45th CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP) 2013 HONG KONG, CHINA, 25th–28th SEPTEMBER, 2013 SIOP ABSTRACTS

1215 abstracts were received in March 2013 and were reviewed by the SIOP scientific committee. The accepted abstracts are printed here in order of:

- 212 Oral presentations (O + number), this includes all Free Paper sessions, 26 Nurses oral presentations, 32 IPSO Oral presentations and 15 ICCCPO Oral presentations.
- 574 Poster presentations (P + number).
- 269 Publications (Pub + number)
- 145 Abstracts were rejected and will not be included in the Journal.

ABSTRACT CONTENTS:

Oral presentations (O + number)

O-0001	O-0004	Neuroblastoma I
O-0005	O-0008	Epidemiology
O-0009	O-0012	Rare Tumours I
O-0013	O-0018	Leukemia I
O-0019	O-0024	Psychosocial I
O-0025	O-0030	Rare Tumours II
O-0031	O-0036	Leukemia II
O-0037	O-0042	Late Effects
O-0043	O-0048	Brain Tumours I
O-0049	O-0054	SIOP Award Session
O-0055	O-0058	Germ Cell Tumours
O-0059	O-0062	Liver Tumours
O-0063	O-0066	Rare Tumours II
O-0066	O-0072	Brain Tumours II
O-0073	O-0078	Psychosocial II
O-0079	O-0084	Renal and Sarcomas I
O-0085	O-0090	Neuroblastoma II
O-0091	O-0096	Bone tumours
O-0097	O-0102	Supportive Care
O-0103	O-0107	Leukemia III
O-0108	O-0113	Neuroblastoma III
O-0114	O-0119	Renal and Sarcomas II
O-0120	O-0125	Lymphoma
O-0126	O-0131	Brain tumours III
O-0132	O-0137	Renal and Sarcomas III
O-0138	O-0163	Nurses
O-0164	O-0196	IPSO
O-0197	O-0212	ICCCPO- Parents/Survivors

Poster presentations (P + number)

P-0001	P-0071	Acute Lymphoblastic Leukaemia
P-0072	P-0102	Myeloid leukemias
P-0103	P-0132	Lymphomas
P-0133	P-0162	Bone tumours
P-0163	P-0182	Soft tissue sarcomas
P-0183	P-0201	Renal tumours
P-0202	P-0208	Germ cell tumours
P-0209	P-0225	Rare tumours
P-0226	P-0238	Liver tumours
P-0239	P-0287	Neuroblastoma
P-0288	P-0303	Surgery (IPSO)
P-0304	P-0305	Radiation Oncology (PROS)
P-0306	P-0322	Retinoblastoma
P-0323	P-0377	Brain tumours
P-0378	P-0418	Others

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P-0419	P-0426	Hystiocytosis
P-0427	P-0448	New drugs/experimental therapeutics
P-0449	P-0458	Epidemiology
P-0459	P-0486	Late effects
P-0487	P-0529	Supportive care/Palliative care
P-0530	P-0548	Psychosocial
P-0549	P-0574	Nursing

Publications (Pub + number)

Pub-0001	Pub-0269	Publication Only

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FREE PAPER SESSION: FREE PAPER SESSION 01 - NEUROBLASTOMA I

O-0001

TREATMENT OF HIGH-RISK NEUROBLASTOMA AND EWING SARCOMA FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION: IMPACT OF BU-MEL ADMINISTRATION ORDER, A CASE CONTROL STUDY AT GUSTAVE ROUSSY

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Purpose/Objective: High dose chemotherapy (HDC) with successive Busulfan and Melphalan (BU-Mel) followed by hematopoietic stem cell transplantation is the reference HDC in the high risk neuroblastoma and high risk Ewing sarcoma european protocols. Regimen related toxicity is a major cause of morbidity. The order of administration of Busulfan and Cyclophosphamide has been demonstrated to impact the treatment related toxicity without any impact on its efficacy. Pharmacological evidence and preclinical studies suggest that Busulfan first can increase the hepatic toxicity of Melphalan and thus the treatment related mortality. This study aimed to assess the influence of administration order on toxicity, for high risk neuroblastoma and Ewing sarcoma.
Materials and Methods: Patients aged under 20 years treated for high-risk neuroblastoma or Ewing sarcoma from 2002 to 2011 at Institut Gustave Roussy had been included in a retrospective study. We considered two administration order: Bu-Mel and Melphalan followed by Busulfan (Mel-Bu). Time to occurrence of hepatic veno-occlusive disease (HVOD) and overall survival were estimated using Kaplan-Meier method. Stratified Cox proportional hazards model was fitted to compare occurrence of HVOD in a sub population of Bu-Mel patients matched with Mel-BU patients of same category of age. In this matched set, toxicity frequencies were compared using adjusted Mantel-Haenszel test
Results: Between 2002 and 2012, 45 and 36 patients were treated with Mel-Bu and Bu-Mel, respectively.
The 5-year Overall Survival were 64% CI95% = (45%-79%) and 62% CI95% = (42%-78%) for Mel-BU and for BU-Mel, respectively.
In the matched set, renal toxicity, mucositis, digestive tolerance and HVO did not differ between the 2 groups (all $p > 0.05$).
Conclusions: This observational study did not show any association between administration order and toxicity. Designs controlling for selection bias (RCTs) should be used to evaluate appropriately toxicity in the two groups.

O-0002

OUTCOME OF PATIENTS WITH FIRST RECURRENCE FROM HIGH RISK METASTATIC NEUROBLASTOMA

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Purpose/Objective: Phase 1/2 studies in neuroblastoma patients mainly include patients with first recurrences from stage 4 disease over 18 months. Little data is available on their outcome with current second line therapies and on the impact of risk factors.
Materials and Methods: Inclusion criteria were GPOH trial participation during 1990 through 2007, first recurrence from stage 4 neuroblastoma, age > 18 months at initial diagnosis. Exclusion criteria were recurrences from high risk stage 1,2,3 and 4S disease, patients with recurrences from the maintenance therapy arm (not anymore standard of care), death from toxicity and tumor-related death before presentation of first recurrence.
Results: 246 patients met the in- and exclusion criteria. The progression-free survival of the total group 3 years after diagnosis of first recurrence (3yPFS) was $7 \pm 2\%$ and the overall survival (3yOS) $12 \pm 2\%$. The median time from the first to the second recurrence was 3.7 months (0.1-53.3) and from first recurrence to death 6.7 months (0.1-77.1). 14% of patients experienced recurrences at primary, 56% at metastatic and 30% at primary and metastatic sites. 34% neuroblastomas showed MYCN amplification (MNA). 35% of patients received palliative care only, 54% underwent second line chemotherapy and 11% chemotherapy plus second ASCT. Children with recurrences later than 18 months after initial diagnosis had a better outcome (3yPFS $10 \pm 3\%$, 3yOS $19 \pm 3\%$) compared to those relapsing before 18 months (3yPFS $4 \pm 2\%$, 3yOS $6 \pm 2\%$, $p < 0.001$). Better prognosis was observed in patients with normal MYCN compared to MNA ($p < 0.001$) and with recurrences in bone/bone marrow (only) compared other metastatic sites ($p < 0.001$). Additional CNS metastases did not further impair the prognosis. Patients with response to second line chemotherapy who could undergo second ASCT had $30 \pm 9\%$ 3yPFS and $42 \pm 10\%$ 3yOS (palliative 2/4%, chemotherapy only 6/12%, $p < 0.001$).
Conclusions: The data of this retrospective study may be useful to evaluate the efficacy of new agents.

O-0003

UPFRONT TREATMENT OF HIGH RISK NEUROBLASTOMA WITH 131I-MIBG THERAPY AND TOPOTECAN. A PHASE I-II PILOT WINDOW STUDY (AMRO-NB-HR-2000/01).

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Purpose/Objective: Patients with high-risk (HR) neuroblastoma (NBL) have a poor prognosis; new treatment strategies are needed. ^{131}I- Meta-Iodobenzylguanidine (MIBG) therapy alone has a significant antitumor efficacy against NBL. Topotecan (TPT) has the ability to potentiate radiation-induced cytotoxicity and can possibly up-regulate the uptake of MIBG *in vitro*.

Haematological toxicity and the effect on harvesting/ feasibility performing autologous stem cell transplantation (ASCT) caused by upfront ^{131}I-MIBG therapy and TPT combination therapy was evaluated. Topoisomerase-1 levels (Topo-1) were measured. Clinical response was scored according to International Neuroblastoma response Criteria (INRC) after 2 courses of MIBG/TPT and after 4 courses of VECI.
Materials and Methods: Multi-centre, prospective (window phase II) study (performed between 2000-2003) in HR NBL patients treated with 2 cycles of upfront ^{131}I-MIBG therapy followed by the addition of TPT 0.7 mg/m^2 for 5 days after each course. Thereafter, patients received 4 courses of VECI chemotherapy, followed by surgery and HD ASCT.
Results: Sixteen patients (10 male), median age 2, 8 yrs. MycN amplified 8/14 (57%) and LOH1P was found in 7/15 (47%). Surgery performed in 12/16 (75%) patients. Harvesting of stem cells in 13/16 patients (79%), mean yield 2, 2 CD34 pos/ kg, 8/16 (50%) underwent HD ASCT. Haematological toxicity was limited, median platelet recovery after HD ASCT was 73

days. Topo-1 activity was measured in 10/16 tumors, increased compared to reference level. Clinical response after 2x MIBG/TPT 14/16 (88%, VGPR/ PR/ MR), 2 PD; after 4x VECI 11/ 16 (69%, CR/ VGPR/ PR/MR), 3 PD, 1 death and 1 unknown. MIBG scans showed more than 50% reduction in MIBG score after 2x MIBG/ TPT and subsequent 4x VECI courses in most cases.
Conclusions: Treatment is feasible; toxicity is limited (haematological). Stem cell harvesting and HD ASCT are manageable. Combination therapy ^{131}I-MIBG/TPT is a good 'first hit' followed by less efficient maintenance chemotherapy.

O-0004

PHASE I STUDY OF 131I-MIBG WITH VORINOSTAT FOR CHILDREN WITH RELAPSED OR REFRACTORY NEUROBLASTOMA: A NEW APPROACHES TO NEUROBLASTOMA THERAPY (NANT) TRIAL

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Purpose/Objective: ^{131}I-metaiodobenzylguanidine (MIBG) is a radiopharmaceutical with activity in neuroblastoma. Preclinical data indicate that vorinostat acts both as a radiosensitizer in neuroblastoma and upregulates expression of the norepinephrine transporter, a key transport protein for MIBG. The goal of this phase 1 study was to determine the maximum tolerated doses of vorinostat and MIBG.
Materials and Methods: Patients $<$ 30 years with relapsed or refractory MIBG-avid neuroblastoma and without prior MIBG therapy are eligible. Patients receive oral vorinostat (planned dose levels 180 and 230 mg/m^2) daily on days 1-14. MIBG (planned dose levels 8, 12, 15, and 18 mCi/kg) is given on day 3 and peripheral blood stem cells are given on day 17. Alternating dose escalation of vorinostat and MIBG was performed using a standard 3 + 3 design.
Results: 21 patients (16 males; median age 6.3 years) have enrolled to dose levels 1-5 and 17 are evaluable for dose escalation. At dose levels 1 (8 mCi/kg MIBG / 180 mg/m^2 vorinostat), 2 (12 mCi/kg MIBG / 180 mg/m^2 vorinostat), and 3 (12 mCi/kg MIBG / 230 mg/m^2 vorinostat), three patients were evaluable per dose level and none had dose-limiting toxicity. At dose level 4 (15 mCi/kg MIBG / 230 mg/m^2 vorinostat), 1 of 6 evaluable patients had dose-limiting toxicity with grade 4 hypokalemia. At dose level 5 (18 mCi/kg MIBG and 230 mg/m^2 vorinostat), two patients were enrolled and both had dose-limiting bleeding (one grade 3 and one grade 5). Evaluation of dose level 5a (18 mCi/kg MIBG / 180 mg/m^2 vorinostat) is ongoing. Among all 21 enrolled patients, the most common grade 3 and 4 non-hematologic toxicities were infection (5 patients) and hypokalemia (4 patients).
Conclusions: As an investigational combination, vorinostat at 230 mg/m^2/dose for 14 days is tolerable with 15 mCi/kg MIBG, but not with 18 mCi/kg MIBG.

FREE PAPER SESSION: FREE PAPER SESSION 02 - EPIDEMIOLOGY

O-0005

ARE WE LOOKING IN THE RIGHT PLACE? A STUDY OF TIME TO DIAGNOSIS OF CANCER IN CHILDREN AND YOUNG ADULTS WITHIN YORKSHIRE SECONDARY CARE SERVICES

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Purpose/Objective: The association between a prolonged time to diagnosis (TTD) for cancer patients and a later stage at diagnosis has been highlighted as a factor contributing to worse outcomes. The majority of early diagnosis research in childhood and young adult (CYA) cancer has focused on primary care. This population-based study investigates TTD in secondary care services for CYA diagnosed with cancer and its effect on survival in Yorkshire, UK.
Materials and Methods: 1098 cases of cancer aged between 0 to 24 years recorded as having a date of diagnosis between 1st January 2004 and 31st December 2009 were identified from the Yorkshire Specialist Registry of Cancer in Children and Young People. Cases were linked to Hospital Episodes Statistics (HES) data, the source for secondary care admissions, only 3 cases were not successfully linked. The International Classification of Diseases-10 codes contained within the in-patient HES episodes preceding or coinciding with the date of definitive diagnosis were reviewed against accepted UK CYA cancer awareness campaigns (Headsmart, TCT awareness, National Health Service referral guidance, Macmillan). The population was analysed for time spent in hospital care, number of alert and non-alert code containing events and 1 and 3-year survival.
Results: In half the patients studied alert code containing episodes preceding their date of diagnosis were identified. These patients were found to have poorer survival at 1 and 3 years compared to patients with no alert codes containing episodes. However the vast majority of alert code containing episodes occurred within the month preceding diagnosis.
Conclusions: CYA cancer cases admitted to hospital with identifiable signs and symptoms preceding their date of diagnosis have a worse survival outcome. However, the majority of cases spent only a short time as in-patients preceding their diagnosis. This research supports the current focus of early diagnosis research and resources at primary care.

O-0006

FEATURES OF CANCER IN TEENAGERS AND YOUNG ADULTS (TYA) PRESENTING TO PRIMARY CARE IN THE UK: A POPULATION-BASED NESTED CASE-CONTROL STUDY

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Purpose/Objective: TYA(15-24 years) with cancer frequently report repeated visits to primary care before referral. Improving early diagnosis is a priority as delayed diagnosis reduces the confidence of patients/parents in their doctor and may influence survival. We investigated the risk of cancer in TYA with symptoms and increased consultation frequency in primary care.
Materials and Methods: Population-based, case-control study using electronic primary care records in the Clinical Practice Research Datalink (CPRD). 1,064 TYA diagnosed with cancer were matched to 13,206 controls. Symptoms independently associated with specific cancers were identified. Likelihood ratios(LRs) and positive predictive values(PPVs) were calculated.
Results: 397(42.9%) cases consulted $\geq$4 times versus 593(11.5%) controls (odds ratio, OR:12.1;95%CI: 9.7,15.1) in the three months before diagnosis, yielding a PPV for any cancer of 0.018%. Symptoms independently associated with specific cancers were identified. The LR of a head/neck mass in a diagnosis of lymphoma was 434(95%CI:60, 3,158), with PPV of 0.5%. Corresponding figures with other diagnoses included: lymphadenopathy (any site) and leukaemia LR 29(8-112), PPV 0.015%; seizure and CNS tumour LR 56(19-163), PPV 0.024%; and lump/mass/swelling and sarcoma LR 79(24,264), PPV 0.042%.
Conclusions: TYA patients with cancer consulted GPs more frequently than controls, particularly in the three months before diagnosis. Features of leukaemia, lymphoma, CNS tumours, bone/soft tissue sarcomas presenting in primary care match secondary care reports of TYA cancer but were very low risk and limited predictive value: nonetheless, some features altered prior probability of cancer substantially and should be taken seriously when assessing a TYA who is unwell or reporting unexplained symptoms, particularly with repeat consultation.

O-0007

CANCER INCIDENCE IN THE FAMILIES OF CHILDREN WITH BONE AND SOFT TISSUE SARCOMAS

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Purpose/Objective: The aims of the study were to investigate the incidence of cancers in the relatives of children with sarcoma.
Materials and Methods: Families of children aged 0 to 14 diagnosed between 1954 and 2008 with Ewing sarcoma (EWS), osteo/chondrosarcoma (Os/Chon) or soft tissue sarcoma (STS) from the population-based Manchester Children's Tumour registry were traced. Interviews were conducted and the medical histories taken and, where possible, verified from hospital records for the grandparents of the case and their descendants. The parents and siblings were flagged for continuous notification of cancers and deaths. Expected numbers of cancers aged 0-84 years were calculated using English national cancer registration data.
Results: There were a total of 10,841 relatives among the 629 families in the study. There were significant excess of cancer in the relatives of STS (observed 280, expected 248, $P = 0.03$) BS (observed 188, expected 158, $P = 0.01$) but not EWS (observed 123, expected 137, $P = 0.89$). The excesses were confined to relatives under 60 with greater relative risk at younger ages ($P < 0.0001$) and, in the relatives of STS cases, younger index cases ($P = 0.005$). The Os/Chon families had significant excesses of embryonal and CNS tumours, STS and melanoma, whereas the STS families had excesses of STS, embryonal and bone tumours, stomach, breast and cervical cancers (all $P <= 0.01$).
Conclusions: The wide range of cancers in excess in relatives of sarcoma cases imply that there may be a variety of either inherited or environmental factors involved. This has implications for both counselling, surveillance and aetiology.

O-0008

DEPRESSION IN SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: Five year survival from childhood cancer is 82% and this population may be at greater risk of developing major depressive disorder (MDD) in later life. The purpose of this study was to investigate the effect of childhood cancer and its treatment on self-reported mental health in adult survivors of childhood cancer in Britain.
Materials and Methods: Responses of a postal questionnaire filled in by 10,488 survivors from the British Childhood Cancer Survivor Study (BCCSS) were analysed. Self-reported anti-depressant use and three Medical Short Form Questionnaire 36 (SF-36) scores were calculated which best measures the mental component of health status - 1) Role limitation due to emotional problems; 2) social functioning; 3) mental health. This was compared between the survivors using a multivariable logistic regression.
Results: Anti-depressant use in survivors of childhood cancer was strongly associated with gender, diagnostic group and attained age but not age at diagnosis or treatment modality. Females were twice as likely to take antidepressant medication compared to men and performed worse in all three SF-36 scores ($p < 0.0001$). Survivors of Non-Hodgkins Lymphoma (NHL) and bone tumours scored significantly lower SF-36 scores (for all three scores for NHL and bone tumours $p < 0.0001$).

A linear correlation was found between age at questionnaire completion and all three SF-36 scores. The likelihood of anti-depressant use also increased with age at questionnaire completion in a non-linear fashion.
Conclusions: This study has highlighted sub-groups within the survivor cohort at particular risk for mental health morbidity, notably depression. Identification of subgroups within the survivor cohort that are at increased risk for mental health conditions in later life will enable rapid engagement with mental health services and subsequently earlier commencement of appropriate therapy. Furthermore, identification of these at-risk subgroups enables more targeted preventative interventions against mental health morbidity.

FREE PAPER SESSION: FREE PAPER SESSION 03 - RARE TUMOURS I

O-0009

CORRELATIONS BETWEEN IGF SYSTEM AND WNT-B-CATENIN PATHWAY IN PEDIATRIC ADRENOCORTICAL TUMORS

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Purpose/Objective: The WNT/b-catenin pathway mediates essential role in normal tissue development, cell proliferation and cell differentiation. However its constant activation has been reported in adrenocortical tumors (ACTs). Alterations in IGF system, an important pathway during adrenal cortex development, have also been found in pediatric and adult ACTs. Recently, studies provided evidences that IGF signaling modulates the canonical WNT pathway at the level of b-catenin, but little is known about this interaction in cancer cells, especially in ACTs.
Materials and Methods: The correlations between the mRNA expression values of IGF system genes and WNT/b-catenin components were determined by the Spearman correlation coefficient (rho) in 57 pediatric ACTs. Non-neoplastic adrenal samples ($n = 19$) were used as controls. Gene expressions were analyzed by RT-qPCR using TaqMan probes by the $2^{-\Delta\Delta Ct}$ method.
Results: ACTs presented increased expression of *IGF2, CTNNB1, WISP2* and underexpression of *DKK3, SFRP1, AXIN1* and *MYCC* genes when compared to normal samples. Higher survival was associated with underexpression of *IGF1R, SFRP1, WNT4* and *TCF7* ($P < 0.05$). A significant positive correlation was found between the *IGF1R* gene expression and the target gene of WNT/b-catenin pathway *MYCC* (rho $= 0.529$; $P < 0.001$) and a trend to *CTNNB1* (rho $= 0{,}276$; $P = 0.05$). Two inhibitors of WNT/b-catenin were also positive correlated with *IGF1R*: *AXIN1* (rho $= 0.375$; $P = 0.009$) and *SFRP1* (rho $= 0.314$; $P = 0.034$). In addition, the major ligant *WNT4* presented a significant negative correlation with *IGF1R* (rho $= -0.316$; $P = 0.031$). Considering the gene expression of *IGF2*, we observed a positive correlation of this ligant with the WNT/b-catenin target gene *WISP2* (rho $= 0.311$; $P = 0.036$). It was also found a positive correlation between *IGF2* and the gene expression of the main mediator of WNT/b-catenin pathway, the *CTNNB1* (rho $= 0.289$; $P = 0.049$).
Conclusions: We observed significant correlations regarding important components of WNT/b-catenin signaling and the receptor *IGF1R* in our pediatric ACTs samples. These results suggest that interactions between both pathways can be related to carcinogenesis process.

O-0010

CONSTRUCTION OF A MOUSE MODEL OF COLORECTAL POLYPS BY TRANS-PLACENTAL RNA INTERFERENCE OF THE BMP4 GENE

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Purpose/Objective: Study have shown that disruption of the BMP signaling pathway is an important cause of intestinal cancers in human and animal models.Thus, the purpose of this study was to construct a Balb/C model of colorectal polyps.
Materials and Methods: Pregnant mice at 9.5 days gestation were transfected with the pSES-Si BMP4 plasmid with three targets and fluorescence via tail vein injection to knockdown the BMP4 gene in first-generation mice (F1 mice). Intestinal fluorescence was detected in 1-, 4- and 8-week-old F1 mice after birth, and RT-PCR and Western-blotting assays were used to determine changes of the BMP4 and Smad4 gene. A dissecting microscope and H&E staining were used to observe polyp appearance and cell morphology. The genotype and phenotype of F1 mice with low BMP4 gene expression were compared.
Results: Intestinal fluorescence was observed in 1-week-old F1 mice in the pSES- BMP4 group. The intestinal BMP4 gene mRNA and protein was downregulated in 1-, 4- and 8-week-old F1 mice ($P < 0.05$). Also, Smad4 gene mRNA is downregulated in 8-week-old F1 mice ($P < 0.05$). In the pSES-BMP4 group, multiple hyperplasic polyps appeared in the colon and rectum of the intestines in 4-week-old F1 mice. The colorectal polyps increased in size at 8 weeks and blood vessels and polyp pedicles were present. H&E staining showed juvenile hamartomatous polyps and pedunculated hyperplasic polyps.
Conclusions: Downregulating BMP4 gene by trans-placental RNAi can induce formation of colorectal polyps in mice model of BMP4 colorectal polyps can be established to study intestinal tumorigenesis and cancer development.

O-0011

MELANOMA IN CHILDREN AND ADOLESCENTS: A SINGLE INSTITUTION EXPERIENCE

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Purpose/Objective: Melanoma in children and adolescents is rare and accounts for less than 1% of all melanomas. Given its rarity, our current understanding of clinical outcomes and management is based on adult literature. We reviewed the clinical features, management and survival outcomes of pediatric patients diagnosed with melanoma and treated at our institution in the past 10 years.
Materials and Methods: Retrospective chart analysis and literature review.
Results: Our study included 33 patients (16 male; 17 female). Median age at diagnosis was 16 years (range; 2.6-20.6 years). Sites of involvement included head and neck ($n = 13$), extremities ($n = 10$), trunk ($n = 7$), eye ($n = 2$), and unknown primary ($n = 1$). Histopathology was superficial spreading ($n = 15$), spitzoid ($n = 9$), nodular ($n = 5$), superficial with spitzoid features ($n = 1$), and choroidal melanoma ($n = 1$). Median Clark level of invasion was 4 and median Breslow thickness was 1.7 mm. Thirty one patients underwent surgical resection. Nine patients had positive sentinel lymph nodes and two had distant metastases. Nineteen patients had Stage I/II disease and 11 had advanced stage (Stage III/IV). Adjuvant treatment for advanced stage included radiation and agents such as interferon alpha-2b, GM-CSF, high dose interleukin-2 and temozolomide. Three patients experienced progression/relapse and died (range; 11.8-25.4 months from diagnosis). Two of those patients received chemotherapy and newer agents such as vemurafenib (BRAF inhibitor) and ipilimumab (monoclonal antibody to CTLA-4). Median follow-up time was 3.2 years (range; 0.3-6.8 years). Four-year overall survival was 87%. Advanced stage and increasing Breslow thickness were associated with poor overall survival ($p = 0.01$ and $p = 0.005$, respectively). Age, gender, and site did not correlate with survival outcomes.
Conclusions: Optimal management of pediatric melanoma, especially advanced stage, is unclear. Clinical trials involving novel agents targeting tumor immune response (ipilimumab) and molecular pathways involved in tumorigenesis (vemurafenib) are currently underway. Large, multi-institutional studies are required for better understanding of this rare disease and to improve management strategies.

O-0012

SOLID PSEUDOPAPILLARY TUMOR OF THE PANCREAS IN PEDIATRIC PATIENTS: 21 CASES OF SINGLE INSTITUTION.

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Purpose/Objective: Solid pseudopapillary tumor (SPT) of the pancreas is a rare neoplasm. The objective of this study was to review our institution's experience and discuss the clinical presentation, pathologic characteristics, management, and outcomes in the pediatric population.
Materials and Methods: We retrospectively reviewed all pediatric patients (age ≤18 years) treated for solid pseudopapillary tumor at ASAN Medical Center between 1999 and 2012.
Results: 21 patients with SPT were identified. 14 patients were female(66.7%) and 7 patients were male(33.3%). Most patients presented with abdominal pain(n = 14, 66.7%) and pain was usually about three months before the diagnosis there were 3months Diagnostic imaging was most commonly an ultrasound or computed tomography. We performed open surgery(n = 13, 61.9%) and laparoscopic surgery(n = 9, 38.1%). Laparoscopic surgery included laparoscopic enucleation of pancreatic mass(n = 3), laparoscopic distal pancreatectomy(n = 3), and laparoscopic spleen saving distal pacreatectomy(n = 3). Median greatest tumor diameter was 4.9 cm (1.5-12 cm). Median length of stay was 15 days (6-35 days). Complications included pancreatic leak(n = 1) and wound seroma(n = 1). Recurrence developed after 2.1 years in 1 patient of enucleation and we performed distal pancreatectomy for recurred mass(diameter: 2.5cm). There were no metastases or deaths. Median follow-up was 4.2 years (0.4-13.5 years).
Conclusions: In our experience, SPT behaves like a low-grade malignancy and has an excellent prognosis. Adequate operative resection including laparoscopic surgery is the mainstay of treatment for SPT.

FREE PAPER SESSION: FREE PAPER SESSION 04 - LEUKEMIA I

O-0013

PEDIATRIC ACUTE MYELOID LEUKEMIA WITH T(8;16)(P11;P13): A DISTINCT CLINICAL AND BIOLOGICAL ENTITY. RESULTS OF A COLLABORATIVE STUDY BY THE INTERNATIONAL BERLIN-FRANKFURT-MÜNSTER AML STUDY GROUP.

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Purpose/Objective: In pediatric acute myeloid leukemia (AML) cytogenetic abnormalities are strong prognosticators. Some recurrent cytogenetic abnormalities, such as t(8;16)(p11;p13), are so rare that collaborative studies are required to define their prognostic impact.
Materials and Methods: From 62 pediatric AML patients with t(8;16)(p11;p13) we collected data on clinical characteristics, morphology and immunophenotype from 18 countries participating in the IBFM AML study group, and used the AML-BFM cohort diagnosed from 1995-2005 (n = 543) as a reference cohort. From 8 samples gene expression profiling was performed, which was compared to 289 pediatric AML samples from diverse cytogenetic background.
Results: Median age of pediatric t(8;16)(p11;p13) AML patients was 1.2 years and they had M4-M5 FAB type in 95%, significantly different from the reference cohort. Erythrophagocytosis (70%), leukemia cutis (58%) and diffuse intravascular coagulation (39%) occurred frequently. Strikingly, spontaneous remissions occurred in 7 neonates with t(8;16)(p11;p13) of which 3 are still in continuous remission. The 5-year overall survival of patients diagnosed after 1993 which received intensive chemotherapy was 59%, similar to the reference cohort (p = 0.14). Gene expression profiles of t(8;16)(p11;p13) pediatric AML cases clustered close to, but distinct from *MLL*-rearranged AML. Highly expressed genes included *HOXA11*, *HOXA10*, *RET*, *PERP* and *GGA2*.
Conclusions: In conclusion, pediatric t(8;16)(p11;p13) AML is a rare entity with distinct clinical features and a unique gene expression signature. Also, spontaneous remissions occur in a subset of neonatal cases.

O-0014

NUP98/JARID1A IS A NEW RECURRENT GENETIC ABNORMALITY IN PEDIATRIC NON-DOWN SYNDROME ACUTE MEGAKARYOBLASTIC LEUKEMIA

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Purpose/Objective: Cure rates in pediatric AML are currently 60-70% despite treatment with intensive chemotherapy. To improve prognosis, new treatment targets need to be identified, hence there is a need to better understand the underlying biology.
Materials and Methods: AML is hypothesized to result from two types of mutations collaborating in leukemogenesis. Type-I aberrations confer a proliferative advantage, type-II mutations lead to impairment of hematopoietic differentiation (Kelly *et al*,2002). We previously reported a patient with *NUP98/JARID1A* in a non-Down Syndrome (DS) AMKL case (VanZutven *et al*,2006). Therefore, samples from 105 pediatric non-DS AMKL cases were obtained from our international collaborators to screen for *NUP98/JARID1A* and other abnormalities. Centrally reviewed clinical and cell-biological data were provided. Dual-colour FISH was performed on *MLL* and *NUP98. NUP98/JARID1A, NUP98/NSD1*, specific *MLL-rearrangements*, *RBM15/MKL1, HLXB9/ETV6, CBFA2T3/GLIS2* and molecular characterization including hotspots in several genes were analyzed using RT-PCR. *HOXA/B* expression was assessed using gene expression profiling (n = 9), and validated and completed with quantitative real-time PCR (n = 37).
Results: *NUP98/JARID1A* was detected in 11 patients (10.5%). One patient was identified with *NUP98/NSD1*, four patients had a *NUP98*-rearrangement based on FISH with unknown fusion partner. In addition, 16/105 patients harboured *RBM15/MKL1*, 13/105 harboured *CBFA2T3/GLIS2*, and 13/96 had an *MLL*-rearrangement. Only 3/45 cases displayed a type-I mutation, all localized in the *RAS* gene. Considering prognosis, outcome in pediatric AMKL is unsatisfactory with a 5-year survival rate of 42%. Comparing *NUP98/JARID1A* positive cases to negative cases, 5-year pEFS was lower (22 ± 14% vs. 36 ± 6%,p = 0.5), but did not differ significantly from all other AMKL patients. Gene expression analysis showed significantly higher *HOXA5/A9/A10* and *HOXB2/B3/B4/B5/B6* expression in *NUP98/ JARID1A* compared to other pediatric AML cases.
Conclusions: In >60% of the AMKL cases a type-II mutation could now be identified. *NUP98/JARID1A* is a new recurrent cryptic translocation present in approximately 11% of pediatric AMKL cases with persistent *HOXA/B* gene expression.

O-0015

NUP98-NSD1 GENE FUSION IS A STRONG POOR PROGNOSTIC FACTOR IN PEDIATRIC AML

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Purpose/Objective: Acute myeloid leukemia (AML) is a heterogeneous disease characterized by the alternation of different pathways affecting cell proliferation and myeloid differentiation. Many important molecular markers have already been discovered in AML that have not only helped to better characterize the patients, but also helped to improve the

risk stratification. However, no cytogenetic changes are detectable with routine cytogenetic analysis in approximately 20% of pediatric AML cases. It was recently reported that the cryptic translocation t(5;11)(q35;p15.5), which creates *NUP98- NSD1* gene fusion, was identified by high-resolution genome-wide copy number analysis and RT-PCR in pediatric and adult AML. Our purpose in this study is to estimate the more accurate frequency and the clinical impact of *NUP98-NSD1* gene fusion in pediatric AML.
Materials and Methods: We examined *NUP98-NSD1* fusion transcript in 533 newly diagnosed AML cases enrolled in two Japan clinical trials (AML99 study and AML05 study).
Results: We identified *NUP98-NSD1* in 17 of 533 cases (3.2%) (7/157 in AML99 and 10/376 in AML05), including eight cytogenetically normal cases (47.1%). Notably, the outcome of *NUP98-NSD1* positive cases was significantly worse than *NUP98-NSD1* negative cases (AML99: 4-years OS, 33.3% vs 80.1%; and AML05: 2-years OS, 20.0% vs 75%, for *NUP98-NSD1* positive vs negative cases, respectively). Furthermore, 6 of 17 *NUP98-NSD1* positive cases (35.3%) failed to achieve complete remission after the first induction therapy.
Conclusions: *NUP98-NSD1* gene fusion is strongly associated with a poor outcome. Routine analysis of *NUP98-NSD1* by PCR is needed for normal karyotype AML cases, and *NUP98-NSD1* positive cases are needed to be classified into high risk group with intensive chemotherapy including stem cell transplantation. In the next Japan pediatric AML clinical trial, *NUP98-NSD1* is planned to be examined in all cases as a poor prognostic marker.

O-0016

UNIQUE BHLHB3 OVEREXPRESSION IN PEDIATRIC ACUTE MYELOID LEUKEMIA WITH T(6;11)(Q27;Q23)

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Purpose/Objective: Pediatric acute myeloid leukemia (AML) is a heterogeneous disease in which cytogenetic aberrations and response to induction-treatment are the most important outcome predictors. Survival of patients with *MLL*-rearranged AML is mainly dependent on translocation partner. Patients with t(6;11)(q27;q23)(*MLL-AF6*) show the worst outcome, which is still poorly understood.
Materials and Methods: To identify important biological factors within t(6;11)(q27;q23), we compared clinical characteristics, mutational status and gene expression profiles (Affymetrix U133 plus 2.0) of 21 pediatric patients with t(6;11)(q27;q23) AML with 285 other pediatric AML cases, including 63 *MLL*-rearranged patients with other translocation partners.
Results: In t(6;11)(q27;q23) AML cases, the median age at diagnosis was 7.2 years, and most prevalent FAB type was M4. In 12/21 patients (57%) the t(6;11)(q27;q23) was cytogenetically cryptic. 45% of t(6;11)(q27;q23) patients had RAS pathway mutations. Using gene expression profiling, supervised clustering revealed highly specific overexpression of *BHLHB3* in t(6;11)(q27;q23) AML, which was confirmed by RT-qPCR and Western Blot. Sequencing the whole coding region of *BHLHB3* did not identify mutations. Sufficient shRNA knockdown of *BHLHB3* did not result in altered proliferation, apoptosis or drug sensitivity, suggesting that although this gene is uniquely overexpressed in pediatric AML with t(6;11)(q27;q23), it is not a driver of leukemogenesis.
Conclusions: This suggests that although *BHLHB3* is uniquely overexpressed in pediatric AML with t(6;11)(q27;q23), it is not a driver of leukemogenesis.

O-0017

GATA1S MEDIATES CLONAL EOSINOPHILIA IN PATIENTS WITH DOWN SYNDROME TRANSIENT LEUKEMIA

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Purpose/Objective: Transient leukemia (TL) is evident in 5-10% of all neonates with Down syndrome (DS) and closely linked to N-terminal truncating GATA1-mutations (GATA1s). We investigated the relationship between GATA1s-mutation and clonal eosinophilia observed in a cohort of TL patients.
Materials and Methods: We sorted TL-blasts and TL-eosinophils from DS-TL patients with and without documented eosinophilia. GATA1 status was assessed in both populations. We examined the myeloid differentiation of human CD34+ fetal hematopoietic stem and progenitor cells (HSPCs) exclusively expressing *Gata1* or *Gata1s* in liquid culture and methylcellulose colony-forming assays. Expression profiling was performed on Agilent SurePrint G3 microarrays.
Results: TL-blasts exhibited an activated eosinophilic genetic program and preferentially differentiated along the eosinophilic lineage in vitro even in the absence of documented eosinophilia. TL-eosinophils carried the same mutation in *GATA1* as the TL-blasts showing their clonal origin. Expression of *Gata1s* in $CD34^{+}$-HSPCs induced a 10-fold higher proliferation rate of granulated progenitor cells accompanied by a monocytic differentiation block and reduction of neutrophils. Atypical colonies were formed upon *Gata1s* expression, consisting of eosinophilic promyelocytes with abnormal pro-eosinophilic granulation, as confirmed by GSEA, chip cytometry and histochemical methods.

Expression profiling demonstrated that Gata1s, unlike Gata1, was not able to repress a number of GATA1 target genes, such as MYC, and the pro-proliferative E2F transcription network. shRNA-mediated knock down of either MYC or the essential E2F-cooperation partner DP1 partially rescued the G1s-induced hyperproliferative phenotype.
Conclusions: We report that eosinophils can be part of the TL cell clone in a substantial fraction of DS patients with TL. As E2F target genes were also upregulated in sorted TL-eosinophils, we propose that the failure to repress pro-proliferative genes while instructing eosinophilic differentiation accounts for *GATA1s*-mediated clonal eosinophilia in TL. Based on our results we propose that the GATA1 status should be assessed in all DS neonates with abnormal eosinophils in their blood smears.

O-0018

IDENTIFICATION OF NOVEL SOMATIC MUTATIONS IN PEDIATRIC ACUTE MYELOID LEUKEIMIA USING WHOLE-EXOME RESEQUENCING

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Purpose/Objective: Currently, a new class of mutational targets have been reported in adult AML, including *CEBPA*, *NPM1*, *DNMT3A*, *IDH1/2*, *TET2* and *EZH2*. However, mutations of the latter class of gene targets are considered to be rare in pediatric AML cases. The recent development of massively parallel sequencing technologies has provided a new opportunity to discover genetic changes across the entire genomes or protein-coding sequences in human cancers at a single-nucleotide level, which could be successfully applied to the genetic analysis of pediatric AML to obtain a better understanding of its pathogenesis.
Materials and Methods: We performed whole exome resequencing of paired tumor-normal specimens from 19 pediatric AML cases using Illumina HiSeq 2000. Although incapable of detecting non-coding mutations and gene rearrangements, the whole-exome approach is a well-established strategy for obtaining comprehensive spectrum of protein-coding mutations. Recurrently mutated genes were further examined for mutations in an extended cohort of 192 pediatric AML samples, using deep sequencing, in which the prevalence and relative allele frequencies of mutations were investigated.
Results: Whole-exome resequencing of paired tumor-normal DNA from 19 patients were analyzed with a mean coverage of more than x100, and 82% of the target sequences were analyzed at more than x20 depth on average. A total of 80 somatic mutations or 4.2 mutations per sample were identified. We newly identified *BCORL1*, and major cohesin components including *SMC3* and *RAD21* in additoion to recurrent mutations such as *FLT3, KIT, CBL, NRAS, EZH2*. We had validated for the clinical significance of these gene mutations in an extended cohort of 192 pediatric cases.
Conclusions: Whole exome resequencing unmasked a complexity of gene mutations in pediatric AML genomes. Our results indicated that a subset of pediatric AML represents a discrete entity that could be discriminated from the adult counterpart, in terms of the spectrum of gene mutations.

FREE PAPER SESSION: FREE PAPER SESSION 05 - PSYCHOSOCIAL I

O-0019

CHILDHOOD CANCER IN INDIA – THE SOCIAL ASPECTS

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Purpose/Objective: Cancer in children represents a significant burden of disease in a developing country such as India. 1.6 to 4.8% of all cancer in India is seen in children. The cure rates for common cancers in children have been over 80% in developed countries. Sadly, outcomes in childhood cancer in our country are abysmal. Lack of access to care, stigma of cancer and financial constraints have been the main reasons to keep our outcomes at an average cure rate of 30%. The economic burden, including the cost of illness, long-term costs, and indirect costs are enormous. After initiation of therapy, interruption of treatment or lost to follow up has been reported in up to 15% of patients.
Materials and Methods: We retrospectively analyzed all cases of newly diagnosed Acute lymphoblastic leukemia (ALL) , admitted in Apollo Specialty Hospital, Chennai from Jan 2002 to September 2012. We analyzed the number of children who had completed their treatment without any financial assistance and how many required financial assistance during treatment and the dropout rate.
Results: A total of 144 patients of ALL were analyzed .The age of the children ranged between 6 months to 17 years. Most of them belonged to lower socioeconomic group. Out of 144 children forty five percent completed treatment without any financial assistance. Seventeen percent of children were covered by medical insurance which helped them in completing their treatment. Thirty eight percent of children needed financial assistance during treatment. After initiation of therapy, interruption of treatment or lost to follow up has been reported in less than one percent of patients.
Conclusions: The outcome of cancers in children in India can be on par with that of developed countries, provided the socioeconomic support required to complete therapy is provided. Paediatric oncologists will be available to function in an optimal manner only with the aid of governmental organizations.

O-0020

INFLUENCE OF HEALTH-INSURANCE STATUS AT DIAGNOSIS ON CHILDHOOD CANCER TREATMENT OUTCOME IN KENYA

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Purpose/Objective: Kenya has a national policy in public hospitals, called 'waiving procedure', by which patients are retained until their hospital bill is cleared. Payment process of hospital bill differs between patients with or without access to National Hospital Insurance Fund (NHIF) at diagnosis.
Our study explores childhood cancer treatment outcome and any influence by health-insurance status at diagnosis in a large Kenyan academic hospital.
Materials and Methods: This was a combined retrospective medical records and case report study. From 2007 to 2009, 222 children were newly diagnosed with a malignancy. Treatment outcome was documented in 180 patients and health-insurance status at diagnosis in 148 patients.
Results: Of all 180 patients with documented treatment outcome, 54% abandoned treatment, 22% had treatment-related death, 4% progressive or relapsed disease, and 19% event-free survival. Health-insurance status at diagnosis was recorded in 148 children: 23% had NHIF and 77% had no NHIF. For children whose families had NHIF compared to those who had not, the relative risk for abandonment of treatment relative to event-free survival was significantly smaller (Relative risk ratio RRR $= 0.31$, 95% CI $= 0.12$ - 0.81, $p = 0.016$). No differences were found in relative risks for death and progressive or relapsed disease relative to event-free survival between both groups. The case report illustrates difficulties Kenyan families face when their child is diagnosed with cancer and retained in a public hospital.
Conclusions: Children with NHIF at diagnosis had a significant lower chance of abandonment and higher chance of survival. Abandonment of childhood cancer treatment was the most important reason for treatment failure. Outcome of childhood cancer treatment could be improved substantially by interventions that help to prevent abandonment of therapy and improve access to NHIF. Nature of waiving procedure should change.

O-0021

DEVELOPMENT AND IMPLEMENTATION OF A CLINICALLY USEFUL MEASURE OF SOCIO-ECONOMIC STATUS FOR FAMILIES OF CHILDREN WITH CANCER IN GUATEMALA.

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Purpose/Objective: The great majority of children with cancer live in low and middle income countries (LMIC) where they experience undue burdens of morbidity (such as malnutrition)[a] and mortality (exacerbated by abandonment of therapy)[b]. These burdens are greatest in the most underprivileged families. To determine their vulnerability, an instrument was developed to measure socio-economic status (SES) using elements reflecting local realities in Guatemala.
Materials and Methods: Based on the experience of social workers and psychologists, a 15 item instrument was constructed addressing marital, educational, and employment status; living arrangements, including dwelling construction and number of occupants; nature of home ownership and energy supply; sanitary facilities and access to drinkable water; distance from the hospital and modes of communication and transportation; monthly income and expenditures on food, education and recreation; and sources of medication. Each factor was divided into 5 levels and assigned a score from 1 to 5 (high to low), providing a summary score for each family.
Results: All families whose children were incident cases at the National Pediatric Oncology Unit in Guatemala City during 2012 ($n > 400$) were assessed and categorized into 5 groups on the basis of the summary scores; the higher the score the lower the overall SES.
Conclusions: The categories of SES afforded the implementation of targeted strategies of psycho-social and material support (such as food supplies), on a sliding scale designed to minimize malnutrition and abandonment of therapy. This instrument and the experience in its utilization should prove to be helpful in other LMIC, with appropriate adaptation to local circumstances including availability of resource support.
a.Sala A et al. Eur J Cancer 2012; 48: 243-252.
b.Bonilla M et al. Int J Cancer 2009; 76: 2144-2146.

O-0022

U-CARE: ECONOMIC LATE EFFECTS FOR MOTHERS AND FATHERS OF CHILDREN DIAGNOSED WITH CANCER

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Purpose/Objective: The diagnosis of childhood cancer often results in an altered life situation for the parents, characterized by difficulties regarding work, family, and household demands. This could have a direct effect on parental long-term health and affect income, time constraints, and economics outcomes. The primary aim is to describe childhood cancer's potential economic late effects for parents of children diagnosed with cancer.
Materials and Methods: 259 parents of children diagnosed with cancer a week previously (T1) were included in a longitudinal study on psychological and economic consequences for parents of children with cancer covering 7 assessments from T1 to 5 years after end of successful treatment (ST)/the child's death (T7). Data on variables such as income, sickness absence, work environment, working hours and health collected via telephone interviews with parents at T7 are presented. The parents answered the same questions as used in the Swedish Living Conditions Survey (ULF). The ULF survey is conducted annually by Statistics Sweden, on behalf of the Swedish Parliament, to obtain data on the living conditions of the Swedish population. Data for parents at T7 ($n = 165$) will be evaluated in comparison with ULF data from a community sample.
Results: Previous results from our longitudinal research show that fewer fathers work and more mothers are on sick leave 1 year after ST than shortly after diagnosis. In this presentation we report the potential economic and health late effects of childhood cancer in terms of e.g. self-rated health, employment, income, and sick leave for mothers and fathers respectively at T7.
Conclusions: The findings will have theoretical implications for the knowledge of economic and health sequel for parents after childhood cancer. This will in a next step inform and facilitate psychosocial work with parents of children with cancer and provide targets for policy interventions.

O-0023

PARENTAL SUBJECTIVE MENTAL FATIGUE AND RESILIENCE IN THE AFTERMATH OF A CHILD'S CANCER: INFLUENCE OF NATION AND SITE-RELATED ORGANISATIONAL FACTORS ON FATIGUE IN TWO NORDIC SAMPLES

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Purpose/Objective: To determine incidence of, and compare parental subjective mental fatigue (SMF) in parents of chilhood cancer (CC) patients treated at centres of different type, organisation and size. To determine the relationship between individual resilience and SMF, and to evaluate fatigue outcomes in the light of nation-, site-, and organisation-related determinants.
Materials and Methods: Participants were 334 parents of 219 CC patients with a child either in or off treatment, recruited from one large specialised CC centre (Sweden), and one smaller general paediatric unit which included CC treatment (Iceland). Parental SMF as a measure of long-term consequence of stress was assessed using the Maastricht Questionnaire (MQ-21),

and individual resilience as potential protective factor against SMF was assessed using the Sense of Coherence (SOC) questionnaire (SOC-13). Clinical groups were compared, comparisons with general population (GP) data were done. Findings were interpreted in the light of nation- and site-related factors.
Results: Unadjusted comparisions of clinical parent groups indicated similar levels of SMF. However, when analyses were adjusted for time elapsed from diagnosis, and child's age at diagnosis, a significant main effect of group (Sweden/Iceland) was found, indicating higher vulnerability for SMF in the Icelandic small center group. Similarly adjusted analyses showed that Icelandic parents scored higher on 4 of 21 SMF-items related to sleep disturbance, feeling weak, and hopelessness. In entire clinical parent group SOC was negatively related to SMF ($r = -0.631$, $p < 0.01$), indicating SOC:s role as boosting resilience against long-term SMF. Compared with GP norms, clinical parents scored significantly higher in the compund SMF measure ($p < 0.0001$), and consistently on item level.
Conclusions: Centre type and orgainsational differences may predict occurrence of parental subjective mental fatigue. Findings provide guidance for addressing organisational targets and developing care to compensate for an increased risk for long-term parental adverse consequences associated with organisational factors at small treatment centers.

O-0024

WHEN RELIGION PROVIDES THE ANSWER: PARENTS WHO ABANDON MEDICAL TREATMENT FOR THEIR CHILD WITH CANCER

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Purpose/Objective: To explore the religious narratives of parents who abandon their child's cancer treatment in El Salvador and how these relate to their living conditions, understanding of cancer and therapy, and the action of abandoning treatment.
Materials and Methods: A paediatric oncologic psychologist, using a medical anthropological perspective, conducted in-depth interviews with ten parents who abandoned their child's treatment. The main topics related to God, faith, cancer and treatment were analysed.
Results: Parents' socioeconomic limitations and emotional distress, together with their perception of their child's cancer and treatment side effects appeared explained and/or solved in the light of a religious narrative. The parents' daily difficulties sustaining their family's needs were perceived to be as imperative as their child's cancer. The parents' religious community appeared more comforting and hopeful than the medical community. The collective belief in miraculous cures without medical intervention provided both support and suitable answers that relieved the economic and emotional burden from treatment. Even parents who were not strongly committed to church/religious-related activities and ideologies used faith-based arguments in favor of their actions regarding treatment. These arguments appeared to be a useful resource to validate treatment abandonment for themselves, the community and medical doctors. Religion not only provided the parents with arguments as valid as medical knowledge for addressing cancer, it was also more suitable for their complicated living conditions, and provided emotional support and reasoning to avoid feelings of guilt or responsibility for the possibility of a bad outcome for their child, which would be God's will.
Conclusions: In the context of the structural vulnerability in which these families live as a natural condition, religious faith and religious community seemed to the parents to be the most suitable resources for coping with their child's cancer as they struggled with multiple daily constraints.

FREE PAPER SESSION: FREE PAPER SESSION 06 - RARE TUMOURS II

O-0025

THE ONCOGENIC PROPERTIES OF THE EWS/WT1 FUSION PROTEIN OF DESMOPLASTIC SMALL ROUND CELL TUMOUR.

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Purpose/Objective: The t(11;22)(p13;q12) translocation is pathognomonic for desmoplastic small round cell tumour (DSRCT). The translocation fuses exon 7 of the *EWS* gene to exon 8 of the *WT1* gene (EWS/WT1). Alternate splicing results in two variants, arising from the presence (+KTS) or absence (-KTS) of three amino acids: lysine, threonine and serine between zinc fingers 3 and 4. The role of the fusion protein in the pathogenesis of DSRCT remains unclear.
Materials and Methods: We over-expressed EWS/WT1 in murine embryonic fibroblasts (MEFs) to examine the ability of EWS/WT1 to transform primary MEFs and those generated from $p53^{+/-}$ or $p53^{-/-}$ mice. Illumina microarray analysis was performed to examine differential expression of genes in cells expressing EWS/WT1. Results were validated in a series of DSRCT.
Results: We demonstrate that neither isoform of EWS/WT1 is sufficient to transform wild type MEFs however the oncogenic potential of both is unmasked by the loss of *p53*. Expression of EWS/WT1 in MEFs lacking at least one allele of p53 enhanced cell proliferation, clonogenic survival and anchorage-independent growth. In addition EWS/WT1 expression in wild type MEFs attenuated several p53-dependent responses, including cell cycle arrest after irradiation and daunorubicin induced apoptosis. We show that DSRCT commonly have copy number amplification of *MDM2* and *MDMX*, suggesting loss of p53 function in the tumours. Expression of either isoform of EWS/WT1 in MEFs induced characteristic mRNA expression profiles, including up-regulation of Wnt ligand7b in cells expressing EWS/WT1 + KTS. Wnt activation was validated in cell lines and in a series of DSRCT.
Conclusions: We show for the first time that both isoforms of EWS/WT1 are oncogenic and that in addition to co-operating with loss of p53 can also further attenuate p53-mediated responses. We provide the first link between EWS/WT1 and Wnt pathway signaling. These data provide novel insights into the function of the EWS/WT1 fusion.

O-0026

DISCRIMINATING PEDIATRIC NON-NEOPLASTIC ADRENAL TISSUE, METASTATIC AND NON-METASTATIC PEDIATRIC ADRENOCORTICAL TUMORS BY MIRNA SIGNATURES

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Purpose/Objective: Although pediatric adrenocortical tumors (ACTs) are very rare malignancies (0.2% of pediatric tumors), in southern of Brazil their incidence is 10-15 times higher and present poor prognosis in metastatic disease. Abnormal miRNAs expression has been shown to play an important role in development and progression of different neoplasias. The present study aimed to evaluate the miRNAs signature in samples from pediatric patients with ACTs.
Materials and Methods: We investigated the global expression of miRNAs in 37 samples of pediatric ACTs compared to 9 pediatric non-neoplastic adrenal cortex using the Human miRNA Microarray Kit (Agilent), with 955 microRNA represented. Changes in miRNA expression levels were detected by microarray analysis and further *in silico* prediction of targets were made using bioinformatics tools to identify predicted miRNA target genes. The expression levels of 4 miRNA were validated by qRT-PCR using TaqMan probes.
Results: A significant modulation of the expression was found in 128 microRNAs with a $P < 0.05$ (false discovery rate corrected) and fold-change ≥ 5. We found the majority (92.2%) of the 128 differentially expressed miRNAs positively regulated in pediatric ACT compared to non-neoplastic samples; among than 10 miRNAs were down regulated and 118 miRNAs up regulated in pediatric ACT. Differential miRNA expression was also observed between the ACTs presenting metastasis at diagnosis compared to those without metastasis (9 down and 19 up regulated). These miRNAs have predicted/validated target genes involved in apoptosis, antigen processing and presentation and several signaling pathway as mTOR, ErbB, Insulin, Shh, Wnt, TGFB, VEGF, GnRH, Notch and p53. Abnormal miRNA expression was confirmed by qRT-PCR to let-7e, miR-128a and miR-196b (up regulated) and miR-92a (down regulated) in ACTs compared to control samples.
Conclusions: Our findings suggest a potential role of miRNAs in tumorigenesis and progression, which can contribute to a better understand and management of pediatric ACTs.

O-0027

MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY: A ROLE FOR CHEMOTHERAPY?

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Purpose/Objective: Melanotic neuroectodermal tumors of the infancy (MNTI) are very rare tumors of young children, mainly affecting the head and neck region, but also many other organs (brain and skull, long bones, testes). In most of cases, the tumor is benign and surgical excision is sufficient for healing. However, in case of metastasis or local recurrence, alternative treatments to surgery have to be considered. There is a crucial lack of data concerning the efficacy of chemotherapy in children with MNTI. The aim of our study was to clarify the potential role of chemotherapy in this indication.
Materials and Methods: We report a retrospective study collecting all the cases of MNTI treated between 1980 and 2012 in the french pediatric oncology centers. Data concerning the clinical history, treatment and outcome were noted.
Results: 27 centers were contacted. 21 cases of MNTI supported in 10 different centers were identified. The mean age at diagnosis was 4.6 months. 47.6% of the lesions concerned the face/head and neck region. One patient had metastatic disease at diagnosis. Six patients experienced one to three relapses. Four patients died of progressive disease. 20 patients underwent surgical resection during the management of the disease. Seven patients received chemotherapy with different regimen. In case of recurrence, neoadjuvant chemotherapy was able to induce significant partial responses allowing to facilitate tumor excision. In case of microscopically incomplete resections, chemotherapy was done in adjuvant setting for two patients with no recurrence within a follow-up ranging from 1 to 4.5 years. Three patients received radiation therapy in the context of recurrence.
Conclusions: Our study confirms the existence of a significant proportion of very aggressive forms of MNTI involving vital and/or functional prognosis of patients, for which no standard treatment exists. Chemotherapy seems to be an interesting therapeutic option in these situations.

O-0028

CHOROID AND RETROLAMINAR OPTIC NERVE INVASION ARE HIGH-RISK FEATURES ASSOCIATED WITH RECURRENCE IN UNILATERAL RETINOBLASTOMA – A CHILDREN'S ONCOLOGY GROUP STUDY (COG) STUDY

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Purpose/Objective: Purpose: The Children's Oncology Group (COG) initiated a prospective trial to determine the prevalence of specific, strictly defined histopathlogic features that are considered predictors of recurrence in children with unilateral retinoblastoma who undergo enucleation. We report here the histopathologic high-risk features in children who developed recurrences.
Materials and Methods: Methods: All patients who underwent enucleation for unilateral retinoblastoma were eligible for the study. Pathology slides were submitted for central review within 21 days of enucleation. Patients with evidence of one or more high-risk features (posterior uveal invasion grades IIC and D, concurrent optic nerve and choroid involvement and post-lamina optic nerve involvement) as determined by central review, received 6 cycles of chemotherapy consisting of carboplatin, vincristine and etoposide. All others were observed.
Results: Results: 93 of 312 children (30%) received chemotherapy. Post-lamina ON involvement occurred in 51 patients, 43 had choroid involvement and 34 had concomitant choroid and optic nerve involvement. Scleral invasion, ciliary body and iris infiltration were not isolated findings. A total of 6 events occurred. One had perforation of the globe during enucleation but the eye had no evidence of high risk features during central review. 2/6 patients had massive choroidal invasion with only prelaminar optic nerve invasion in one. The above 3 patients are alive after treatment for recurrence. Of the 26 patients with tumor at least 1.8 mm or more in post lamina optic nerve, 3 had recurrence and died. All 3 had concomitant massive choroidal invasion (>3mm), 1/3 had sclera invasion and 0/3 had anterior uveal invasion. These 3 also represent 3/15 with concomitant post lamina optic nerve invasion and choroidal invasion$\geq$3 mm.
Conclusions: Conclusions: The findings in this prospective trial suggest that post lamina optic nerve invasion of 1.8 mm or greater and choroidal invasion $\geq$3 mm could predict recurrence after enucleation.

O-0029

SURGERY OF THE THYROID DISEASE IN PEDIATRIC AGE: OUR EXPERIENCE OF 253 CASES.

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Purpose/Objective: Currently there are still no clear guidelines for the surgical approach of the thyroid disease in pediatric age as instead there are for adults. In this study we report our experience.
Materials and Methods: From January 2002 to December 2010, 253 pediatric patients with medium age 15.1 years (range 5-18 years), 51 male and 202 female, underwent surgery at the Department of Surgery of the University of Pisa. Age, sex, preoperative diagnosis, extension of the surgical approach, final histological diagnosis, local invasion, multifocality, bilaterality, TNM staging, node metastasis and postoperative complications are the parameters we analyzed.
Results: A total thyroidectomy has been performed in 147 patients: 140 with Differentieted Thyroid Cancer (DTC) (of which 72 cases had preoperative evidence of nodal involvement so the operation has been completed with a nodal dissection) and 7 cases for MEN 2A. A near-total thyroidectomy has been performed in 78 cases (45 multinodular goiter, 33 Graves disease) and lobectomy in 28 patients with nodular goiter.

Infiltration of thyroid capsule occurred in the 45% of PTC (Papillary Thyroid Cancer). We found multifocality in 58/131 (44.3%) PTC and 3/6 (50%) MTC (Medullary Thyroid Cancer); bilaterality in 42/131 (32.1%) PTC and 1/6 (16.7%) MTC. DTCs were at T3 or T4 stage in 71/147 cases (48.3%). Lymph node metastasis occur in 42.0% of PTC and 16.7% of MTC and involved central and lateral compartment in 75% of cases while only the central compartment in 25%.

Postoperative complications occurred only in patients with DTC. We recorded 5 cases (2%) of recurrent nerve injury (1 case of bilateral paralysis) and 52 cases (20.6%) of hypoparathyroidism (14 cases -5.5% - of permanent hypocalcemia).
Conclusions: It's vitally important a correct preoperative diagnosis and staging to guide the surgeon to the best choice since most radical approaches are associated with higher complications rate.

O-0030

KAPOSIFORM HEMANGIOENDOTHELIOMA AND TUFTED ANGIOMA: SUCCESSFUL TREATMENT WITH A NATIONAL THERAPEUTIC GUIDELINE

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Purpose/Objective: To evaluate the clinical and laboratory data of patients with kaposiform hemangioendothelioma (KHE) and tufted angioma (TA) +/− Kasabach-Merritt phenomenon (KMP) treated with a national protocol in the last 6 years, and the response to antiaggregants and vincristine.
Materials and Methods: A retrospective review of registered patients with KHE and TA. Treatment was according to guidelines of Rare Tumors and Vascular Tumors Committee of SEHOP (prednisone: 3-5 mg/kg/day $\pm$ aspirin and ticlopidine, both to 10 mg/kg/day. If not response in two weeks; discontinue corticosteroids and begin with vincristine: 0.05 mg/kg in weekly intervals).
Results: Eighteen cases were registered; eight male (44.4%) and ten female (55.6%). Thirteen patients had biopsies (69% KEH, 23% TA and 8% both). Mean age at time diagnosis was two months (range 0-9 months). Tumors were located in the head and neck (6), chest wall (7), extremities (1) and retroperitoneum (4). Twelve patients (66.6%) had a greater than 10 cm size tumor and fifteen (83%) had associated KMP. Prior to start of treatment; the average platelet count was 15,000 (range 4,000 to 36,000) and the fibrinogen level was 75 mg/dl (range 0-170 mg/dl). 15 cases were treated with vincristine, aspirin and ticlopidine, and ten had received previously prednisone. The mean vincristine dose was 0.048 mg/kg/week. All patients had an increase in platelet count and fibrinogen level with an average response time of 25 $\pm$ 17 days. Duration of vincristina treatment was 20 weeks (range 6-24 weeks). Five patients (38.5%) relapsed. All were rescued with vincristine. Vincristine related side effects occurred in 38.5%. The survival rate was 100%, with a mean time of the follow-up of 20 months (range 6-58 mo): 66.6% complete remision and 33.4% decrease in size.
Conclusions: Antiaggregants (aspirin and ticlopidine) in combination with vincristine is an effective and safe treatment option in the KMP management associated with KHE and TA.

FREE PAPER SESSION: FREE PAPER SESSION 07 - LEUKEMIA II

O-0031

STRATEGIES TO PREVENT ABANDONMENT AND THEIR OUTCOMES AT A PEDIATRIC CANCER CENTER (PCC) OF THE SCHOOL OF MEDICINE (SM) IN PARAGUAY

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Purpose/Objective: *Purpose:* In Paraguay, about 300 cases of new cancer in children occur every year. Through the ReNACI network, national referrals of children increased to 78% on 2012 almost doubling the number of children with cancer cared at the PCC * SM. Abandonment, an important problem in cancer care in Paraguay, poses a risk for cancer relapse and death. Interventions to decrease abandonment at the PCC included: (1) identification of risks groups; (2) patient follow ups; (3) supports to family in their communities; (4) engagement of local child protection services; (5) education of parents and teachers. Here we report our results.
Materials and Methods: *Method:* From January 2009 to August 2012, we used prospectively a validated tool that assesses indicators for abandonment in consecutive children newly diagnosed with cancer during interviews with family members and visits at family households. Risk indicators included patient's place or origin (rural vs. urban), family composition ($>$ 4 family members) and characteristics (separated vs. married), parental education ($<$ primary school) and salary (without fixed salary), and house characteristics (precarious vs. good). We used Excel software for data collection and analysis.
Results: *Results:* From 404 patients studied, $>$ 50% of the households was at risk for abandonment. To prevent abandonment, we telephoned parents 837 times (2010 = 568; 2011 = 221; 2012 = 48), visited 25 households, and referred 11 children to child protection services; we also trained 450 parents and teachers in adhering to the cancer treatment. Abandonment decreased gradually, in 2009, 3 children of 114 (2.6%), in 2010, 1 children of 132 (0.75%), in 2011, 0 abandonment, and in 2012, 1 of 64 (1.5%) abandoned the treatment.
Conclusions: *Conclusions:* Through a careful and concerted action of clinicians and psychosocial support and the participation of community resources we decreased abandonment to $<$ 2% in 4 years. Constant vigilance is needed to sustain successful program for preventing abandonment.

O-0032

IMPROVEMENTS IN OVERALL SURVIVAL (OS) IN CHILDREN WITH NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) ENROLLED IN CHILDREN'S ONCOLOGY GROUP (COG) TRIALS IN 2000-05 VS. 2006-09

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Purpose/Objective: To compare OS rates for children enrolled in risk-adapted COG ALL trials in 2000-05 (n = 7835) and 2006-09 (n = 6530).
Materials and Methods: We estimated OS using the Kaplan-Meier method with standard errors (SE) calculated per Peto and curves compared using the log-rank test.
Results: Five-year OS increased from 90.4% (SE 0.4%) in 2000-05 to 91.9% (SE 0.6%) in 2006-09 (p = 0.0213). OS increased in most subsets examined, with statistically significant improvements for those 1-9 years (94.0% SE 0.3% vs. 95.2% SE 0.5%, p = 0.0252), and dramatic OS improvements for T-ALL patients (81.5% SE 2.0% vs. 89.8% SE 5.5%, p = 0.0015). Non-significant trends toward improved survival were observed for the 10+ year, male, female, and B-lineage subgroups, while non significant trends toward inferior survival were seen in infants $<$ 1 year and adolescents 16+ years. In 2006-09, 5-year OS was similar for patients 16-21 (n = 391; 76.2% SE 4.8%) and 22-30 years (n = 36; 73.9% SE 21.8%). Differences in outcome based on race decreased over time with 5-year OS rates for whites and blacks of 91.0% SE 0.4% (n = 6039) and 86.6% SE 1.7% (n = 486) in 2000-05 and 92.3% SE 0.7% (n = 4884) and 91.0% SE 2.5% (n = 451) in 2006-09. Survival rates were unchanged among Hispanics, 88.0% SE 0.9% (n = 1481) in 2000-05 and 88.2% SE 1.6% (n = 1354) in 2006-09. In 2000-05, survival rates were only modestly lower at 8- vs. 5-years (88.5%, SE 0.5%, and 90.4%, SE 0.4%), suggesting that 5-year OS provides a good estimate of long-term survival.
Conclusions: Survival continues to improve for children enrolled in COG ALL trials. Results are particularly impressive for T-ALL with the difference in 5-year OS rates between T- and B-ALL dropping from 9.6% in 2000-05 to 2.3% in 2006-09. No recent improvements have occurred in OS of infants and older teenagers, identifying these as subgroups in particular need of new therapies.

O-0033

MIR-124 REGULATES GLUCOCORTICOID RECEPTOR EXPRESSION AND PLAYS A ROLE IN TREATMENT RESPONS TO GLUCOCORTICOID IN ACUTE LYMPHOBLASTIC LEUKEMIA.

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Purpose/Objective: Recent studies revealed that aberrant expression of some miRNAs are associated with the prognosis of leukemia; however, the role of miRNA in regulating treatment response to glucocorticoid (GC) in acute lymphoblastic leukemia (ALL) remains to be explored.
Materials and Methods: A total of 31 prednisone good response (PGR) and 9 prednisone poor response (PPR) pediatric ALL patients were enrolled, and GC-sensitive and GC-insensitive ALL cell lines (CCRF-CEM and CEM/C1) were used in this study.
Results: Firstly, there are 5 leukemia/cancer-associated miRNAs including miR-124 potentially targeting GC receptor gene according to prediction using biology softwares and the literature available. Secondly, western blot and qRT-PCR showed that the expressions of GC receptor (NR3C1 protein) and its mRNA significantly increased in GC sensitive cells (CCRF-CEM), and decreased in GC insensitive cells (CEM/C1), which were contrary to the expression of miR-124. Thirdly, the expression of NR3C1 was inhibited after up-regulating the expression of miR-124 in CCRF-CEM cells transfected with mimics-miR-124 (P
Conclusions: This study strongly suggests that miR-124 targets GC receptor gene and negatively regulates its expression, playing an important role in treatment response to GC in ALL. MiR-124 could be a potential prognostic marker of ALL and a potential target of therapy.

O-0034

OUTCOME FOR CHILDREN WITH HYPODIPLOID ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) ON CONTEMPORARY CHILDREN'S ONCOLOGY GROUP (COG) CLINICAL TRIALS

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Purpose/Objective: To determine event-free survival (EFS) rates for children with hypodiploid ALL, defined as $<$ 44 chromosomes and/or a DNA index $<$ 0.81, and the role of minimal residual disease (MRD) and other factors in predicting outcome for this high-risk ALL subtype.
Materials and Methods: We assessed outcome of 122 (1.5%) hypodiploid ALL patients among 8,399 children, adolescents, and young adults 0-30.99 years old with B-ALL enrolled on COG trials AALL0331 (NCI standard risk, n = 5,307) and AALL0232 (NCI high risk, n = 3,092) between 2004 and 2011. MRD was determined via flow cytometry in one of two central COG ALL reference labs. EFS was estimated using the Kaplan-Meier method with standard errors (SE) calculated per Peto and survival curves compared using the log-rank test.
Results: The 5-year EFS was 46.6 $\pm$ 7.3% in hypodiploid ALL patients vs. 84.5 $\pm$ 0.7% in the remaining patients (p $<$ 0.0001). End induction MRD was highly predictive of 5-year EFS among hypodiploid patients using an MRD cutoff of 0.01% (55.3 $\pm$ 8.9% (n = 82) vs. 28.3 $\pm$ 10.7% (n = 40), p $<$ 0.0001) or 0.1% (53.5 $\pm$ 8.2% (n = 94) vs. 26 $\pm$ 15.8% (n = 28), p $<$ 0.0001). This was true among NCI standard risk and NCI high risk patients, respectively. Among MRD negative (0.01% cutoff) patients, outcomes were significantly worse for hypodiploid patients compared to others (55.3 $\pm$ .9% vs. 90.4 $\pm$ 0.7%, p $<$ 0.0001). In multivariate analyses age, initial white blood cell count, NCI risk group, MRD status, and hypodiploid status among all patients, were all prognostic of outcome (p $<$ 0.0001). When analyses were limited to those with hypodiploid ALL, only MRD status was prognostic of outcome (p $<$ 0.0001).
Conclusions: Outcome is poor for patients with hypodiploid ALL, which is a strong negative independent prognostic factor. Outcome for hypodiploid ALL patients who have MRD $\geq$0.01% at end induction is particularly poor. New treatments are needed for this high risk ALL subset that has unique genomic properties (Holmfeldt et al, Nature Genetics 2013).

O-0035

BONE MINERAL DENSITY AT DIAGNOSIS DETERMINES FRACTURE RATE IN CHILDREN TREATED ACCORDING TO THE DCOG-ALL9 PROTOCOL

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Purpose/Objective: To elucidate the incidence and risk factors of skeletal toxicity in children with ALL treated with the dexamethasone-based DCOG-ALL9 protocol.
Materials and Methods: Prospectively, the cumulative incidence of fractures was assessed in 672 patients and compared between different subgroups using the Log-Rank test. Serial measurements of bone mineral density of the lumbar spine (BMD_{LS}) were performed in 399 ALL patients using dual energy X-ray absorptiometry (DXA). We evaluated risk factors for a low BMD using multivariate regression. Osteoporosis was defined as having a $BMD_{LS} \leq$-2 SDS combined with clinical significant fractures.
Results: The cumulative incidence of fractures at 3 years was 17.8%. At diagnosis, mean BMD_{LS} of ALL patients was lower than that of healthy peers (mean BMD_{LS} = -1.10 SDS, $P < 0.001$), and this remained significant lower during and after treatment (8 months: BMD_{LS} = -1.10 SDS, $P < 0.001$; 24 months: BMD_{LS} = -1.27 SDS, $P < 0.001$; 36 months: BMD_{LS} = -0.95 SDS, $P < 0.001$). Multivariate linear regression analysis showed that age at diagnosis, weight and B-cell-immunophenotype were associated with a lower BMD_{LS} at diagnosis. After correction for weight, height, gender and immunophenotype, stratification to the HR protocol arm and older age had a significant independent larger decline of BMD_{LS} during treatment (HR group: β = -0.52, $P < 0.01$ and age: β = -0.16, $P < 0.001$) Cumulative incidences of fractures between ALL risk groups and age groups were not significantly different. Patients who developed fractures had a lower BMD_{LS} during treatment than those without fractures. Treatment-related bone loss was similar in patients with and without fractures (respectively: ΔBMD_{LS} = -0.36 SDS and ΔBMD_{LS} = -0.12 SDS; interaction group time, $P = 0.295$). Twenty of the 399 patients (5%) met the criteria of osteoporosis.
Conclusions: This large prospective study shows that a low absolute value of BMD_{LS} both at diagnosis and during treatment, rather than the treatment-related decline of BMD_{LS}, determines the markedly increased fracture risk of 17.8% in children with ALL.

O-0036

THE DEVELOPMENT OF THROMBOEMBOLISM MAY INCREASE THE RISK OF OSTEONECROSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: Osteonecrosis (ON) is a recognized complication of anti-leukemic therapy, specifically long-term corticosteroid use. A prothrombotic state is thought to underlie corticosteroid-related ON. Hence, we explored the relationship between ON and thromboembolism (TE) along with other variables, including age and obesity, in children with acute lymphoblastic leukemia (ALL).
Materials and Methods: Data were collected on a prospectively-assembled cohort of children (2 to $<$18 years) treated on Dana-Farber Cancer Institute (DFCI) ALL protocols from 1992*2009. Given the lack of validated body mass index (BMI) Z-scores, children $<$2 years were excluded. Regression analyses were used to evaluate the influence of age (continuous variable), gender, ALL risk-category, steroid and asparaginase type, BMI at diagnosis and objectively-confirmed TE on the development of ON.
Results: The mean age of the study cohort ($n = 182$) was 6.1 years and male:female ratio 1.28:1. One-hundred-ten patients (60%) had standard-risk ALL and 107 (59%) received dexamethasone post-induction. Seventeen patients (9.3%) developed ON and 34 (19%) TE. Gender, ALL risk-category, steroid type and BMI did not predict ON. Older age was significantly associated with ON ($p = 0.0001$). Nine of 34 patients with TE (26%) had ON versus 8 of 148 without TE (5.4%) (OR 6.30, 95% CI 2.22*17.88, $p = 0.0005$). Diagnosis of TE preceded that of ON in 7 of 9 patients. Because older age is a known risk factor for both TE and ON, we undertook a multivariate analysis, which showed that age ($p = 0.003$) and TE (OR 3.80, 95% CI 1.24*11.69, $p = 0.02$) are independent predictors of ON.
Conclusions: In addition to the known impact of older age, we identified TE as an independent risk factor for ON in children with ALL. This observation suggests overlap in the etiopathogenesis of ON and TE. We recommend future studies to confirm the association of TE with ON and assess the impact of hypercoagulability on the development of ON.

FREE PAPER SESSION: FREE PAPER SESSION 08 - LATE EFFECTS

O-0037

LONG-TERM NEUROCOGNITIVE FUNCTIONING IMPAIRMENT IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) WHO RECEIVED ONLY CHEMOTHERAPY

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Purpose/Objective: Studies are inconsistent regarding the severity, if any, of neurocognitive impairment in children treated for ALL on chemotherapy-only regimens. This systematic review and meta-analysis sought to assess this important question for the domains of intelligence, working memory, processing speed, and visual motor coordination.
Materials and Methods: We conducted an iterative search of the literature with disease-specific, treatment-specific, and outcome-specific search terms. To be included, studies were required to measure neurocognitive function in childhood ALL survivors with CNS1 status in CR1 who did not receive cranial radiation and who were $\geq$3 years off-therapy, compared to a healthy comparison group.
Results: 11 articles were included in our final analysis, with 8 articles assessing IQ level, 8 assessing working memory, 5 assessing processing speed, and 4 assessing visual motor coordination. Overall, nearly every study found at least some neurocognitive impairment. Meta-analysis was performed on the results of all five domains, finding a strong statistically significant ($p < 0.0001$) negative effect associated with chemotherapy-only across all measures: mean difference in Full Scale IQ ($n = 348$) of -11.24 points [-14.47, -8.68], Performance IQ ($n = 381$) of -7.68 points [-10.73, -4.64], Verbal IQ ($n = 381$) of -11.57 points [-14.47, -8.68], working memory via the Wechsler Digit Span Subtest ($n = 415$) of -1.45 [-1.98, -0.92], processing speed via the Wechsler Coding Subtest ($n = 209$) of -2.30 [-2.96, -1.64], and visual motor coordination via the Wechsler Block Design Subest ($n = 220$) of -1.71 [-2.50, -0.92].
Conclusions: Our results suggest that even with contemporary therapy for childhood ALL with chemotherapy only, patients experience a significant decrease in intelligence in the range of 7 to 11 IQ points, representing half to two-thirds of a standard deviation compared to population norms. There is also a measurable decrease in the domains of working memory, processing speed, and visual motor coordination. Our data suggest that further studies are warranted to investigate cognitive late effects in children treated for ALL.

O-0038

FINE AND VISUAL-MOTOR SKILLS AS PREDICTORS OF ACADEMIC ACHIEVEMENT AMONG PEDIATRIC SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) ENROLLED ON COG TRIALS

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Purpose/Objective: Children with ALL often develop impairment in fine and visual motor abilities as a result of standard treatment, skills that are associated with academic performance in healthy children. We aim to determine if performance on these measures predicts reading and math achievement in pediatric survivors of ALL.
Materials and Methods: This 22-site cross-sectional study included 256 children in first remission for standard-risk precursor-B ALL previously enrolled on COG protocols between 1993 and 2000. Patients had no history of CNS leukemia, did not receive cranial radiation, were $\geq$1 year off-therapy, were 6-16.9 years at evaluation, and had no history of pre-existing neurodevelopmental disorders. Patients were administered tests of 1) fine motor skills, Lafayette Grooved Pegboard (LGP); 2) visual-motor skills, Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI); and 3) math and reading from the Wechsler Individual Achievement Tests*II. Impaired performance was defined as worse than 1 SD from the normative mean.
Results: VMI performance is significantly associated with math achievement ($p = < 0.0001$), older age at diagnosis ($p = 0.006$), and higher maternal education ($p = 0.0008$). VMI performance and higher maternal education ($p = 0.02$) are significantly associated with reading achievement ($p = < 0.0001$). Impaired VMI performance was significantly associated with impaired math performance (OR, 5.854; 95%CI, 2.72-12.59) and impaired reading performance (OR, 2.852; 95%CI, 0.963-8.443). Performance on the LGP is associated with math ($R2 = 0.10$; $p = 0.0336$) but not reading achievement.
Conclusions: Our data suggest that visual-motor coordination contributes to academic success among pediatric survivors of ALL, and children treated at a younger age are more likely to have poorer math abilities. Fine motor dexterity is related to math, but not reading skill, consistent with the use of finger counting in math. Since ALL patients are at increased risk to experience peripheral neuropathies with treatment, close monitoring of this medical condition and development of these skills are warranted.

O-0039

LONG TERM FOLLOW UP OF HEALTHCARE VISITS IN ADULT SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: The high survival rates of patients with childhood cancer require increased knowledge of the late complications of the diseases and their treatment.
The aim of this work was to determine the in- and outpatient hospital visits during the years 2009-2011, in adult survivors of childhood cancer.
Materials and Methods: All individuals diagnosed with cancer before the age of 18 in the time period 1985-2001 in the Western region of Sweden, older than 18 years, at least 5 years past treatment and still living in the region in January 2009 (452 individuals) were identified. Of them, 170 had leukaemia/lymphoma (LL), 141 central nervous system tumours (CNST) and 141 solid tumours (ST). 1000 age- and gender-matched controls were identified in the Population Register of Sweden. We evaluated and compared their healthcare visits during 2009-2011. One leukaemiapatient was considered as outlier due to extensively many visits, and therefore excluded in all calculations.
Results: Compared to controls, adult survivors of cancer had in total 2.1 times more hospital visits per individual during the years 2009-2011. In the adult survivor group 75% had hospital visits compared with 56% in the control group. Evaluation of each subgroup showed equal results; LL 1.8, CNST 2.2 and ST 2.3 times more often hospitals visits. The stay in the hospital care was 2.5 times longer for survivors of cancer in comparison with controls. The health care costs were for the adult survivors in general 2.8 times higher per year.
Conclusions: This population-based study shows that survivors of childhood cancer have greater demand for healthcare contacts in adulthood. They have both higher frequency of hospital visits and increased length of stay in hospital. The higher health care costs indicate a high burden of chronic health conditions and motivates structured follow-up. Further analysis of the specific health conditions will be presented.

O-0040

LATE EFFECTS IN CHILDREN AND ADOLESCENTS TREATED FOR RETINOBLASTOMA

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Purpose/Objective: Overall survival of children with retinoblastoma in Germany is $>95\%$. This study investigates the impact of prognostic factors at presentation and different therapy strategies on late effects in children and adolescents treated for retinoblastoma.
Materials and Methods: Basic follow-up data were collected for 281 (64.0%) of 439 survivors of retinoblastoma (age >6 to <18), comprising 154 (54.8%) with unilateral and 127 (45.2%) survivors with bilateral retinoblastoma. Of these, 228 (51.9%) survivors participated in an interview and/or clinical examination.
Results: Median follow-up was 9.6 years (range 1.4-17.3 years). Previous treatment was enucleation or focal treatment alone in 163 children, chemotherapy in 53 children, external beam radiotherapy (EBRT) in 47 children and both (chemotherapy and EBRT) in 18 children. Without showing significant differences between treatment subgroups, current discomforts were reported by 12.2% (24/173) and 10.2% (20/177) of survivors required permanent medication. At follow-up examination, 1.2% (3/228) had bilateral enucleation and 2.6% (5/198) of survivors needed hearing aids after chemotherapy and EBRT. Six children developed a second malignancy (median age 7.5 years, range 3.0-8.5 years) that comprised 1 meningioma, 1 osteosarcoma, 2 rhabdomyosarcomas and 2 acute leukemias (1 myeloid, 1 lymphatic). All children with second malignancies had heritable bilateral retinoblastoma; one child with second malignancy suffered from 13q deletion syndrome. The child with meningioma had received enucleation and focal treatment including brachytherapy for retinoblastoma. All other 5 children had been treated with EBRT. Both children with leukemia had additional chemotherapy with carboplatin, etoposide, vincristine and cyclophosphamide. The 10-year cumulative incidence of second malignancies was 5.5% for all survivors of bilateral retinoblastoma and 9.3% in the subgroup treated with EBRT.
Conclusions: Late effects affects children and adolescence in very different extent depending on treatment strategies for retinoblastoma. Late effects of established and experimental retinoblastoma therapies need to be assessed prospectively to allow informed treatment decisions.

O-0041

TESTICULAR VERY SMALL EMBRYONIC-LIKE STEM CELLS (VSELS) MAY BE TARGETED FOR FERTILITY RESTORATION IN CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: Infertility is a major concern in childhood cancer survivors due to treatment related gonadal toxicity which affects actively dividing cells. Based on experiments in chemo ablated mice testis, we propose that Pluripotent Very Small Embryonic like Stem Cells (VSELs) exist in gonads of azoospermic childhood cancer survivors.These VSELs escape oncotherapy insults (as they are very slow dividing) and remain quiescent because surrounding somatic microenvironment is destroyed. If we attempt to restore somatic niche, spermatogenesis may be restored & survivors may achieve biological parenthood.
Materials and Methods: Young adult azoospermic survivors of childhood cancer with normal pubertal development were enrolled in the study. After obtaining written informed consent, 10 * 12 pieces of testicular biopsy were collected from 4- 6 different sites from testes in a sterile manner.
Results: Seven married men, survivors of childhood cancers (2 Hodgkin Lymphoma, 4 Non-Hodgkin Lymphoma, 1 Wilms tumor) were included in the study. Median time since treatment completion is 23 years (21-27) All received alkylating agents and/or Radiation. H & E stained testicular sections confirmed azoospermia by presence of empty tubules with no signs of germ cells and sperms. In all, Pluripotent VSELs were identified based on typical morphological characteristics &markers (Nuclear OCT4, STELLA, CD133) which was further confirmed by RT-PCR.

Further studies done in chemo ablated mice to restore somatic niche by transplantation of healthy Sertoli or mesenchymal cells are positive, Spermatogenesis was restored overcoming meiotic block and producing functional sperm.
Conclusions: Pluripotent Very Small Embryonic like Stem Cells (VSELs) exists in the gonads and persist in azoospermic testis despite aggressive oncotherapy. The compromised somatic microenvironment renders VSELs non-functional. Transplanted Sertoli or mesenchymal cells possibly act as a source of growth factors essential for differentiation of VSELs (human trial awaited). Since sperm formation mimics natural spermatogenesis,this study offers an altogether newer perspective to the field of oncofertility.

O-0042

LOWER DOSES OF CHEST RADIATION TO LARGE FIELDS MAY INCREASE BREAST CANCER RISK AMONG FEMALE CANCER SURVIVORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Purpose/Objective: Women treated with high doses of radiation to the chest for a childhood cancer have a high risk of breast cancer (BC). How the chest radiation field modifies BC risk is unknown.
Materials and Methods: We studied 1229 female 5-year survivors of a childhood cancer who were diagnosed 1970-1986 and were treated with chest radiation. Radiation treatment information, including dose and field, were abstracted from medical records. Relative risk of BC was assessed with standardized incidence ratios (SIRs) estimated using age- and calendar year-specific rates from population registries.
Results: With a median follow-up of 26 yrs (range 5-39), 174 women were diagnosed with BC at a median age of 38 yrs (range 24-53) and a median latency of 23 yrs (range 7-38). The cumulative incidence of BC by age 50 was 24% (95% confidence interval [CI] 20-28%). The chest radiation fields and associated median doses used to treat the 1229 survivors included: mantle field (40 Gy, n = 603), mediastinal/involved field radiation therapy/hemithorax fields (IFRT, 30 Gy, n = 292), whole lung (14 Gy, n = 116), total body irradiation (12 Gy, n = 69), abdominal fields extending above the diaphragm (20 Gy, n = 77), posterior thoracic or para-vertebral fields (31 Gy, n = 54), and other fields (n = 18). BC risk was significantly elevated in women treated using the mantle field (SIR = 21.7, 95% CI 18.4-25.6), IFRT (SIR = 10.4, 95% CI 6.6-16.3), and the whole lung field (SIR = 31.4, 95% CI

17.8-55.3). Treatment with ovarian radiation lowered BC risk, but the incidence of BC was still elevated in these women (n = 128) compared with the general population (SIR = 7.1, 95% CI 3.5-14.2).
Conclusions: Women with a large extent of breast tissue exposed to moderate doses of radiation using the whole lung field had an increased risk breast cancer warranting consideration of surveillance strategies similar to current recommendations for women treated with > 20 Gy.

FREE PAPER SESSION: FREE PAPER SESSION 09 - BRAIN TUMOURS I

O-0043

RESULTS OF MEDULLOBLASTOMA TREATMENT IN CHILDREN OVER THREE YEARS OLD

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Purpose/Objective: To improve the survival in patients with medulloblastoma (MB) over 3 yo and to determine the prognostic factors.
Materials and Methods: From 2000 to 2009 a cooperative randomized study was organized. Patients with a residual tumor and/or stages M+ were stratified into two arms depending on the type of CHT. All pts after the surgery received CSI 35 Gy, boost on PF 55 Gy and on metastases: 50 Gy on cerebral, 45 Gy on spinal cord with weekly VCR 1.5 mg/m^2 and once CCNU 100 mg/m^2. CHT regimes consist: 8 cycles of maintenance CHT (CCNU, CDDP and VCR) or 4 cycles of cyclic CHT (2 cycles of VCR + CPM and 2 cycles of VP-16 + CDDP). 222 pts were enrolled: 153 male, 69 female. The median age was 10 years (range, 3 to 15 yrs). Histological types were identified in 146 pts: desmoplastic * 4, classic - 115, large-cell - 27, 10 pts were MYC+. There were 90 pts (40.54%) with M0; 127 pts with M+ (57.2%); 5 pts - Mx. 38 pts (17%) underwent total tumor resection, 184 (83%) - subtotal. 109 pts (49%) received maintenance CHT, 113 pts (51%) cyclic therapy.
Results: 173 pts (77.92%) are still alive; PD was observed in 46 pts (20.72%). Toxicity death - 14 cases (6.30%). LFU - 8 pts. 3 pts (1.3%) developed a secondary tumor (median 35 months). The OS and PFS were 0.75 $\pm$ 0.03 and 0.77 $\pm$ 0.03, respectively (median observation 67 months, median PFS 16 months). PFS in pts with M0 was 0.84; M+, 0.72 ($p = 0.01$). PFS in pts with MYC amplification - 0.1, without - 0.85 ($p = 0.00001$). PFS in large-cell MB was 0.27, in classic - 0.9, desmoplastic - 1.0 ($p = 0.000001$).
Conclusions: The prognosis was significantly influenced by the presence of metastases, large-cell MB and MYC amplification. No significant differences were found between cyclic and maintenance CHT.

O-0044

SUBGROUP SPECIFIC PATTERNS OF RECURRENCE IN MEDULLOBLASTOMA

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Purpose/Objective: Recurrent medulloblastoma remains an enormous treatment challenge, and is almost uniformly fatal. Recent studies confirmed that medulloblastoma comprises four distinct subgroups. We sought to delineate subgroup-specific differences in medulloblastoma recurrence patterns.
Materials and Methods: We identified a screening cohort of all recurrent medulloblastomas at the Hospital for Sick Children between 1994-2012, and sub-grouped the cases from FFPE tissues using a nanoString-based gene expression class predication algorithm. Our findings were confirmed through analysis of two independent non-overlapping FFPE validation cohorts.
Results: A screening cohort of 30 recurrent medulloblastoma was assembled; 9 with local tumor bed recurrences, and 21 metastatic recurrences. Notably, SHH tumors recurred much more frequently in the tumor bed (8/11, 73%) whereas Group 3 and Group 4 recur more exclusively with metastases (16/18, 89%; $p = 0.001$). The subgroup-specific location of recurrence was confirmed in a multicenter validation cohort ($p = 0.012$, $n = 53$), and an independent validation cohort comprising 96 recurrences (SHH in 21/24 local recurrences, Group 3/4 tumors represented 69/72 metastatic relapses) ($p < 0.001$). Survival post recurrence was significantly longer in Group 4 patients ($p = 0.03$) and was confirmed in a multicenter validation cohort ($p = 0.02$). Strikingly, in all 35 cases where matched primary and recurrent pairs were available, the subgroup affiliation remained stable at recurrence.
Conclusions: Medulloblastoma does not change subgroup at the time of recurrence. Significant differences in the pattern of recurrence exist across medulloblastoma subgroups, further highlighting the clinical differences between the four principle subgroups. Intensified local (posterior fossa) therapy should be considered upon initial treatment for SHH patients. Refinement of therapy for Groups 3 and 4 should focus on the metastatic compartment.

O-0045

ADOPTIVE LYMPHOCYTE THERAPY (ALT) PLUS DENDRITIC CELL VACCINATION (DCV) AFTER MYELOABLATIVE (MA) OR NON-MYELOABLATIVE (NMA) CONDITIONING IN PATIENTS WITH RECURRENT CENTRAL PNET (C-PNET)

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Purpose/Objective: Patients with c-PNET have a dismal prognosis and alternative treatment approaches are needed. We have developed a novel platform for the expansion of polyclonal tumor-specific T cells using amplified tumor RNA pulsed DCV targeting a broad repertoire of undefined and patient specific tumor antigens. This strategy showed considerable efficacy in preclinical models of CNS malignancies and led to a phase I/II study (Re-MATCH) assessing feasibility, safety, and efficacy of ALT + DCV following recovery from either MA or NMA chemotherapy in patients with recurrent c- PNET (FDA IND BB-14058, Duke IRB #18020).
Materials and Methods: In 2 concurrent phase I studies (3 + 3 design), eligible patients undergo surgery to obtain tumor for total RNA extraction, amplification, and vaccine preparation. All patients receive 4 cycles of induction chemotherapy. Patients with localized disease (Group A) then receive MA (carboplatin, thiotepa, and etoposide) plus peripheral blood stem cell (PBSC) rescue and those with metastatic disease (Group B) NMA (Cyclophosphamide + Fludarabine) followed by DCV +ALT. Three dose levels of single dose ALT are to be evaluated (3×10^6, 10^7, or 10^8 cells/kg) followed by a dose of intradermal DCV (10^7 cells) and then every 2 weeks x 2. Dose limiting toxicity (DLT) will be assessed 2 weeks following the third biweekly DCV.
Results: Tumor RNA was successfully amplified from 13/13 recurrent tumors. We generated sufficient DCV ($\geq$ 3 vaccines) and T cells to the targeted dose in 12/13 patients. Seven patients have received immunotherapy: 4 at 3×10^6 T cells/Kg (Group A-1, Group B-3), and 3 at 3×10^7 T cells/Kg (Group B-3). No DLTs have been observed.
Conclusions: ALT + DCV therapy is a novel, feasible therapeutic approach and preliminary evidence corroborates the safety of this promising intervention as accrual continues on the phase I component with ongoing clinical and immunologic evaluation.

O-0046

IMPROVING RISK STRATIFICATION OF PATIENTS WITH NON-METASTATIC MEDULLOBLASTOMA: BIOMARKER ANALYSIS IN THE SIOP-EUROPE PNET4 CLINICAL TRIAL

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Purpose/Objective: Optimizing outcome and minimizing late side effects by a risk-adapted treatment of medulloblastoma patients is a major goal. This requires an accurate stratification of the disease-risk. A series of validated molecular and pathological prognostic markers have now been identified for medulloblastoma including the favourable-risk WNT activation.
Materials and Methods: In the recent multicenter SIOP-PNET4 medullobastoma trial, non-infant patients without metastatic disease at diagnosis have been defined as 'standard-risk' group. We undertook a systematic analysis of biomarkers of reported prognostic significance, alongside clinical and pathological variables, within the PNET4 cohort. Formalin-fixed paraffin-embedded (FFPE) tumour tissue was collected for centralised pathology review ($n = 338$) and analysis (up to $n = 236$) of WNT activation status (b-catenin immunohistochemistry, *CTNNB1* mutation analysis), copy-number alterations (chromosome 17, *MYC/MYCN*, *PTCH1*) and DNA ploidy status.
Results: Standard (77 ± 4%) and hyperfractionated (78 ± 4%) radiotherapy were found equivalent regarding five-year event-free survival ($p = 0.8$). b-catenin nuclear positivity predicted a favourable outcome ($p < 0.05$), while chromosome 17p loss or 17q gain ($p < 0.01$), and significant residual tumour after surgery ($p < 0.01$) were associated with a poor outcome. Chromosome 17p/q defects were heterogenous, and predicted a poor prognosis when they occurred against a diploid, but not polyploid, genetic background. All three factors were supported as independent markers in multivariate testing. Notably, previously identified poor prognosis markers (*MYC or MYCN* amplification) were not significantly associated with adverse outcome in this 'standard-risk' cohort. In survival models of patients with non-metastatic, completely resected medulloblastoma (R0), chromosome 17p/q defects predicted a poor outcome.
Conclusions: These findings demonstrate that routine testing of chromosome 17 and WNT status may help to improve the accurate definition of disease-risk in 'standard-risk' medulloblastoma patients.

O-0047

TREATMENT OF YOUNG CHILDREN WITH CLASSIC OR LARGE-CELL/ ANAPLASTIC MEDULLOBLASTOMA WITHIN THE PROSPECTIVE MULTICENTER TRIAL HIT 2000.

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Purpose/Objective: In contrast to desmoplastic variants, classic and large-cell/anaplastic medulloblastoma are associated with an unfavorable prognosis in young children. We evaluated different strategies aiming to delay or avoid craniospinal irradiation in these high-risk patients.
Materials and Methods: From 2001-2011, 86 eligible children below 4 years (median age: 2.8 years) with classic (n = 75) or large-cell/anaplastic (n = 11) medulloblastoma confirmed by central pathology were registered. Children with nonmetastatic disease (n = 46) were treated with 3 cycles of postoperative HIT-SKK chemotherapy. Before 2006, children in remission received 2 additional cycles of SKK chemotherapy, elsewise CSI plus maintenance chemotherapy. Since 2006 all patients received local radiotherapy (54 Gy) after HIT-SKK induction, and maintenance chemotherapy in case of residual disease. Children with metastatic disease (n = 40) received postoperative induction with 3-4 courses carboplatin/etoposide, further intensified since 2006 (cisplatin/vincristine/ cyclophosphamide/etoposide/methotrexate). After complete or partial response, therapy proceeded with tandem-HDCT (carboplatin/etoposide; thiotepa/cyclophosphamide) and ASCT. CSI was given after poor response to induction or if there was residual disease after HDCT, and optional if non-CR before HDCT.
Results: Four-year event-free (EFS) and overall survival (OS) rates were 37% ± 6% and 57% ± 6%, respectively (median follow-up: 3.8 years). Nonmetastatic medulloblastoma patients did not differ in their EFS (p = 0.323) and OS (p = 0.151) from metastatic medulloblastoma patients. In case of metastatic disease induction was followed by tandem-HDCT, n = 18; tandem-HDCT and CSI, n = 9; CSI only, n = 5; and no tandem-HDCT or CSI, n = 8. In the latter group, 2 patients succumbed to toxic death and 6 patients had an early disease progression. Four-year CSI-free and radiotherapy-free survival was 29% ± 5% and 15% ± 4%, respectively.
Conclusions: Survival rates of young children with classic or large-cell/anaplastic medulloblastoma remain low. Metastatic disease was not associated with a lower survival, possibly due to the more intensive therapy applied. Children with nonmetastatic disease may benefit from therapy intensification with HDCT. Neuropsychological assessments are ongoing.
Supported by Deutsche Kinderkrebsstiftung

O-0048

INTEGRATIVE CLUSTERING REVEALS FOUR SHH MEDULLOBLASTOMA SUBTYPES

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Purpose/Objective: Sonic hedgehog (SHH) medulloblastomas account for one-third of all patients and comprise the majority of infant and adult tumors. Although all tumors in the SHH subgroup show over-activity of the SHH pathway, this subgroup exhibits remarkable heterogeneity in their somatic copy number alterations, transcriptional and mutational signatures. To date, few genomic studies have profiled sufficient cases to reveal distinct molecular subtypes within this subgroup, making it difficult to define molecular targets for the development of novel treatment strategies.
Materials and Methods: To specifically address these issues, we performed comprehensive genome-wide gene expression analysis using the Affymetrix GeneChip Human Gene 1.0 ST Array and a high-resolution methylation profiling analysis using the Illumina Infinium HumanMethylation450 BeadChip in a discovery cohort of over 250 primary SHH medulloblastomas. Molecular subtypes were delineated using unsupervised clustering algorithms for each of the datasets. Integrative clustering was performed to incorporate profiling data from different platforms. We used Ingenuity and Cytoscape to identify subtype-specific pathways.
Results: Unsupervised consensus clustering analyses of methylation and transcriptomic data revealed four distinct SHH subtypes. SHH tumors show characteristic methylation and gene expression signatures in infant and adult tumors further underlining age-specific difference in SHH tumor biology. Notably, infant tumors can be further separated into two clusters, while pediatric and adult SHH tumors form distinct subtypes. The pediatric cluster is associated with increased metastatic dissemination and inferior prognosis, while adult tumors define an intermediate risk group compared to the prognostically favorable infant clusters.
Conclusions: Collectively, our integrated analysis identifies four clinically, epigenetically, transcriptionally, genetically, and prognostically distinct SHH subtypes. A refined understanding of these subtypes may help to develop novel outcome prediction algorithms and define novel targets for molecular-based therapies.

PRIZE SESSION: SIOP AWARD SESSION

O-0049

GENOME SEQUENCING OF SHH MEDULLOBLASTOMA PREDICTS AGE-DEPENDENT RESPONSE TO SMOOTHENED-INHIBITION AND RATIONAL THERAPEUTIC COMBINATIONS

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Purpose/Objective: Smoothened (SMO)-inhibitors have recently entered clinical trials for SHH-driven medulloblastoma (SHH-MB). Early evidence suggests that even within this molecularly defined patient subgroup response to therapy is highly variable. To better understand the mechanism(s) of primary resistance to conventional SMO-inhibitors and identify other pathways coopting aberrant SHH signaling, we conducted a comprehensive next-generation study of 125 SHH medulloblastomas obtained from patients between 0 and 49 years of age.

Materials and Methods: Tumor and blood DNA of 57 SHH-MBs (31 pediatric [< 16 years of age] and 26 adult [≥16]) were subjected to whole-genome or whole-exome sequencing. Two independent non-overlapping replication cohorts (41 pediatric and 27 adult) were sequenced for at least ∼400 prioritized candidate genes. Gene expression (n = 112), DNA copy number (n = 266), and DNA methylation (n = 55) data complement this integrative genomics approach. SHH-MB models with different underlying genotypes were used to evaluate response to SMO inhibition and other drugs.
Results: Three age-related subgroups exhibiting highly discriminate genomic profiles were identified. Mutations in the SHH-pathway involved *PTCH1* (young children and adults), *SUFU* (infants, including germline), and *SMO* (adults). Children (10-15 years) harbored excess downstream *MYCN* and *GLI2* amplifications, and frequent *TP53* mutations, often in the germline, all of which were exceedingly rare in infants and adults. Based on recurrent mutations in other pathways, rational candidates for combination therapies include PI3K-inhibition in infants and adults, GLI-inhibitors in children, and epigenetic modifiers in adults. Functional assays demonstrated that adult SHH-MBs were responsive to SMO inhibition, whereas pediatric counterparts harboring *MYCN/GLI2* amplifications were not.
Conclusions: Our data show that (i) response to SMO inhibition can be predicted by thorough molecular analysis of the primary tumor, (ii) tumor predisposition (Gorlin«s Syndrome in infants and Li-Fraumeni-Syndrome in older children) is highly prevalent in patients with SHH-MB, and (iii) rational age group-specific combination therapies may be derived from these findings.

O-0050

DISSECTING PROGNOSTIC AND BIOLOGICAL SUBTYPES OF GROUP 3 AND GROUP 4 MEDULLOBLASTOMAS

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Purpose/Objective: Integrated genomics approaches revealed four medulloblastoma subgroups with distinct genetics, transcriptomics, and prognosis. Clinically, Group 3 and Group 4 tumors are frequently metastatic at diagnosis and are associated with an unfavorable prognosis. These tumors exhibit a remarkable clinical and biological intertumoral heterogeneity suggesting subtypes within Group 3 and Group 4. Previous attempts to identify the underlying tumor biology driving these subtypes, and to define prognostic subtypes have been underpowered because of small samples sizes included in earlier genomic studies.
Materials and Methods: To elucidate these subtypes, we performed a high-resolution genome-wide methylation profiling analysis using the Infinium HumanMethylation450 BeadChip in a discovery set of 361 frozen primary Group 3 or Group 4 tumors. Comprehensive genome-wide copy number and gene expression analysis was performed for matching samples. We identified biological subtypes using unsupervised consensus clustering approaches for each of the datasets. Next, we integrated information across platforms using integrative clustering approaches, and delineated key driver genes and pathways. Clinicopathological associations were assessed for each subtype.
Results: Unsupervised consensus clustering analyses of transcriptomic and methylation data identified three distinct subtypes within both Group 3 and Group 4. Subtype-specific distributions of genomic, epigenomic and transcriptional characteristics were elucidated using integrated genomics. Poor prognosis was observed in a Group 3 cluster enriched in LCA histology, and *MYC* amplification. *MYC* status or M stage were not prognostic within this cluster. Group 3 infants defined an intermediate risk group. Intriguingly, a cluster comprising one third of Group 3 tumors comprised patients with a favorable prognosis, who would be considered high-risk based on current molecular outcome prediction models.
Conclusions: Integrated analyses of transcriptomic and genomic alterations delineate distinct subtypes within Group 3 and Group 4. Future research on medulloblastoma and the development of clinical trials should take these subtypes into consideration to improve risk stratification, and to define future avenues for rational, targeted therapy.

O-0051

IKZF1 DELETIONS PREDICT RELAPSE IN BCR-ABL1-POSITIVE CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS WHO WERE TREATED WITH OR WITHOUT IMATINIB

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Purpose/Objective: The *BCR-ABL1*-translocation(Philadelphia-chromosome) predicts for an unfavorable outcome in childhood acute lymphoblastic leukemia(ALL). *BCR-ABL1*-positive ALL frequently carries an *IKZF1* deletion(70%). *IKZF1* deletions are correlated to an unfavorable outcome in *BCR-ABL1*-negative ALL. We studied the prognostic value of *IKZF1* deletions in children with *BCR-ABL1*-positive ALL who were treated with and without Imatinib.
Materials and Methods: The *IKZF1*-status was evaluated by multiplex ligation-dependent probe amplification in 191 newly diagnosed patients; 84 cases were diagnosed before the introduction of Imatinib and 107 cases were enrolled in the European Philadelphia-chromosome positive ALL trial. 63 EsPhALL cases were stratified in the good-risk arm and were randomized for Imatinib, 44 EsPhALL cases were stratified in the poor-risk arm and all received Imatinib.
Results: 66%(126/191) of the *BCR-ABL1*-positive patients had an *IKZF1* deletion; 36.5% of these deletions resulted in haplo-insufficiency(covering mono-allelic loss of at least exon 2), 52.4% had an exon 4-7 deletion(dominant-negative variant). The frequency of hematopoietic stem cell transplantation(HSCT) did not differ between the *IKZF1*-deleted and wild-type group(both ∼70%). In patients that were treated before the introduction of Imatinib, *IKZF1*-deleted patients had a poor 4-yr disease free survival(DFS) (30.0 ± 6.8%) compared to wild-type patients(57.5 ± 9.4%; p = 0.01). IKZF1-deleted patients treated according to the EsPhALL good-risk protocol had a poor 4-yr DFS(51.9 ± 8.8%) compared to wild-type patients(78.6 ± 13.9%; p = 0.03), and this was also evident for those who received Imatinib(4-yr DFS 55.5 ± 9.5% for *IKZF1*-deleted versus 75 · 0 ± 21.7% for *IKZF1* wild-type good-risk patients, p = 0.05).
Conclusions: This is the first study demonstrating that *IKZF1* deletions are correlated to a poor outcome in a relative large cohort of childhood *BCR-ABL1*-positive ALL. We advocate that *IKZF1*-deleted patients need a more intensified or alternative therapy. In addition, since *IKZF1* wild-type *BCR-ABL1*-positive patients treated with Imatinib have a good outcome comparable to *BCR-ABL1*-negative ALL, the absence of an *IKZF1* deletion may be used as marker to exclude HSCT.

O-0052

CHILDREN'S HEPATIC TUMOR INTERNATIONAL COLLABORATION (CHIC): NEW HEPATOBLASTOMA INTERNATIONAL RISK GROUPS (HB-IRG)

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Purpose/Objective: Four major study groups have coordinated clinical research in hepatoblastoma (HB): SIOPEL (International Childhood Liver Tumors Strategy Group), COG (Children's Oncology Group), GPOH (German Association of Pediatric Hematology and Oncology), and JPLT (Japanese Study Group for Pediatric Liver Tumors). Prognostic risk factor analysis by individual study groups has been statistically limited by small patient numbers. To address this challenge Childhood Hepatic tumors International Collaboration (CHIC) set out to create a shared database in order to develop common international risk groups in hepatoblastoma
Materials and Methods: In cooperation with the data management group CINECA, the CHIC steering committee created the International Pediatric Liver Tumors Warehouse, that includes data from all children treated on nine separate trials between 1989 and 2008: 1605 patients. Univariate analysis was used to identify prognostic variables. They were then included in a backwards elimination multivariate analysis to identify those constellations of factors most predictive of outcome.
Results: Univariate analysis identified the following factors, present at diagnosis, that significantly predicted event-free survival (EFS): Pretreatment Extent of Disease (PRETEXT); AFP < 100; AFP 100-1000; metastatic disease; age; macrovascular involvement retrohepatic IVC and/or all three hepatic veins (+V); macrovascular involvement portal bifurcation (+P); contiguous extrahepatic tumor (E); tumor multifocality; and tumor rupture at diagnosis. A hierarchical assessment of these factors led to selection of a prognostic backbone based upon PRETEXT I/II, PRETEXT III, PRETEXT IV, AFP < 100, and metastatic disease. Within each of these backbone groups, patients with the presence or

absence of the remaining risk factors were further stratified into low risk (EFS > 90%), intermediate risk (EFS 70-90%), high risk (EFS 50-70%), and very-high risk (EFS < 50%).
Conclusions: CHIC has created the largest database reported to date for such a rare pediatric tumor. These new Hepatoblastoma International Risk Groups (Hb-IRG) are an important step towards international collaborative study and individualized treatment in HB.

O-0053

EARLY DETECTION AND TRACKING OF PATIENTS MISSING APPOINTMENTS: CONSEQUENCES FOR ADHERENCE AND ABANDONMENT OF TREATMENT

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Purpose/Objective: In El Salvador, the national pediatric cancer program diagnoses 200 new cases every year, and has around a 70% cure rate. Although treatment is available at no cost, abandonment of therapy has been a problem with 13% of cases abandoning yearly during the last decade. In 2011 a protocol was designed to track sporadic absences to the hospital and early detection of possible cases of abandonment.
Materials and Methods: The protocol involved psychologists, social workers, and an educating nurse. Absences to both medical appointments and weekly outpatient treatment were registered daily. Patient information was entered into a Google Drive database, including name and diagnosis, date, type, and reason of absence and status of treatment. A three-category urgency classification was introduced based on status of treatment. ALL patients in induction therapy were to be contacted by telephone within the first 24 hours, all other patients in treatment within 48 hours, and patients off treatment within a week to reschedule an appointment. Patients who showed up at the hospital and whose reason for absence was not obtained during the telephone call were interviewed. If a patient failed to show up within a few days, local health clinics and municipalities were contacted to conduct a search for the patient. Many patients received either transportation or travel expenses from these institutions.
Results: Absences were efficiently registered and families in need of information or economic support were detected and helped. Abandonment rates dropped from 13% to 3%. Institutional costs were reduced in cases in which local institutions were involved. Internal problems in the process of giving appointments and follow up were detected.
Conclusions: There is a link between sporadic absences and abandonment of treatment that needs to be addressed. A multidisciplinary and multi-institutional involvement proved to be successful in reducing abandonment and non adherence.

O-0054

ABANDONMENT HAZARD IS DEPENDENT ON TIME, AGE AND TUMOR TYPE IN CHILDREN WITH CANCER: A REPORT OF VIGICANCER PEDIATRIC CANCER SURVEILLANCE SYSTEM FROM CALI, COLOMBIA.

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Purpose/Objective: Treatment abandonment is a key determinant of cure in children with cancer in developing countries. We describe the variations of abandonment hazard related to time, and other variables in children with cancer in Cali, the third largest city in Colombia.
Materials and Methods: VIGICANCER-Childhood Cancer Outcomes Surveillance System- was established in Cali in 2009. We prospectively enrolled children with a new diagnosis of cancer and collected data from January 2009 to December 2012. Data sources included medical records, pathology reports, direct patient observation, parental interviews and death certificates. Outcomes measured in real-time included cancer relapse, death, secondary tumors and treatment abandonment. Active follow-up was done every 3 months. Instantaneous hazard of abandonment was estimated by time and stratified into different variables. Independent predictors of abandonment were calculated with multivariate Cox's regression analyses.
Results: There were 802 children (≤15 years) included in the analysis and 758 (94.5%) were actively followed-up. Thirty-six month overall survival was 57% (95%CI:52, 62). Globally, 8% (95%CI: 6, 10) of patients abandoned treatment. Abandonment was higher in patients with governmental insurance when compared to private insurance (16% vs 2%), with a hazard ratio of 9.7 (95%CI: 4, 22). Hazards curve for abandonment showed the highest peak (4.2‰) at 18-20 weeks from diagnosis in children < 10 years with Acute Lymphoblastic Leukemia. Patients with age 10-15 years with Acute Myeloid Leukemia showed a steady increasingly hazard with a maximum of 1.5‰ occurring 70-80 weeks. Other types of cancer showed a peak (2.6‰) at 15-29 weeks.
Conclusions: Our findings suggest that interventions aiming to decrease abandonment should be carefully planned to take into consideration patient age, time since diagnosis and tumor type, in addition to other complex social issues. Tailored interventions are urgently needed to be further investigated and implemented.

FREE PAPER SESSION: FREE PAPER SESSION 10 - GERM CELL TUMOURS

O-0055

LONG-TERM FOLLOW-UP IN CHILDREN FOLLOWING TESTICULAR SPARING SURGERY

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Purpose/Objective: Testicular tumors account for 1% to 2% of all pediatric solid tumors, and benign lesions represent a greater percentage of cases in children than in adults. Prepubertal testicular tumors are distinct from those of adults in histologic characteristics, molecular biology and clinical behavior. As most tumors in children tend to be benign, testis sparing surgery for these benign lesions appears an attractive proposition. We took up this study to look at long term safety of this procedure and, as well as to study the effects of this procedure on testicular volume.
Materials and Methods: Children undergoing testis preserving surgery for testicular tumor were prospectively included into the study. All these children were followed up at 3 monthly intervals in the first year, and yearly thereafter following surgery. At follow-up visits the children were questioned regarding pain (orchalgia), appearance of any mass or swelling at the operated site. Physical examination was done in all to rule out abnormalities on palpation. Scrotal ultrasonography was done in all. Testicular size was calculated by using the Lambert formula. An atrophy index for the operated testis was calculated.
Results: During the study period Jan 1999 to Dec 2011, a total of 26 children with a mean age of 4.6 years underwent testicular preserving surgery. None of the children had any recurrences. There was no evidence of testicular dysmorphia, although the affected testis was smaller with a mean atrophy index of 15%. Utrasonography confirmed normal appearing parenchyma with no evidence of previous surgery or recurrent lesions.
Conclusions: Testicular sparing surgery is an attractive option in the management of benign testicular tumors in children. Long term follow-up confirms safety of this technique and also acceptable atrophy index. Children reported satisfaction with cosmetic appearance.

O-0056

EFFECT OF TRANSCATHETER ARTERIAL INFUSION CHEMOTHERAPY COMBINED WITH INTRAVENOUS CHEMOTHERAPY FOR VAGINAL MALIGNANT TUMORS IN CHILDEN: A SINGLE-CENTER EXPERIENCE

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Purpose/Objective: Evaluate the effect of transcatheter arterial infusion chemotherapy (TAIC) combined with intravenous chemotherapy for the treatment of vaginal malignant tumors in children.
Materials and Methods: Between Sept.2002 and Jan. 2013, TAIC was performed on 6 patients aged 3 months to 3 years (median 1.3 years) with vaginal malignant tumors. All of them were confirmed by biopsy pathology. The histopathologic types were endodermal sinus tumor in 3 cases and rhabdomyosarcoma in 3 cases. Neoadjuvant therapy was taken with alternate application of TAIC and intravenous chemotherapy. For TAIC, cisplatin 80mg/m^2, pirarubicin 40mg/m^2, and vindesine 3mg/m^2 were administered intraarticularly via both internal iliac arteries using the Seldinger method. Intravenous chemotherapy used ifosfamide, etoposide, and vindesine 3-4 weeks later. The alternative treatments of TAIC and intravenous chemotherapy were repeated for 2 to 4 courses. Then changed to two sets of alternating intravenous chemotherapy using carboplatin, pirarubicin, vindesine and ifosfamide, etoposide, vindesine.
Results: No drug-induced complications such as cardiotoxicity, nephrotoxicity or hepatic dysfunction were observed except for moderate bone marrow suppression. Partial resection of the vaginal tumors were performed in 2 cases. Four cases were only vaginal tumor biopsy. Finally, vaginal tumors completely disappeared in all cases. Two patients undergone pelvic surgery and radiation therapy due to accompanied by pelvic tumor infiltration.
All patients were followed up to January 2013 with the follow-up time of 10 months to 122 months (median 54 months). One patient was found right inguinal lymph nodes and bladder wall metastasis 46 months later. After inguinal lymph node dissection, partial cystectomy and radiation therapy, the patient has survival. The remaining five patients were so far free survival.
Conclusions: Transcatheter arterial infusion chemotherapy combined with intravenous chemotherapy for the treatment of vaginal malignant tumors in children is safe and highly effective. It can avoid extended radical hysterectomy and improve the prognosis.

O-0057

CLINOCIPATHOLOGICAL PROFILE OF PEDIATRIC AND ADOLESCENT GYNECOLOGICAL MALIGNANCIES AND ITS OUTCOME: A TEN YEAR EXPERIENCES IN A NATIONAL CANCER CENTER OF NEPAL.

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Purpose/Objective: To study the clinicopathological profile and treatment outcome of gynecological malignancies among pediatric and adolescent group seeking treatment at B.P. Koirala Memorial Cancer Hospital (BPKMCH), Nepal.
Materials and Methods: Descriptive study was done at BPKMCH Nepal. All available case records of pediatric and adolescent females diagnosed to have gynecological malignancies from 2002 to 2011 were collected and analyzed in term of age, presenting symptoms,type, treatment modalities and outcome.
Results: Total 60 females were eligible for the study. There were five patients (8.3%) below 5 years, 14 (23.3%) between 6-12 years and 41 (68.4%) patients between 13-19 years. Gynecological malignancies observed among the study group were: ovarian cancer in 46 (76.66%), gestational trophoblastic disease(GTD) in 11 (18.33%), uterine cancer in two (3.33%) and vaginal cancer in one (1.66%). Among the ovarian cancers, 42 had malignant germ cell cancer (91.3%), three had epithelial ovarian cancer (6.5%) and one had juvenile granulosa cell tumor. Commonest presentation was abdominal distension and pain in 70%. Onset of symptoms ranged from 3 days to 730 days (mean 95 days). Disease stage at presentation was early stage 18 (30%) and advanced disseminated disease 42 (70%). In treatment modalities, 8 (13.33%) underwent fertility sparing surgery only, 21(35%) underwent chemotherapy only and 31(51.66%) underwent multimodality treatment. There were 20 (33.33%) dropped out and 40 (66.66%) received recommended treatment among which progressive disease and mortality was recorded in seven (17.5%) patients and 33(82.5%) attended cure.
Conclusions: Malignant germ cell cancer is the commonest gynecologic malignancy among pediatric and adolescent females. In country where childhood marriage is still prevalent, GTD is also more common among adolescent females. Early presentation and prompt appropriate treatment would offer chances of cure even with preservation of fertility.

O-0058

CURRENT OUTCOMES OF BENIGN AND MALIGNANT GERM CELL TUMOURS (GCT) IN INDIA: RESULTS OF A SYSTEMATIC REVIEW

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Purpose/Objective: The outcome of children with cancer in India is inferior to resource-rich nations. Little is known about the outcome of children with GCT and their subtypes in India. Hence this study was conducted to assess the current outcomes of childhood GCT in India.
Materials and Methods: A comprehensive search of MEDLINE, EMBASE, SCOPUS and Web of Science was conducted to identify studies published from year 2000 onwards. SIOP (2000-2012), ASCO (2000-2012) and PEDICON (2007-2012) annual meeting abstracts were hand-searched. Separate analysis was done for malignant GCT and mature/immature teratomas.
Results: Eighteen studies (11 published and 7 abstracts) were selected from 1319 unique studies including one population-based cancer registry (PBCR) report and 17 cohorts/case-series from 10 centers in 8 cities with a total of 607 patients.
Malignant GCTs (10 studies, n = 447) - More than 50% were gonadal and of advanced stage (stage III/IV). Treatment consisted of surgery (upfront or in between chemotherapy) and 4-6 cycles of chemotherapy (bleomycin, etoposide, cisplatin) in most cases. The 5-year overall survival was 38% (n = 45) in the single PBCR report. The overall survival (OS) and event-free survival (EFS) ranged from 36-96% (median 87%) and 14-95% (median 65%) respectively with variable follow-up. Mortality, progression/relapse rates and treatment abandonment rates were 1-64% (median 12%), 0-35% (median 13%) and 0-50% (median 27%) respectively.
Mature/Immature Teratomas (9 studies, n = 157) - 83% were extragonadal and treatment included surgical resection and follow-up with clinical/radiological/tumour marker monitoring. OS and EFS ranged from 86-100% (median 100%) and 89-100% (median 100%) respectively.
Conclusions: Outcomes of malignant GCTs vary across India and are generally inferior to that reported from resource-rich nations. As treatment strategies were similar and the differences in outcomes may be related to disease biology, patient or centre-related characteristics.

FREE PAPER SESSION: FREE PAPER SESSION 11 - LIVER TUMOURS

O-0059

GENOME-WIDE COMPARATIVE STUDY OF DNA COPY NUMBER ALTERATIONS IN HEPATOBLASTOMA AND HEPATOCELLULAR CARCINOMA

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Purpose/Objective: Pediatric tumors are often characterized by a few but highly significant genomics changes compared to the many genomic alterations observed in adult carcinomas. As part of an on-going study of chromosomal aberrations in hepatoblastoma, we undertook an analysis by oligonucleotide array comparative genomic hybridization (oaCGH) in a large series of hepatoblastoma tumors between 2005 and 2012.
Materials and Methods: A total of 196 hepatoblastoma tumors were studied by oaCGH. Data was analyzed using a segmentation algorithm by Nexus Copy Number (v6). Selected samples were also analyzed by fine-tiling microarrays for regions with frequent copy number alteration in hepatoblastoma. In addition, four of the tumors analyzed also underwent whole exome sequence analysis.
Results: We observe high frequency alterations (+/− 0.2 fold) in chromosome 1p (loss), 1q (gain), whole chromosome 2 gain, lose of distal chr4, loss of focal region near centromere of chr9, and whole chromosome gains of chromosome 8, 17, and 20. Comparing to published copy number data on adult hepatocellular carcinoma (HCC), we observe a common the gain/loss trend in chr1, 4, and 20, although with much higher frequency in HCC (Chr1q gain: HB: ∼40%, HCC: ∼70%; Chr4 loss, HB: distal ∼10%, HCC: q-arm ∼60%; Chr8, HB: whole chromosome ∼10%, HCC: q-arm ∼60%). Absent from hepatoblastoma compared to HCC are characteristics HCC copy number alterations such as gains on chr6p, 17p and losses on 8p, 13, 16, and 17q. Comparisons also revealed that the majority of chromosomes were characterized by segmental changes in HCC, while HB tumors has characteristically dominant whole chromosomal changes with a much lower frequency of segmental copy number alteration as compared to HCC.
Conclusions: Hepatoblastoma is marked by recurring whole chromosomal changes, some of which are shared with hepatocellular carcinoma, however the spectrum and number of copy number changes is low in HB compared to HCC.

O-0060

FURTHER STUDY: IDENTIFICATION OF NEW CANDIDATE GENES IN PROGRESSION OF HEPATOBLASTOMA USING GENOME-WIDE ASSOCIATION STUDY

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Purpose/Objective: Hepatoblastoma (HBL), the most common pediatric liver cancer, demonstrates various grade malignancies, from pure fetal type to small cell undifferentiated type. To identify useful molecular markers for hepatoblastoma biology, we examined genome-wide aberrations and expression in samples using microarray in JPLT2 hepatoblastoma cases.
Materials and Methods: In 109 out of 331 HBL cases registered in JPLT-2, normal and tumor DNA was analyzed by Affymetrix SNP 6.0 array. Of these cases, 34 were also analyzed by gene expression array. This microarray data was analyzed using several software programs (GeneSpring, Partek, IPA). According to PRETEXT classification, 12 were classified as I, 33 as II, 41 as III and 24 as IV tumors. Distant metastasis was detected in 35 cases. Of those, 13 cases whose tumors proved fatal were defined as unfavorable cases.
Results: Using the data of SNP array, comparison of gene aberrations in favorable and unfavorable cases revealed variation in cell signaling, molecular transport, cell morphology, cell death and survival, DNA replication, and cancer pathways. Interestingly, the core of cell signaling may be the GPCR gene located at 1q32. The core genes involved in cell death and survival signaling were the ATM and XRCC genes located at 11q and 2q, respectively. These chromosomes had already been identified as highly aberrant loci in HBL. Expression analysis revealed high activity in the genes located lower down in these pathways in unfavorable tumors.
Conclusions: SNP array analysis revealed the main activated pathway caused by chromosomal aberrations in hepatoblastoma. Aberrations of gene dosage may regulate the expression of genes and correlate to tumorigenesis and progression of HBLs. Further analysis of genome aberration provided important candidates for indicators for risk assessment and of therapeutic targets for HBLs.

O-0061

GENOME-WIDE ANALYSIS OF LONG NONCODING RNA EXPRESSION IN HEPATOBLASTOMA

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Purpose/Objective: In recent years, long noncoding RNAs (lncRNAs) have been shown to have critical regulatory roles in cancer biology. However, the contributions of lncRNAs to hepatoblastoma remain largely unknown. The aim of this study was to reveal potential lncRNA regulatory mechanism in hepatoblastoma.
Materials and Methods: Liver samples were obtained from hepatoblastoma patients and paired peritumoral tissues. The genome-wide analysis of lncRNA expression in hepatoblastoma and paired peritumoral tissues was completed by microarray assay and validated by quantitative real-time reverse transcriptase polymerase chain reaction (real-time qRT-PCR) analysis. Differentially expressed lncRNAs and mRNAs were identified through fold-change filtering. Gene ontology analysis and pathway analysis were performed with the standard enrichment computation method. The relationship between lncRNAs and adjacent protein-coding genes was determined by complex transcriptional loci analysis.
Results: We identified thousands of lncRNAs and mRNA that were differentially expressed in hepatoblastoma patients. Some lncRNAs are transcribed in complex loci with overlapping and antisense patterns relative to adjacent protein-coding genes. Differential expression of endothelial cell-specific molecule 1 (ESM1) and TCONS_00014512 (ESM1-ncRNA) was confirmed by real-time qRT-PCR.
Conclusions: Some lncRNAs and their associated protein-coding genes are closely related and may be part of a potential regulatory mechanism of hepatoblastoma, and lncRNAs will provide additional opportunities to advance our understanding of the basic biology of hepatoblastoma.

O-0062

IDENTIFICATION OF SOMATIC AND GERMLINE MUTATIONS USING WHOLE EXOME SEQUENCING OF HEPATOBLASTOMA

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Purpose/Objective: Hepatoblastoma (HB) is a rare and rapidly progressive childhood malignancy. If confined to the liver, HB can be cured by radical surgical resection and chemotherapy, but still approximately 20% of HBs remain unresectable with a poor prognosis. It is mainly affecting young children in the first 4 years of life, underscoring the unique sensitivity of the immature liver to tumorigenesis. The unique age range affected by this embryonal tumor suggests that developmental factors contribute to the tumor development; however, the exact mechanism by which normal hepatic developmental processes are altered by mutational events is an area of current research and the definitive contribution to tumorigenesis is unclear.
Materials and Methods: To explore the gene mutations underlying the pathogenesis of HB, the coding regions in the HB genome were captured, and whole-exome sequencing using Illumina HiSeq 2000 was employed for the identification of single-nucleotide variants and small insertions and deletions in the 10 primary HB tumors. Reads were aligned to the human reference genome and sequencing data was analyzed by Genomon-exome. All the candidates for somatic and germline mutations were validated by Sanger sequencing.
Results: With a mean coverage of 121.2, 95.8% of the target sequences were analyzed at more than x20 depth on average. The somatic mutation rate was 20 (range of 2-76) per tumor with median of 0.5 non-silent mutations per megabase. Overall, HBs have low mutation rates consistent with other pediatric solid tumors. In our cohort, recurrent somatic mutations with high frequency was not detected, but overlapping germline mutations in Wnt signaling pathway were found, even if they were not affected with familial adenomatous polyposis (FAP)
Conclusions: This study disclosed comprehensive genetic features of HB and identified potentially important therapeutic targets, as well as insight into possible cancer predisposition genes.

FREE PAPER SESSION: FREE PAPER SESSION 12 - RARE TUMOURS II

O-0063

THE GENETIC LANDSCAPE OF PLEUROPULMONARY BLASTOMA

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Purpose/Objective: Pleuropulmonary blastoma (PPB) is a rare type of pediatric lung tumor and has highly aggressive clinical behaviors. Recently, germline mutations of *DICER1* were reported frequently in familial PPB and also in non-familial PPB. However, other genetic changes have been poorly studied. Thus, to elucidate the genetic alterations underlying the pathogenesis of PPB, we applied to genome-wide approach to a series of PBB.
Materials and Methods: Sanger sequencing for *DICER1* screening and 250K SNP array analysis were performed in 11 non-familial PPB. Exome sequencing was performed in 3 cases which primary/relapsed tumors and normal pairs were available. In addition, deep sequencing was performed for validation of candidate genes.
Results: Sanger sequencing revealed recurrent *DICER1* mutations in 10 of 11 cases. Notably, frequent compound heterozygous mutations and two homozygous mutations of *DICER1* were observed in our series, and subsequent SNP array analysis disclosed loss of heterozygosity of 14q lesion harboring *DICER1* in the cases with homozygous mutations. Of note, two recurrent somatic mutations in a Wnt signal-related gene and a receptor gene for adrenomedullin were detected by exome sequencing. These mutations shared in the tumors with and without *DICER1* mutations, suggesting that these genes contribute to pathogenesis of PBB independently *DICER1* pathway. In SNP array analysis, recurrent amplification of 19q lesion including 5 candidate genes was detected. Among these, we found overexpression of *PDCD2L* gene, negative regulator of TNF-α, in the cases with 19q amplification, indicating that *PDCD2L* might be a candidate target for PPB.
Conclusions: Most non-familial PPB analyzed in this study harbored *DICER1* mutations, confirming that *DICER1* is a diver gene not only in familial PPB but also in sporadic PPB. Across the genome-wide approach, we found recurrent gene mutations and amplifications in our cohort, suggests that these genes could be additional novel gene targets involved in PPB development.

O-0064

PROGNOSTIC FACTORS FOR PLEUROPULMONARY BLASTOMA: AN ANALYSIS FROM THE EXPERT (EUROPEAN COOPERATIVE STUDY ON PEDIATRIC RARE TUMORS) GROUP

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Purpose/Objective: Pleuropulmonary Blastoma (PPB) is an aggressive embryonal malignancy believed to arise from pleuropulmonary mesenchyme and presenting in early childhood. To improve our knowledge of this tumor EXPeRT analyzed their shared data set.
Materials and Methods: Patients aged 0-17 yrs with a histologically confirmed PPB and registered up to 2008 in national databases in Italy, France, United Kingdom and Poland, were included in this analysis. All lesions were classified as type I, II and II according to the Dehner classification.
Results: the analysis included 65 patients (13 type I, 24 type II and 28 type III). Most tumors were large (91% >5 cm), and invasive extending to pleura (29) mediastinum (10), major vessels (4) or pericardium (3). Nodal involvement was present in 2 children and metastasis in 3. Median follow up was 5 (0.6-22) years.

For type I, 5-yrs PFS was 83.3% and OS 91.7%: 6 patients did not receive any further treatment after surgery but 2 relapsed.

All type II/III PPB received chemotherapy (CT): 20 patients according to the CEVAIE regimen, 14 VAIA, 7 IVA, 6 IVADo, and 5 other regimens. The 5-year PFS was 69.5% (42.7-85.6) and 49.5% (30.1-66.3) for patients with type II and III PPB, respectively.

With univariate analysis, favorable prognostic factors for PFS were complete tumor resection at diagnosis ($p = 0.008$) and non invasiveness ($p = 0.02$). Restricting the analysis to type II/III tumors CT emerged as a significant factor: patients receiving a doxorubicin-containing regimen (VAIA or IVADo) had a superior outcome with a 5-year PFS of 70%.
Conclusions: Type I PPB demonstrate a good outcome, some of whom have received CT. Doxorubicin containing CT regimens seems to be important for type II/III PPB. These results will inform the EXPeRT group's treatment guidelines for PPB.

O-0065

CLINICAL SIGNIFICANCE OF DNA REPAIR GENES EXPRESSIONS IN NEUROFIBROMATOSIS TYPE 1 CASES

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Purpose/Objective: Neurofibromatosis Type 1 (NF1) is a a common autosomal dominant genetic disorder that has a variable phenotype. DNA repair genes are responsible for proofreading the missing in the DNA. We aimed to analyze expression of DNA repair genes and their clinical significance in NF1 patients; comparing exsistance of neurofibroma or hamartomatous lesions or other tumours or existance of NF1 in the family.
Materials and Methods: This study included 46 cases. 36 NF1 patients (30 children; 6 parents), 8 control, two cases with rhabdomyosarcoma without NF1. 17 of them are female, and 19 are male. The mean age is 10 for children and 40 for parents. Among 36 patients, 17 had neurofibromas, 17 had hamartomatous lesions. Rhabdomyosarcoma was observed in one patient, breast cancer in one patient and four patients suffered optic glioma.After RNA isolation from mononuclear cells and cDNA converting, expressions of 84 genes related with DNA Repair were determined by Real-Time PCR. Fold changes and p values comparing groups were evaluated.
Results: In NF1 cases PNKP, RAD18, XAB2, XRCC3, XRCC4 and XRCC5 genes were downregulated compared with control group. In NF1 cases having neurofibromas, POLB was overexpressed; while ERCC3,LIG1,MGMT, MRE11A, MPG, MSH6, PARP2, PRKDC, RAD51B, RAD52, RPA3, SMUG1, TREX1, UNG were downregulated compared with the NF1 cases without neurofibromas ($p < 0.05$, T test). RAD18 is the downregulated and statistical significant gene for existance of NF1 in the family. There are gene expression fold change differences when malign tumor cases with/without NF1 were compared. DDB2, MGMT, MLH1, POLB UNG, XPA are overexpressed. Six genes (DDB2, MGMT, MLH1, POLB, UNG, XPA) are overexpressed in rhabdomyosarcoma (RMS) case with NF1 compared with RMS cases without NF1.
Conclusions: Our results may point toward a role of gene expression changes of DNA repair system to be predictive for clinical manifestations in NF1 cases.

O-0066

PROTONTHERAPY (PT) IN PEDIATRIC SKULL BASE AND CERVICAL CANAL CHORDOMAS. LONG TERM OUTCOME OF THE ORSAY SERIES.

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Purpose/Objective: Skull base chordomas are challenging tumors requiring resection, followed by high doses radiation. Successful series report the use of protons, although remain controversies on optimal doses, and long-term outcome, esp. in children.
Materials and Methods: Between 1995 and 2010, 34 children were managed using proton/photon (29) or proton alone (5) radiotherapy (RT) following single (11) or multiple (23) surgical resections. Mean age at diagnosis was 12 years, and at RT, 13.5 (6-17). M/F sex ratio was 1.4. Most common presenting symptoms were headaches, and diplopia. At the time of radiation, 33 had a gross residue. Anatomical sites involved were the clival area (19), cervical spine (2), or both (13). A stereotactic (fiducial-based) approach was syst*matic to spare: brain stem (9), cervical cord (8), optic pathway (5), and/or pituitary (1). Mean total dose was 70 CGE (CGE = Physical dose X RBE of 1.1), fractionated. 29/34 children received a combination of high energy photons (med: 34Gy), and protons (mean: 36 CGE), and five exclusive protons.
Results: With a mid 52 months follow-up, 7/34 children failed locally, and 1/34 both locally and distantly. Mean time to progression was 2.5 years (max: 10). Most failing children had an initial cervical extension (87.5 vs 23%). An effective salvage program could be performed in 5/7. 7-year OS and DFS were 76 and 93% respectively. Acute toxicity was recorded in most patients (31), but with no G 3 or 4. It included dermatitis, mucositis, and hydrocephalus. Likewise long-term side-effects were recorded in half cases, with only 1 visual, 2 auditory, and 2 hormonal > G2.
Conclusions: Our experience confirms the excellent outcome of high dose PT in young chordoma-patients beyond 5 years. A dose of approx. 70 CGE, conventionally fractionated, seems appropriate. Follow-up extended to 10 years or more is warranted to detect delayed local failures, and long term sequelae.

FREE PAPER SESSION: FREE PAPER SESSION 13 - BRAIN TUMOURS II

O-0067

WEEKLY VINBLASTINE IN CHEMOTHERAPY NAÏVE CHILDREN WITH UNRESECTABLE OR PROGRESSIVE LOW GRADE GLIOMA: A CANADIAN COOPERATIVE STUDY

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Purpose/Objective: Background: vinblastine has shown promising activity in a phase II study in children with recurrent/refractory low grade glioma. The aim of this study was to assess the activity of vinblastine in chemotherapy naïve children.
Materials and Methods: Methods: Patients < 18 years old with unresectable or progressive low grade glioma were eligible if they had not received any previous treatment with chemotherapy or radiation. Vinblastine was administered weekly at a dose of 6 mg/m^2 over a period of 70 weeks. Patients who showed progression or on 2 consecutive imaging studies or evidence of clinical progression were off study.
Results: Results: 54 patients (24 female) were enrolled between 2007 and 2010. Mean age at inclusion was 8.4 years. 27 had chiasmatic/hypothalamic tumours, 6 had evidence of dissemination. 13 had neurofibromatosis type 1. Histology was Pilocytic astrocytoma (25), Pilomyxoid astrocytoma (4), low grade astrocytoma variant (7), gangliogliomas (1). 17 patients had no histological diagnosis. Treatment was well tolerated. However, only 14 patients received the full dose for the duration of the study. The most common toxicity was haematological with 40 patients who experienced grade 3+ neutropenia. There were only 6 episodes of febrile neutropenia and 3 RBC tranfusions. No patient died of treatment related toxicity. Best response to chemotherapy was assessed centrally by an independent radiologist: There were 1 CR, 3 MR, 10 PR, 28 SD, 12 PD, for a response rate of 24.5%. Progression free survival at 2 years was 72.1% (CI: 58.1-82.2). On patient with disseminated disease died of uncontrolled progression despite multiple lines of treatment.
Conclusions: Conclusion: Weekly vinblastine is well tolerated in paediatric patients with low grade glioma. Although the response rate appears inferior to other common LGG regimens, the progression free survival at 2 years favourably compares to most currently used regimens.
Supported by a grant from the Ontario Institute Cancer Research

O-0068

A PROSPECTIVE MULTI-INSTITUTIONAL PHASE II STUDY OF EVEROLIMUS (RAD001), AN MTOR INHIBITOR, IN PEDIATRIC PATIENTS WITH RECURRENT OR PROGRESSIVE LOW-GRADE GLIOMA. A POETIC CONSORTIUM TRIAL

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Purpose/Objective: The ras/raf signaling pathway is crucial in the development of pediatric low-grade gliomas. Aberrant ras/raf signaling is involved in tumorigenesis through promotion of cell proliferation, survival, and differentiation in sporadic LGG. Everolimus (RAD001) is a potent and selective inhibitor of mTOR, a downstream element of the ras/raf pathway. The activity, safety and pharmacokinetics of everolimus in pediatric patients with radiographic recurrent/progressive low-grade glioma are presented.
Materials and Methods: Pediatric patients with radiographic progressive or recurrent low-grade gliomas without neurofibromatosis type I were treated with oral everolimus 5mg/m^2/day once daily. Therapy was provided for 28 days (one cycle) and could be repeated for a total of 12 cycles. Response, as determined by standard 2-D MRI criteria was assessed for all patients. Pharmacogenetics, preliminary correlations of response with changes in pharmacodynamic parameters including p70s6 kinase activity as well as the toxicity profile and phamrmacokinetics of everolimus were also evaluated.
Results: Twenty-three patients with a median age of 9 years (range, 3*17 years) were enrolled, all of whom had received prior chemotherapy (average # regimens = 2.7) including progression after a carboplatin-containing regimen. Median number of cycles of therapy were 10 (range, 1-12). Responses were determined by blinded central review and included 4 patients with PR (>50% decrease) and 13 with stable disease (neither progressive disease (>25% increase) nor partial response (50% decrease). Six patients had progressive disease by one year. Overall therapy was well tolerated; two patients discontinued therapy due to mouth sores (n = 1) and withdrawal of consent (n = 1). PK parameters were similar to those previously reported in both adult and pediatric patients for this agent.

Conclusions: Everolimus was well tolerated in pediatric patients with progressive or recurrent low-grade gliomas and demonstrated activity in this patient population. A similar trial of everolimus in NF1 associated low-grade gliomas is currently underway. Incorporation of everolimus into frontline LGG therapy is being proposed.

O-0069

GENE EXPRESSION ANALYSIS OF 163 PEDIATRIC LOW-GRADE GLIOMAS REVEALS THEIR MOLECULAR HETEROGENEITY

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Purpose/Objective: Low-grade gliomas (LGGs) represent the most frequent brain tumors of childhood. Clinically, they constitute a broad and heterogenous group of diseases. Histologic diagnoses are often controversial due to a lack of reproducibility. Recurrent genomic alterations of *BRAF* have recently provided significant insights in the genesis of these tumors. However, little is known about the molecular characteristics associated with their clinical and histological heterogeneity.
The aim of the study was to describe the expression patterns of a large cohort of pediatric LGGs and to compare them to patterns of expression in normal brains.
Materials and Methods: We performed gene expression profiling on 163 paraffin-embedded pediatric and 20 adult LGGs across 6100 selected genes known to be dysregulated in cancer. We applied unsupervised and supervised clustering methods to distinguish molecular features associated with age, location, histologic subtype, and *BRAF* genomic status of the tumors. We also performed multivariate analyses to specify differences associated with each clinical feature, and compared those differences with a large cohort of normal brain samples (BrainSpan database).
Results: NMF (Non-negative Matrix Factorization) clustering distinguished three molecular groups, associated with location, *BRAF* genomic status, and histological subtype. Differences between tumors with these clinical features were confirmed using principal component analysis. Distinct molecular patterns were not detected between *BRAF*-duplicated and wild-type pilocytic astrocytomas. After controlling for tumor location, we found that 75% of the genes differentially expressed between adolescent and adult LGGs were similarly differentially expressed between normal adolescent and adult brains ($p < 0.0001$).
Conclusions: This large cohort of pediatric LGG expression profiles indicates differences associated with location, histologic subtype and *BRAF* genomic status. Most of the molecular differences between adolescent and adult LGGs are reflected in normal brain development, suggesting that normal development from adolescence to adulthood may influence tumor development.

O-0070

IDENTIFICATION OF NEW DRUG TARGETS IN PILOCYTIC ASTROCYTOMA – MORE HITS IN THE MAPK PATHWAY

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Purpose/Objective: Pilocytic astrocytoma (PA), the most common childhood brain tumor, arises throughout the CNS. PAs typically harbor oncogenic alterations of the MAPK/ERK pathway. While most cerebellar tumors show alterations of *BRAF*, a substantial fraction of cases residing outside the cerebellum lack such alterations. Although survival rates are generally excellent, these cases are often not amenable to complete resection, resulting in multiple recurrences and a considerable loss of life quality. Using deep sequencing techniques, we aimed to identify additional genetic lesions in tumors without classical MAPK pathway changes.
Materials and Methods: A total of 90 pairs of PA tumor and matched germline samples were subjected to whole-genome sequencing. This was complemented with RNA sequencing, expression profiling, and array-based DNA methylation profiling for a subset of samples.
Results: As previously seen in PA, a majority of cases showed tandem duplications at the *BRAF* locus leading to oncogenic KIAA1549-BRAF fusion genes. Most interestingly, sequencing analysis allowed us to detect alterations in the MAPK pathway in $>95\%$ of samples (higher than the $\sim$80% reported in most previous studies), including novel fusions with alternative partners (sometimes involving balanced translocations rather than duplications), and recurrent mutations in *PTPN11* and *FGFR1*. The latter are of particular interest since they occurred in two mutational hotspots (i.e., can be easily tested in clinical samples) and comprise a promising drug target, with some anti-FGFR drugs already in the preclinical or clinical pipeline. Perhaps the most striking finding of this extensive cancer sequencing study, however, is the fact that no recurrent mutations were detected outside of the MAPK pathway - further supporting the concept of PA as a prototypic single pathway disease.
Conclusions: In conclusion, our results not only expand the spectrum of MAPK changes observed in PA, but also reveal novel therapeutic targets with readily available drugs in clinically relevant subsets of patients.

O-0071

EGFR ACTIVATION CONFERS RESISTANCE TO MAPK PATHWAY INHIBITORS IN GLIOMA

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Purpose/Objective: Recent discoveries in cancer research have implicated activating alterations in the MAPK pathway, including BRAF-V600E missense mutation, NF1 loss, and KIAA1549:BRAF fusions, in pediatric gliomagenesis. Potent inhibitors of BRAF-V600E and MEK are being used to target this pathway in pre-clinical and clinical studies. Negative feedback loops downstream of MEK have been demonstrated in multiple tumor types, however, and may limit the efficacy of MAPK pathway inhibitors. Here we have sought to investigate the activation and consequences of this feedback loop in treating pediatric gliomas with MAPK pathway inhibitors.
Materials and Methods: Using the BRAF-V600E inhibitor PLX4720, as well as MEK inhibitors AZD-6244 and PD-0325901, we treated BRAF-V600E mutant (AM-38, DBTRG-05MG), NF1-mutant (LN229), and BRAF + NF1- wildtype glioma cell lines and their derivative xenografts, in vitro and in vivo, respectively. Treated and untreated cell lines and xenografts were compared for EGFR activation as well as other pathway signaling changes.
Results: Both BRAF inhibition and MEK inhibition resulted in a dose-dependent increase in EGFR phosphorylation in glioma cell lines and their derivative xenografts. This activation was associated with an increase in AKT activity and may also contribute to MAPK recovery from inhibitor treatment of BRAF-mutant gliomas. Addition of an EGFR kinase inhibitor to either BRAF or MEK inhibitor prevents EGFR/AKT activation, resulting in increased anti-tumor effect against BRAF-V600E cell lines and xenografts.
Conclusions: BRAF or MEK inhibition results in EGFR activation in glioma cell lines with BRAF-V600E mutation. This appears to be a consequence of repressing a negative feedback loop downstream of MEK. Combined EGFR and MEK (or BRAF) inhibition prevents EGFR activation, resulting in improved efficacy from combination treatment, both in vitro and in vivo.

O-0072

IMPACT OF PERSISTENT LATE EFFECTS ON PHYSICAL SELF-IDENTITY IN ADULT SURVIVORS OF CHILDHOOD CNS TUMOURS: POPULATION-BASED OUTCOMES FROM THE SWEDISH LIFE STUDY

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Purpose/Objective: As part of the larger Swedish LIFE research project, this study investigated body-image (BI) and physical self-confidence (PSC) in adult central nervous system (CNS) tumour survivors, and the extent to which illness- and/or treatment related late effects predicted these outcomes which are critical components of mental health and quality of survival.
Materials and Methods: A nation-wide multi-centre cohort of 603 adult survivors, >18 years old, and >5 years from diagnosis date, was studied. The survivors, diagnosed 1982*2001 with a primary CNS tumour before their 19th birthday, were identified through the national childhood cancer registry. Illness- and treatment-related late effects regarding sensation, mobility, and global health status were assessed with the Health Utilities Index2/3^{TM} (HUI2/3). Psychological outcomes were assessed using the Body Image and Sports/Athletics subscales of the multidimensional Self-Esteem Questionnaire (SEQ-42).
Results: Females had significantly poorer BI and PSC than males. Females generally had a negative PSC, while males' PSC was more positive. There was no regular difference between males and females regarding the impact of health/functional status on psychological outcomes. Positive BI was significantly associated with better sensation and global health. PSC was positively related to sensation, mobility, and global health. Only global health predicted PSC in both females and males. In males, also sensation was related to PSC. BI and

PSC were significantly poorer among survivors diagnosed in pre-pubertal age, compared to later diagnosed.
Conclusions: Health and function-related sequelae following childhood CNS tumour diagnosis affect confidence in physical capability and contribute to body image disturbance, with females at heightened risk for both late effects and affected physical self-identity. To minimise cancer-related self-identity disturbance, compensatory measures integrated in psychological follow-up should address patients with apparent illness-related disability, female survivors, and patients diagnosed at young age. Interventions addressing self-identity would sustain long-term mental health in this vulnerable population.

FREE PAPER SESSION: FREE PAPER SESSION 14 - PSYCHOSOCIAL II

O-0073

PARENTING STRATEGIES AND THEIR ASSOCIATION WITH CHILD SLEEP, EATING AND DIFFICULT BEHAVIOUR AMONGST PRE-SCHOOL CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose/Objective: Problems with child sleep, eating and behaviour are markedly affected during cancer treatment. The aim of this study was to examine a) group differences in parenting practices between parents of children with acute lymphoblastic leukaemia (ALL) and parents of healthy controls and b) the association between parenting practices and child sleep, eating and difficult behaviour, amongst parents of children with ALL.
Materials and Methods: A sample of 36 parents of pre-school children in maintenance phase ALL treatment and 21 parents of healthy pre-school children completed a survey that included validated measures of parenting practices, child diet, child sleep difficulties and child behavioural and emotional difficulties.
Results: Parents of children with ALL reported higher use of parental overprotectiveness, spoiling/bribing, emotional feeding, sleep strategies and laxness compared to parents of healthy children. There were no group differences in parental use of positive parenting, parental warmth, inconsistent discipline and use of food as a reward for behaviour. Children with ALL whose parents used emotional feeding (e.g. providing children with food as emotional support when the child is upset) were less likely than children with ALL whose parents did not use emotional feeding to consume a healthy diet. Children with ALL whose parents used sleep strategies to help get them to sleep (e.g. co-sleeping) and lax parenting strategies (e.g. limited boundaries/rules) were more likely than children with ALL whose parents did not use these parenting strategies to experience sleep difficulties and clinical levels of problem behaviour respectively.
Conclusions: Results from this study demonstrate that certain parenting practices are more pronounced amongst families experiencing ALL and these practices are associated with poorer child sleep, diet and behaviour outcomes. These results may inform psychosocial interventions such as parenting interventions or information-based resources, aimed at alleviating child behaviour problems and improving quality of life for children and families.

O-0074

GENERAL ANESTHESIA, CONSCIOUS SEDATION OR NOTHING. WHY THE CHILD CANNOT CHOOSE?

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Purpose/Objective: Children with cancer need repeated painful procedures and can be frightened by different aspects of the experience: pain perception, anaesthesia, separation from caregiver, loss of control. Caregivers and medical providers approach can make an important difference in children's level of anxiety and pain perception. We developed a standardized support modality to prevent children's experience of painful procedures as a repeated trauma.
Materials and Methods: Participants were a consecutive sample of 85 children performing painful procedures, whose caregiver signed the consent. Support was offered by psychologists: before procedures, creating a 'listening time' when children express their needs for reassurance and can choose among general anesthesia, conscious sedation or no anesthesia; during, inducing distraction, relaxation, guided imagery according to children's requests and personality; after, helping children to elaborate the whole experience. Through an assessment tool, we evaluated how pain management technique and caregiver's support influenced on children's experience of the procedure.
Results: During 2012, 247 procedures were monitored. 39.3% of children choose general anesthesia, 26.7% conscious sedation, 2% no anesthesia and 32% could not make a choice because of age, fear or agitation. We observed that children's capacity to be in tune with their needs and become able to make the most adequate choice for reassurance, depended on the caregiver's containment modality and operators respect for their choice. Children experiencing their preference for support to be satisfied become more reassured, collaborative and less anxious.
Conclusions: Support modality that respects child's self-regulation and personality style can prevent repeated trauma and lack of continuity in their identity development. It helps to establish a trusting relationship among children, caregivers and multidisciplinary equip. We also observed that it potentially prevents burnout syndrome facilitating responsibility distribution among the equip operators involved and improves their well-being.

O-0075

DISCREPANCIES IN FERTILITY RISK AND PRESERVATION DISCUSSION COMFORT AMONG PROVIDERS AND FAMILIES WITH ADOLESCENT MALES NEWLY DIAGNOSED WITH CANCER

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Purpose/Objective: The American Academy of Pediatrics recommends that health care providers discuss treatment-related infertility and offer cryopreservation to patients when possible. Several factors may impact these sensitive discussions, including physician (dis)comfort. This study examined differences in providers' reports of their discussion comfort compared to patient and parent perceptions of provider comfort.
Materials and Methods: Information regarding infertility and preservation discussions was collected among 51 health care providers (attending oncologists, nurses, fellows) and at-risk patients/families under their care, as part of a multisite, NIH-funded study investigating sperm banking practices in this group. Participants completed 7-items assessing provider comfort specific to discussions addressing infertility risk and fertility preservation. When multiple adolescent or parent reports were available regarding a specific provider, scores were aggregated within provider. Multivariate analyses of variance were performed to examine provider-adolescent and provider-parent discrepancies on comfort items.
Results: Overall models revealed discrepancies in provider-adolescent and provider-parent reports of provider discussion discomfort ($ps < 0.01$). Post hoc analyses revealed no differences in provider, patient, and parent ratings specific to physician comfort in discussion of infertility risk (3 items). However, when assessing comfort in fertility preservation discussions, providers reported significantly less comfort than was perceived by adolescents and parents (all $ps < 0.05$). Furthermore, providers reported being significantly less comfortable discussing the process of fertility preservation than was reported by adolescents ($p < 0.05$).
Conclusions: Adolescents newly diagnosed with cancer and their parents have discrepant perceptions of providers comfort when discussing fertility preservation, but not infertility risk, with providers rating being lower than that of families ratings. Hypotheses to explain these discrepancies as well as implications for training and professional development will be discussed.

O-0076

WHAT ARE THEY WORRIED ABOUT? THE CONTENT OF EMOTIONAL CONCERNS EXPRESSED AT FOLLOW-UP CONSULTATIONS WITH ADOLESCENTS AFTER CHILDHOOD CANCER: A VIDEO-BASED OBSERVATIONAL STUDY

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Purpose/Objective: Studies based on self-report show that many childhood cancer survivors are concerned about cancer related issues such as recurrence, late effects and secondary cancers. However, little is known to what extent such concerns actually are expressed by survivors during follow-up consultations after cancer treatment. Medical communication research indicates that patients concerns are more often expressed implicitly, rather than explicitly, as subtle hints to underlying emotions.
The present study aimed to explore the content of concerns expressed by adolescents during follow-up consultation after cancer treatment.
Materials and Methods: Consultations between 67 consecutively included adolescents aged 12-20 (mean 16) and their paediatric oncologists (n = 11) were video-recorded during follow-up after treatment from lymphoma, leukaemia and/or allogeneic stem-cell transplant at the paediatric department at Oslo University Hospital in Norway. First, we identified and coded cues and concerns using the Verona Definition of Emotional Sequences. Second, a thematic analysis of these cues and concerns were conducted.
Results: In more than half of the consultations neither cues nor concerns were identified. In total, 99 cues and concerns from 29 consultations were coded. Four main categories were identified in the thematic analysis of cues and concerns: Medical (bodily symptoms, body image, pain, problems with eating or sleeping; 31%), psychological (anxiety, fear, stress, fatigue; 31%), social (family, school, friends; 16%) and explicitly cancer related (recurrence, late effects, coming to the follow-up consultation; 22%).
Conclusions: Despite findings in the literature indicating that many patients worry about cancer related issues, few such concerns were expressed by the patients during the follow-up consultations. This may indicate an underreporting of cancer related concerns in follow-up care with adolescents. Our findings indicate that oncologists should actively elicit potential

emotional concerns in follow-up consultations in order to uncover patients worries and provide adequate support.

O-0077

TELEPHONE AUTOMATED COMPUTER ASSISTED SELF INTERVIEWS (TACASIS) TO ASSESS PSYCHOSOCIAL OUTCOMES OF PEDIATRIC CANCER SURVIVORS: ASSESSING USABILITY AND SURVIVOR PREFERENCE

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Purpose/Objective: TACASI (Telephone Automated Computer Assisted Self Interviews) are an innovative means to collect patient reported outcomes. Advantages may include cost effectiveness, convenience, and increased sense of privacy, but TACASIs have not been widely applied in pediatric cancer populations. Our objective was to evaluate the utility of TACASIs for assessing psychological outcomes in this population.
Materials and Methods: We surveyed 83 young adult (YA) survivors of childhood cancer (age 18-39, median = 21) using both TACASI and paper questionnaires of anxiety and depression. Participants completed paper checklists measures (BSI-18 and PROMIS short forms), and a structured interview (PRIME-MD) by TACASI, followed by a survey asking them to evaluate the two administration methods. In addition, participants were randomized to receive sensitive items about sexuality and suicidality either on paper or by TACASI.
Results: 95% of participants agreed that both TACASI and paper assessments of anxiety and depression were easy to understand and to complete, and 75% of survivors gave them identical ratings. Among those who rated the formats differently however, survivors rated paper measures significantly easier to understand and less frustrating to complete ($p < .05$). Survivors who answered sensitive items by TACASI did not report differences in survey clarity or ease of use compared to those who answered the same items on paper. When asked for an overall preference, survivors strongly prefer paper surveys over TACASI ($p < .001$) for all outcomes measured. Of note, preliminary analysis on 45 survivors indicate those who responded on paper reported more sexual activity than those who responded by TACASI ($p < .05$).
Conclusions: TACASI is an acceptable survey method for YA cancer survivors, but the majority prefer paper surveys when given the choice. Contrary to expectation, survivors may be more likely to report sensitive information on paper surveysÑa finding that will be further analyzed in an expanded cohort of 125 survivors.

O-0078

DIAGNOSTICS OF THE LEVEL OF BURNOUT IN PEDIATRICS HEMATOLOGISTS ONCOLOGISTS

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Purpose/Objective: Emotional burnout is a reaction of the body to continuous professional stress of moderate intensity and it is also an acquired pattern of professional behavior. The purpose of the study was to evaluate the level of burnout in Pediatric Hematologists Oncologists.
Materials and Methods: Eight female physicians ranged in age from 35 to 50 years old with duration of service from 10 to 25 years, were enrolled in the present study. Personality questionnaire designed by V. Boyko (2003) was used. The questionnaire was previously validated in the population of primary care physicians. Three phases of emotional burnout such as tension, resistance, and the phase of exhaustion were diagnosed. The severity of each symptom was assessed on a scale 0 to 30 points.
Results: Dominant symptoms of burnout for each phase were identified and the severity was assessed. Dominant symptoms of the first phase were: the experience of stressful circumstances present in 5 (62.5%) and personal dissatisfaction present in 2 (25%). In 6 (75%) cases predominant symptoms indicated generating tension phase. In one physician the tension phase was already formed.Dominant symptoms of the resistance phase were present in 6 physicians, specifically, inadequate selective emotional reaction in 4 (50%) and emotional thriftiness in 2 (25%). The resistance phase was fully formed in one person (12.5%).Phychosomatic alterations as dominant symptoms of the phase of exhaustion were revealed in one physician (12.5%), and in 2 (25%) physicians as a fully formed symptom. Emotional deficit was present in one physician. Emotional deficit was noted in one case (12.5%). The exhaustion phase was in the process of formation in all physicians.
Conclusions: Therefore, symptoms of the formed phase of tension and forming phase of resistance were present and reflect the level of burnout in physicians Pediatric Hematologists Oncologists.

FREE PAPER SESSION: FREE PAPER SESSION 15 - RENAL AND SARCOMAS I

O-0079

CLEAR CELL SARCOMA OF THE KIDNEY (CCSK) REGISTERED ON SIOP 93-01 AND SIOP 2001 PROTOCOLS: A REPORT OF THE SIOP RENAL TUMOUR STUDY GROUP

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Purpose/Objective: Clear Cell Sarcoma of the Kidney (CCSK) is a rare childhood renal tumour. So far, only a few large and homogeneously treated cohorts have been reported. This study aims to evaluate clinical characteristics and survival of CCSK patients treated according to recent SIOP trials.
Materials and Methods: We analysed the prospectively registered data of all patients with a histological verified and reviewed CCSK, entered onto the SIOP 93-01 and SIOP 2001 trials from 1993 until 2011.
Results: A total of 183 CCSK patients (66% male) were identified, with a median age at diagnosis of 31 months, and a median follow-up time of 6 years. Stage distribution for stage I, II, III and IV was respectively 41%, 24%, 28% and 7%. The most common site of metastasis at diagnosis was the bone (9/13). Pre-operative chemotherapy rather than initial nephrectomy was administered in 88% of the patients. Additional treatment with radiotherapy was applied in 2/75 stage I patients, 33/44 stage II patients, 43/51 stage III patients and 6/13 stage IV patients. Overall 5-year event-free survival and overall survival were respectively 79% (95% CI 73-85) and 86% (95% CI 80-92). Relapses occurred in 28 patients. Most relapses occurred in the brain (n = 13) and the lungs (n = 13). Stage IV was a significant adverse prognostic risk for event-free survival. Factors such as age, gender, tumour volume at diagnosis or at surgery and type of initial treatment were not found to be prognostic for event-free or overall survival.
Conclusions: In this largest European CCSK cohort described so far, overall outcome of CCSK is reasonable, although treatment of patients with advanced-stage disease is still challenging. As further intensification of treatment is hampered by direct and late toxicity, future directions should include biomedical approaches that will lead to the development of targeted therapy based on specific molecular aberrations.

O-0080

OUTCOME OF BLASTEMAL TYPE NEPHROBLASTOMA PATIENTS TREATED ACCORDING TO INTENSIFIED TREATMENT IN THE SIOP 2001 PROTOCOL, A REPORT OF THE SIOP RENAL TUMOUR STUDY GROUP (RTSG)

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Purpose/Objective: From previous pre-surgery chemotherapy based SIOP protocols, blastemal type Wilms tumour(WT-BT) has been identified as a poor prognostic subgroup. Therefore, in the SIOP 2001 protocol, post-operative treatment was prolonged and intensified ((VCR/ActD/Dox) in stage I, (VP16/Carbo/Cyclo/Dox) in stage II, III, IV). Here, we present the characteristics, and outcome analysis of WT-BT patients treated with the intensified regimen.
Materials and Methods: Response and survival analysis of all WT-BT patients treated from 2001-2012 (SIOP-2001 study) were compared with the historical control from SIOP 93-01 (n = 182).
Results: In total, among all nephroblastoma patients (n = 3671) registered in SIOP-2001 282 (8%) were WT-BT patients (44% male). Median age at diagnosis was 43 months (IOR

23-68 months). Pre-operative chemotherapy reduced tumour volume with a median of 276 mL (IQR 117-447 mL). Stages were: I (n = 84, 30%), stage II (n = 67, 24%), III (n = 77, 27%) while 19 patients presented with stage IV (7%) and 33 had bilateral disease (12%).

Univariate analysis showed a 5-year event-free survival(EFS) of localised WT-BT cases of 81%(95% CI: 75-87%) compared to 64% in SIOP 93-01(95% CI: 54-75; p = 0.004) and an overall survival (OS) of 88%(95% CI: 82-93) compared to 80%(95% CI: 72-89; p = 0.13) in SIOP 93-01. Treatment protocol, tumour volume at surgery, age and stage (III vs I/II) were prognostic variables for EFS in the multivariate analysis. Prognosticators for overall survival were age and tumour volume. Patients with metastatic WT-BT (n = 22) showed a similar improvement, with 5-year EFS of 51%(95% CI: 33-78) in SIOP 2001 compared to 20%(95% CI 6-69) in SIOP 93-01 (n = 10), and an OS of 54%(95% CI 36-82) in SIOP 2001 compared to 30%(95% CI 12-77) in SIOP 93-01.

Conclusions: Blastemal type nephroblastoma, uncovered by pre-operative chemotherapy, benefits from more intensive chemotherapy as reflected by the occurrence of less events and better OS.

O-0081

RESULTS OF NEPHRON SPARING SURGERY FOR UNILATERAL WILMS' TUMOR IN WT1 RELATED DISEASE AND OTHER DEVELOPMENTAL ANOMALIES.

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Purpose/Objective: Wilms' tumor is known to occur in various predisposition syndromes such as WT1 related disease but also in patients with uropathy and other developmental anomalies. The anatomy of the lesions encountered, the risk of contralateral tumor development, the potentially associated nephropathy and the overall less aggressive features of WT in this population encouraged nephron-sparing surgery (NSS). We report our experience and try to delineate the criteria allowing performing this approach.

Materials and Methods: The study is a retrospective review of patients with predisposing syndromes who underwent surgery for Wilms' tumor over a period of 14 years in a single institution. Data collected consisted of age and sex of the child, diagnostic and work-up tools, treatment and surgery, follow-up and recurrences.

Results: Thirty out of 137 patients (21%) treated for Wilms' tumor were diagnosed with syndromes or associated malformations. There were three WAGR syndromes, two Denys-Drash syndromes, six isolated hemi hypertrophies, one Leber amaurosis, three uropathies and fifteen other isolated malformations. All received preoperative chemotherapy according to SIOP protocols and were considered as potential candidates for NSS. After preoperative MRI, NSS was finally indicated in 9 patients (30%). After a median follow-up of 4 years (1-11) all patients are alive and free of disease.

Conclusions: This series allowed us to delineate criteria for NSS in this particular population of patients and showed that this approach is safe and effective provided that indications are well set. A more precise identification of this subpopulation of Wilms' tumor should be encouraged at a European level in order to define clear criteria for NSS that can be included in treatment protocols.

O-0082

DOES THE NUMBER OF THE LYMPH NODES INFLUENCE THE OUTCOME OF WILMS' TUMOR PATIENTS; REVIEW OF 204 CASES FROM A SINGLE INSTITUTION?

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Purpose/Objective: Wilms' tumor is the most common pediatric renal tumor with several prognostic factors influencing its survival outcome. Lymph node (LN) involvement is one of the factors and it's been incorporated in pathological staging; however number of LN required to be sampled from renal hilum and paraaortic is not well established. We analyzed the relationship between the number of LN sampled during staging and the survival outcome in patients with Wilm's tumors.

Materials and Methods: After obtaining Institutional Review Board (IRB) approval, we reviewed all Wilm's tumor cases diagnosed at our institution from 1992-2012. The data was analyzed for tumor histology, stage, number of LN sampled, and their metastatic status and survival outcomes.

Results: A total of 204 cases were identified, 187 had favorable histology, 17- anaplasia (unfavorable histology). Stage distribution was as following: I-49, II-47, III-56, IV-38, V-14. Patients with unfavorable histology tend to present with more advanced stage tumor. Number of LNs sampled varied from 0 to 31 (mean 4.4) for the entire group. In the favorable group, the number of sampled LNs ranged from 0-29 (mean of 4.3), while in the unfavorable group they ranged from 0-31 (mean 9.8). There were a total of nine deaths observed, 5 out of 187 (2%) in the favorable histology group, and 4 out of 17 (23%) in the unfavorable histology group. Number of LN sampled for each group did not have any statistically significant correlation with survival outcome. Additionally, our results showed poor correlation between stage, number of positive LN and survival rate, however it confirmed that the histological subtype is the most significant predictor of clinical outcome.

Conclusions: Number of sampled LN in Wilm's tumor appears to have no significant correlation with patient survival. The most predictive factor is the pathological grading of favorable vs. unfavorable.

O-0083

INTRA-OPERATIVE TUMOR SPILL AND OUTCOME OF PATIENTS WITH STAGE II, FAVORABLE HISTOLOGY WILMS TUMOR. A REPORT FROM THE NATIONAL WILMS TUMOR STUDY GROUP

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Purpose/Objective: Intra-operative tumor spill has been reported to increase the risk of local recurrence among children with Wilms tumor. Previous reports were based on institutional acceptance of review tumor stage which may differ from stage based on central review.

Materials and Methods: Surgical checklists, operative notes, institutional pathology reports, central pathology review and flow sheets of 602 patients registered between August 1986 and September 1994 on National Wilms Tumor Study * 4 as randomized, followed or switched and coded as Final Stage II/favorable histology (FH) following central pathology review were reviewed by GJD, MHM or AEE. All were reviewed by DMG, who was blinded to the results of the other reviews. Relapse-free (RFS) and overall (OS) survival were estimated using the Kaplan-Meier method. Hazard ratios (HRs) were estimated using the Cox model and tested for statistical significance by the log-rank test.

Results: 499 patients were found after review to have stage II/FH Wilms tumor. The eight-year RFS percentages were 85.0% (95% confidence interval (CI) * 81.1%, 88.1%) for those with no spill compared to 75.7% (65.8%, 83.2%) for those with spill. The eight-year OS percentages were 95.6% (93.1%, 97.3%) for those with no spill compared to 90.3% (82.2%, 94.9%) for those with spill. 23 relapses were observed among patients with spill compared to 16.3 expected (HR = 1.55 (95%CI * 0.97,2.51), p = 0.067). 10 deaths were observed compared to 6.1 expected (HR = 1.94 (0.92,4.09), p = 0.077).

Conclusions: Among patients with stage II/FH Wilms tumor, RFS and OS were lower in those who had intra-operative tumor spill, but confidence intervals for the corresponding HRs included the null value of 1.0. Augmenting therapy for these patients with doxorubicin or flank irradiation, with their potential adverse late effects, in attempts to improve RFS and OS must be balanced against the relatively good outcomes after two drug chemotherapy without irradiation.

O-0084

GENETIC AND PATHOLOGICAL ANALYSES OF BILATERAL OR FAMILIAL WILMS TUMORS INDICATE THE INHERITANCE MODE OF WT1 GERMLINE MUTATION AND RESPONSE TO CHEMOTHERAPY

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Purpose/Objective: To identify the incidence of *WT1* abnormality, the mode of inheritance of *WT1* germline mutation, and pathological features in Japanese bilateral or familial Wilms tumors (FWT or BWT)

Materials and Methods: We studied *WT1* abnormality in 26 patients with BWT, and 3 infants with familial unilateral WT (UWT). DNA was sequenced for *WT1*, and deletion was detected by SNP array or PLPA analysis. Pathological studies were performed on 28 tumors with *WT1* abnormality, and 4 with normal *WT1*.

Results: *WT1* abnormality was found in 28 (88%) of 32 bilateral or familial tumors, or 22 (85%) of the 26 BWT patients. The most mutations resulted in truncated WT1 protein. Two twin-infants and their father without the past history of WT and an infant with the father having the past history of WT had R390X in exon 9, indicating that the mutation was inherited from their father. Another two twin-infants had Y48X in exon 1 and uniparental disomy of the paternal allele in tumors, while their parents had normal *WT1* sequences,

indicating that the mutation occurred de novo. Of the 28 tumors with *WT1* abnormality, 13 had the stromal predominant type, and 8 had the triphasic type. None of 4 tumors with normal *WT1* had the stromal predominant type. None of the tumors showed anaplasia.
Conclusions: The present study showed the great majority of Japanese bilateral and familial WTs had *WT1* germline mutation. *WT1* mutation found in BWT or FWT was inherited from the father or developed de novo in the father's germ cell. One half of WTs with germline *WT1* mutation had the stromal predominant type that is known to show favorable outcome but poor response to chemotherapy. When *WT1* mutation was found in tumor cells, peripheral blood of patients and parents are required to determine the possible inheritance of the mutation.

FREE PAPER SESSION: FREE PAPER SESSION 16 - NEUROBLASTOMA II

O-0085

RISK CLASSIFICATION OF NEUROBLASTOMA BASED ON GENOMIC PROFILES: FOR FUTURE TAILOR-MADE THERAPEUTIC STRATEGIES IN JAPAN

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Purpose/Objective: Neuroblastomas (NBs) exhibit wide ranges of clinical behavior. We previously proposed the tumor risk classification of NB based on the genomic profiling. It uses three genomic groups (GGs) of copy number aberrations in NB: silent (S), partial (P) and whole (W). Each GG was further segregated into subgroups with different prognostic risk clearly defined by *MYCN* amplification (*MYCN*-amp), 1p loss, 11q loss and 17q gain. In this study, we conducted the clinical validation of our GG risk classification combined with the *ALK* genomic aberrations.
Materials and Methods: Array CGH (44k array) and mutation analysis of *ALK* gene of 343 sporadic NB (sent to Chiba Cancer Center from 1995 to 2007; stage 1: 48; stage 2: 29; stage 4s: 27; stage 3: 60; stage 4: 179) were performed and the clinical impact of the genomic signatures was assessed by using the outcome information of the patients.

In the analysis of 343 NBs, GG-P or GG-S with *MYCN*-amp exhibited very poor prognosis, however, only GG-Pa with 1p loss (P1a) showed intermediate risk (8-year survival rates: 33% in P1a vs. 0% in the other rest, $p = 0.07$). *ALK* gene mutations and amplification were found in 16 (4.7%) and 5 tumors (1.5%) in our dataset, respectively, whose distribution among the GGs was nonrandom: Those were frequently found in P1a, GG-Ps with 11q loss (P3s) and GG-Ws. *ALK* abnormalities also cause the patients' outcome worse ($p = 0.0061$), especially in those with *MYCN*-amp ($p = 0.16$) as well as in P3s (p
Conclusions: These results suggested that the genomic signatures efficiently predict the prognosis of the patient with NB and are useful for the quality control of the clinical studies.

O-0086

A GENE SIGNATURE PREDICTS THE CLINICAL OUTCOME IN STAGE 4 NEUROBLASTOMA ACROSS INDEPENDENT DATA SETS

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Purpose/Objective: Most of the neuroblastoma (NB) gene classifiers are built on heterogeneous patients without differentiating among INSS stage and other clinical and genetic markers. We created a robust and reproducible gene predictor of clinical outcome restricted to stage 4 NB patients using microarray and quantitative Real Time (qRT)-PCR based on different and innovative strategy.
Materials and Methods: We developed and validated a specific-stage 4 signature using genes included in three published signatures (Oberthuer et al., 2006, Asgharzadeh et al., 2006, Vermeulen et al., 2009), and gathered by Medline search and by reanalysis of public microarray data from retinoic acid-treated NB cells (GSE9169). Four hundred genes were selected for further analyses. To find the optimal combination of genes able to predict survival, Cox regression and area-under-the curve (AUC) analyses were performed in two independent microarray datasets (GSE2446 and R2: microarray analysis and visualization platform (http://r2.amc.nl)) composed of 102 and 40 patients with stage 4 NB, respectively.
Results: A 20-gene signature, including genes only from the published signatures and Medline search, resulted to be an independent predictor of survival. The survival prediction ability of this signature was validated in four microarray datasets of stage 4 NB (Kaplan Meier; $P = 9.1 \times 10^{-17}$, $P = 2.0 \times 10^{-3}$, $P = 1.0 \times 10^{-4}$, $P = 6.5 \times 10^{-10}$). Finally, in the same datasets, the 20-gene signature increased the prediction value of the well-known clinical markers such as age and *MYCN* status (increase of AUC = 6.1%, 12.9%, 10%). qRT-PCR of 43 additional samples confirmed the survival prediction of 20-gene signature.
Conclusions: We have generated a reliable 20-gene predictor signature that significantly predicts, survival in patients with stage 4 NB. Since the risk evaluation of patients at stage 4 is still elusive, the 20-gene signature discovered by us will be useful fir the appropriate therapy of this group of patients.

O-0087

GENOME-WIDE DNA METHYLATION ANALYSIS IDENTIFIES DISTINCT EPIGENETIC RISK GROUPS IN NEUROBLASTOMA

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Purpose/Objective: In recent years, there was emerging evidence that epigenetic alterations including DNA methylation play an essential role in the development and progression of various cancers. In neuroblastoma, the most common extracranial solid tumor in infancy and childhood, this was underlined by the identification of the CpG island methylator phenotype (CIMP), which is closely associated with unfavorable prognosis.
Materials and Methods: To further dissect the role of DNA methylation in neuroblastoma pathogenesis, global DNA methylation profiles of 106 neuroblastoma samples were generated by using the Illumina 450k methylation array. Furthermore, this comprehensive methylome analysis was complemented by generating Agilent 44k gene expression data of the same tumor samples.
Results: As a result, unsupervised hierarchical clustering of DNA methylation data reveals that the epigenome of MYCN amplified neuroblastomas strikingly differs from tumors without this key genomic alteration. However, our data demonstrates that genome-wide DNA methylation data can be used to refine the neuroblastoma CIMP phenotype by detecting new CIMP-specific gene loci. Moreover, we identified distinct epigenetic subgroups within the cohort of MYCN non-amplified tumors, which were significantly associated with disease staging and patient survival. By integrating methylome and transcriptome data, we found differentially regulated genes within these subgroups, which represent potential novel prognostic biomarkers.
Conclusions: In conclusion, this study sheds light on the epigenetic basis of clinical heterogeneity of neuroblastoma. Our integrative approach identified distinct epigenetic risk groups and corresponding biomarkers within MYCN non-amplified tumors, which might offer the opportunity to develop tailored treatment protocols, improving patient outcome and minimizing treatment induced deleterious consequences.

O-0088

GENE EXPRESSION PROFILING OF HUMAN NEURAL CREST STEM CELLS AND NEUROBLASTOMAS IDENTIFIES DIFFERENTIAL EXPRESSION OF EMBRYOLOGIC AND NEURAL DEVELOPMENT GENES

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Purpose/Objective: Neuroblastoma (NB), the most common extracranial solid tumor of childhood, is derived from neural crest stem cells (NCSC). Because the neural crest is a transient embryologic structure, there have been few studies comparing NB tumors to normal human NCSC. Recent advances have enabled the *in vitro* differentiation of NCSC from pluripotent stem cells. We compared gene expression profiles of pluripotent stem cells, NCSC, and NB cell lines and tumors to identify differentially expressed genes that may be relevant in NB pathogenesis.
Materials and Methods: Induced pluripotent stem (iPS) cells were differentiated to NCSC *in vitro* using established protocols. We performed RNA expression profiling of iPS cells, NCSC, twelve NB cell lines and 39 non-*MYCN* amplified primary NB tumors (3 stage 1, 5 stage 2, 3 stage 3, 24 stage 4, and 4 stage 4S. 32 tumors were from patients diagnosed at $>$ 18 months of age.) on Illumina HT-12 arrays. Results were normalized and analyzed with principle components analysis (PCA); differential expression was tested using Limma.
Results: PCA showed that undifferentiated iPS cells and NCSC cluster closely together and away from NB cell lines. The NB cell lines and primary tumors do not cluster closely together suggesting there are significant differences between them. Comparison between NCSC and NB cell lines plus primary tumors, adjusted for differences between cell lines and tumors, identified 182 differentially expressed genes (FDR ≤ 0.05) . Nine of the top ten genes are regulators of embryologic and/or neural development (*SOX3, DPPA4, HES5, LIN28,*

IRX2, SOX21, PAX6, FABP7, and OTX2). All are overexpressed in normal NCSC compared to NB cell lines and tumors.
Conclusions: *In vitro* derived NCSC represent an excellent model to study early NB pathogenesis. Gene expression profiling identified decreased expression of multiple developmentally important genes in NB compared to NCSC. Further investigations of these pathways are underway.

O-0089

DRUGGING MYCN THROUGH AN ALLOSTERIC TRANSITION IN AURORA KINASE A

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Purpose/Objective: Neuroblastoma is the most common extracranial solid tumor of childhood. Amplification of MYCN is common in high risk disease and confers a particularly poor prognosis. Stabilization of MYCN protein proceeds through a kinase-independent function of Aurora Kinase A. Here we describe a novel class of inhibitors and show a novel strategy for targeting MYCN for degradation through pharmacologic induction of a large structural shift in Aurora Kinase A.
Materials and Methods: An array of MYCN-amplified cancer cell lines were acquired through the UCSF Cell Culture Core. Lentiviral and bacterial constructs were generated to express MYCN and mutants were generated by PCR-based site-directed mutagenesis (Stratagene). Aurora A was purified from overexpressing bacteria, crystals were generated by hanging drop vapor diffusion. Standard chemical synthesis, cell free kinase assays, and crystallography were performed as described previously.
Results: We synthesized and screened a novel class of inhibitors to identify agents that finessed degradation of MYCN protein across several MYCN-expressing cell lines. To clarify mechanism, we solved the crystal structure of ligand-free Aurora Kinase A, as well as the structure of Aurora Kinase A bound to our most active compound, CD532. These structures demonstrate that a bulky chemical moiety in CD532 clashes sterically with structures in the amino terminus of Aurora Kinase A, resulting in a hinge-like opening of the kinase domain. In comparing structures of free Aurora Kinase, Aurora Kinase bound to clinical inhibitors, and Aurora Kinase bound to CD532, the degree of hinge movement correlated directly with degradation of MYCN. These structural data, coupled with mechanistic studies and biochemical assays, show potent MYCN protein degradation above the effects of simple nanomolar level inhibition of Aurora Kinase A kinase activity.
Conclusions: This class of inhibitors, which disrupts stabilizing interactions between Aurora A and MYCN, represents new candidate agents to target neuroblastoma and other MYCN-driven cancers.

O-0090

MIR-221 TARGETED NLK AND ENHANCED N-MYC LEVEL IN NEUROBLASTOMA

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Purpose/Objective: Amplification of *N-myc* oncogene is closely associated with malignant phenotype and progression of neuroblastoma (NB). Wnt signaling induces transcriptional activation and persistent amplification of N-myc. Our aim is to investigate the correlation of N-myc expression with the clinical relevence of children neuroblastoma, and further determine the effect of miR-221 by targeting of NLK on the Wnt signaling pathway in NB.
Materials and Methods: The correlation of *N-myc* expression with the clinical relevence was measured by fluorescence in situ hybridization (FISH) in 60 children neuroblastoma patients. MiR-221 target site in *NLK* 3' untranslated region (3' UTR) was detected by using the dual glo luciferase assay system. The effect of miR-221 on the expression of NLK and N-myc protein was determined by Western blot.
Results: The FISH results showed that *N-myc* expression and copies were positively associated with the clinical relevence and prognosis of 60 children neuroblastoma patients. Transcripts carrying the *NLK* 3'UTR exhibited 53.78% reduction in luciferase activity in the presence of miR-221 mimics ($P = 0.013$). In contrast, the mimics control had no significant effect on the luciferase activity ($P = 0.094$). Western blot assay demonstrated that *NLK* was significantly reduced, whereas *N-myc* was markedly enhanced in cells transfected with miR-221 mimics, when compared with untreated cells and cells transfected control mimics ($P < 0.001$).
Conclusions: Our results indicated that *N-myc* expression and copies were positively correlation with the clinical relevence and prognosis of children neuroblastoma patients. *NLK*, one of the vital control factor of Wnt signaling pathway, was a target for miR-221, and overexpression of miR-221 caused an enhancement of *N-myc*. Whether miRNA-221 activates Wnt pathway by targeting of NLK, and thus, induces N-myc amplification, and thereby may contribute to the progress of NB, is ongoing. This work was supported in part by the National Natural Science Foundation of China (NSFC, 81201543) and Natural Science Foundation of Chongqing (CSTC, 2010BA5008).

FREE PAPER SESSION: FREE PAPER SESSION 17 - BONE TUMOURS

O-0091

DOUBLE HIGH-DOSE CHEMOTHERAPY BY THIOTEPA TO TREAT POOR PROGNOSIS OSTEOSARCOMA

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Purpose/Objective: To evaluate efficiency/tolerance of tandem high-dose chemotherapy by Thiotepa followed by stem cell rescue and tumor resection in patients with poor prognosis metastatic osteosarcomas.
Materials and Methods: Double high-dose Thiotepa (900mg/m^2) and autologous stem cell rescue preceded or not with conventional dose chemotherapy. Surgery of all disease sites was performed after the first Thiotepa. Between 1995 and 2012, 37 patients with multimetastatic osteosarcomas at diagnostic ($n = 3$) and relapsed osteosarcomas (14 first, 19 second and 1 third relapse) were enrolled.
Results: This strategy was interrupted after the first course of thiotepa in 15 cases (40%), because of progressive disease (11/37) or toxicity (4/37 patients, including 3 due to post-surgery complications after first Thiotepa). Toxicity was acceptable and not significantly increased for the second thiotepa: neutropenia and thrombopenia lasted in median 8 and 9 days, respectively and 50% of the patients presented digestive toxicity. At the end of the strategy, 15 patients were in complete remission, 4 in partial remission, 2 had stable disease. Among the 22 patients who received both thiotepa, 15 developed further relapses and 14 died. However, in these patients with very poor prognosis, some patients did benefit hugely of the strategy (e.g. patients with mediastinal lymph nodes). The 24-month overall survival was 32% (95%CI, 19-49) and the disease-free survival was 23% (95%CI, 12-40). The patients who did not benefit of the strategy (survival < 6 months) are either those with early relapse (< 12 months) or those with more than 5% of residual viable tumor cells in the tumor resected after the first course of thiotepa. Six patients are still alive in complete remission with 5.6 years follow-up.
Conclusions: Tandem high-dose Thiotepa is feasible. Identification of patient who will benefit from the procedure is difficult. Further evaluated in a prospective study for selected patients with specific prognosis factors should be performed.

O-0092

PHARMACOGENETICS OF MICRORNAS IN OSTEOSARCOMA

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Purpose/Objective: Methotrexate (MTX) is a key component in the treatment against osteosarcoma. Treatment with high-dose MTX (HD-MTX) often causes toxicity. In those cases, dose reduction or cessation of treatment is needed. In the last years, the relationship between genetic variation and MTX-toxicity has been investigated,. but most of these studies are focused in coding regions.

Recent studies have provided evidence that SNPs in pre-miRNAs and in genes of miRNA processing machinery may affect the expression of genes involved in drug response. In fact, MTX transporters as ABCC2 and ABCC4 could be regulated by miRNAs.

The aim of this study was to determine the potential role of SNPs in pre-miRNAs or their processing genes as markers of MTX-toxicity in children with osteosarcoma.
Materials and Methods: We analyzed 99 blood samples from osteosarcoma patients. MTX plasma levels were used as objective and quantifiable toxicity markers. Cut-off values for toxicity were set at $3{,}5 \times 10^{-6}$ at 24h and/or $3{,}5 \times 10^{-7}$ at 48h post-infusion. We studied 118 SNPs in premiRNAs and in genes of the miRNA biogenesis pathway with the Taqman OpenArray platform. The effect of these SNPs in miRNA expression was evaluated by QRT-PCR.
Results: Of the 118 SNPs analyzed, 8 were significantly associated ($p < 0{,}05$) with MTX plasma levels. One of them was located in a pre-miRNA and seven in miRNA biogenesis pathway genes.
Conclusions: Our results suggest that polymorphisms in both pre-miRNAs and processing machinery genes may affect toxicity due to HD-MTX in osteosarcoma.

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O-0093

TARGETING METASTATIC SARCOMA IN THE YOUNG

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Purpose/Objective: Cancer patients mostly do not die of the primary tumour, but of metastasis. Sarcomas of childhood are rare but highly malignant, because of early and frequent metastatic spread. They are characterized by low genetic complexity and, hence, pivotal mechanisms of metastasis may be straightforward to decipher. Metastasis and stemness are intimately linked processes in childhood sarcomas.
Materials and Methods: We have identified critical genes criticalfor metastasis and stemness by transcriptomics and epigenomics. In contrast, exome sequencing did not reveal additional targets so far. Candidate gene function was evaluated by RNAi. Functionally relevant targets EZH2, CHM1, and STEAP1 were next addressed by T cell receptor (TCR) transgenic, major histocompatibility complex (MHC) haplotype disparate T cells, recognizing the candidate peptide in the allo-MHC context of the recipient. Tumour selective allorestricted TCRs were cloned and expressed as transgenes.
Results: We were able to generate transgenic T cells recognizing tumour selected petides in an allorestricted context. The approach was translated into the clinic by haplo-disparate stem cell transplantation followed by infusion of donor parent-derived tumour selective, allo-restricted TCR cytotoxic T cells against EZH2, CHM1, and STEAP1. The yielding targeted therapy thus engaged parent cells to combat the children's cancers by recognizing newly identified, tumour-associated peptides in the haplo-disparate MHC context of the non-donor parent.
Conclusions: These advances may give rise to novel personalized precision therapies in metastatic sarcoma and open some horizons for cure of cancer in general.

O-0094

IMPACT OF GENDER ON EFFICACY OF ALKYLATING AGENTS AND THEIR ACUTE TOXICITY IN PATIENTS WITH STANDARD RISK LOCALIZED EWING SARCOMAS (EWS) IN THE EURO-EWING99-(EE99)-R1 TRIAL.

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Purpose/Objective: Patients were randomized for cyclophosphamide vs. ifosfamide-based consolidation (VAC vs. VAI) in the Euro-EWING99-R1 trial. Overall, the efficacy of the two agents was similar [PBC,57,p710;2011). Based on the EE99R1 gender-stratified randomization, gender impact on efficacy and acute toxicity was explored.
Materials and Methods: Gender impact on Event-Free Survival (EFS) and acute toxicity by course, switches between treatment arms, and cumulative dose of alkylating agents was evaluated in multivariable models including tests for heterogeneity of treatment effect by gender, on the intention-to-treat population.
Results: 856 patients (347 females) were randomized between 2000 and 2010: 425 VAI and 431 VAC. Overall EFS was not gender dependent. ($p = 0.33$). Marginal variation of treatment effect on EFS was seen between genders ($p = 0.083$): In males VAC exhibited poorer EFS than VAI, HR(VAC/VAI) $= 1.34$ [0.96 - 1.86]. In females, VAC was slightly better than VAI, HR $= 0.83$ [0.54 - 1.28]. Equivalently, males had poorer EFS than females with VAC, HR(M/F) $= 1.42$ [0.97 * 2.08]. Results by gender were similar with VAI, HR $= 0.91$ [0.62 * 1.33]. Severe hematological toxicity was more frequent with VAC. Tubular renal impairment was more frequent with VAI. Severe toxicity was more frequent in females, for all toxicity types, with no significant treatment-gender interaction. Thirty patients switched from VAI to VAC (21 F, 9 M), mostly due to renal toxicity, and 3 from VAC to VAI (1 F, 2 M). A reduction of either alkylating agent cumulative dose $>20\%$ was more frequent in females (15% vs. 9%, $p = 0.01$).
Conclusions: Gender impact on EFS and acute toxicity from an alkylating agent requires further study. Effects of gender-dependent polymorphism/activity of metabolic enzymes (e.g. CYP2B6) of ifosfamide vs. cyclophosphamide should be explored.

O-0095

MAINTENANCE OF STEMNESS: A RECURRING FEATURE IN THE CLINICAL BIOLOGY OF EWING SARCOMA

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Purpose/Objective: Ewing sarcomas (ES) are highly malignant, localized in bone or soft tissue and are molecularly defined by ews/ets translocations.
Materials and Methods: Microarray analysis revealed histone methyl-transferase Enhancer of Zeste, Drosophila, Homolog 2 (EZH2), BRICHOS domain containing proteins important for chondrogenic differentiation and canonical Wnt agonist Dickkopf, Xenopus, Homolog of, (DKK) 2 critical for terminal bone development, to be over-expressed in ES.
Results: While BRICHOS domain containing protein Chondromodulin-I (CHM1) and histone methyl-transferase EZH2 seem directly induced in ES via EWS/FLI1, DKK2 and Integral Membrane Protein 2A (ITM2A) are independently induced in ES.RNA interference experiments disclosed histon-methyltransferase EZH2 to maintain an epigenetically regulated undifferentiated, aggressive, invasive, immature phenotype incapable for endothelial and neuroectodermal differentiation (Richter et al., 2009; Burdach et al., 2009). DKK2 (Hauer et al., 2013) and BRICHOS domain-containing genes CHM1 and ITM2A on the other hand preserve the immature, invasive chondro-osseous characteristics of this disease.DKK2 was critical for malignant outgrowth in an orthotopic xenograft mouse model *in vivo*, while BRICHOS proteins, CHM1 and ITM2A seemed essential for the maintenance of a precursor state of chondrogenic differentiation. Gene expression analyses proved DKK2 to induce genes important for osteolysis, like HIF1α, IL6, JAG1, RANKL and VEGF, while BRICHOS domain containing proteins suppressed the expression of such genes. Clinically, high DKK2 expression seems associated with increased bone infiltration and decreased survival of ES patients.
Conclusions: Thus, EZH2 as well as DKK2 and BRICHOS proteins orchestrate and promote different aspects of *stemness* and metastatic spread of this tumour, and provide significant conceptual progress in understanding both the pathogenesis and immature phenotype of this disease.
References
Burdach S, et al., 2009. *Cell Cycle* 8(13): 1991-6.
Hauer K, et al., 2013 *Cancer Res.* 73(2): 967-77.
Richter, GHS, et al., 2009 *Proc Natl Acad Sci USA* 106(13): 5324-9.

O-0096

TIME TO DIAGNOSIS OF EWING SARCOMA IN CHILDREN IS ASSOCIATED WITH TUMORAL VOLUME BUT NOT WITH METASTASIS OR SURVIVAL: A PROSPECTIVE MULTICENTER STUDY

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Purpose/Objective: To study the determinants of duration between first symptoms and diagnosis (time to diagnosis: TtD) of Ewing tumours and its impact on disease extension at diagnosis and outcome.
Materials and Methods: We conducted an ancillary analysis of prospectively collected data of 2 clinical trials (EW88 and EW93) that included patients younger than 21 years, with osseous Ewing tumors treated in France between 1988 and 2000. Relations between TtD and clinical features, disease stage and survival were studied using uni- and multivariate analyses.
Results: The median TtD of the 436 cases was 70 days (interquartile range 27 days * 5 months), without any decrease during the study period. The factors associated ($p \leq 0.001$) both in uni- and multivariate analyses with a longer TtD were an older age (median 13 weeks for children >12 years vs 6), the presence of pain at diagnosis (11 weeks vs 6), and the tumor localisation (longer TtD for pelvis and extremities of limbs). A longer TtD was associated with a larger tumoral volume both in uni- and multivariate analyses (12 weeks for volume >200 ml vs 9; $p = 0.02$) and with a decreased histological response to induction chemotherapy in the univariate analysis (12 weeks for cells $>10\%$ vs 8 weeks for better response; $p = 0.03$) but not after adjustment for tumoral volume. We did not found any significant association ($p > 0.10$) between TtD and the presence or type of metastasis, surgical resection, complete resection, mutilating surgery, or survival (10-years survival of 56% for patients with TtD shorter than the median (10 weeks) vs 50%).
Conclusions: TtD of Ewing tumors in children were long and stable during the study period. They were associated with pain and tumoral volume but not with metastasis or survival. These findings should be used to inform parents at diagnosis and educate primary care physicians to decrease the TtD.

FREE PAPER SESSION: FREE PAPER SESSION 18 - SUPPORTIVE CARE

O-0097

PROTEOMIC BIOMARKERS FOR RISK-STRATIFICATION OF PEDIATRIC PATIENTS WITH FEVER-NEUTROPENIA

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Purpose/Objective: Fever-Neutropenia (FN) is leading cause of hospitalization among patients receiving chemotherapy and is associated with significant morbidity and mortality. We hypothesize that upon FN presentation, select serum proteins may generate a distinctive proteomic signature which could be used as biomarker to predict clinical outcome.
Materials and Methods: High risk FN (HR-FN) patients were defined with either of two clinical outcomes: prolonged hospitalization (>7 days) or clinical sepsis requiring management in Intensive care unit. Low risk FN (LR-FN) patients had none of the above. Blood samples were collected upon FN presentation (40 FN events), pooled proteomic data (20 LR-FN and 20 HR-FN samples) were generated using mass spectroscopy and correlated with clinical outcome. Each candidate protein was compared between the HR-FN and LR-FN patients using exact nonparametric test. To measure false discovery rate, Q-values were calculated based on resulting p-values. Q-values equal to or less than 0.05 were considered to be statistically significant.
Results: Subject's median was age 11 years and malignancies included leukemia (52%), CNS (22%) and bone (17%). Median hospitalization days were 4 (LR-FN) and 11 (HR-FN). We identified a specific proteomic signature in the sera of patients with HR-FN in which median levels of C-reactive protein, beta-2-microglobulin, fibrinogen-like protein 1, intercellular adhesion molecule 1, amyloid A protein and tenascin were significantly elevated as compared to LR-FN patients. In contrast, median serum proteins levels for Protein S100-A9 were significantly higher in the LR-FN group compared to the HR-FN group (p-value 0.0079, Q-value 0.055).
Conclusions: Serum protein analysis upon FN presentation demonstrates unique proteomic profile which show significant differences that associates with HR or LR-FN clinical outcomes. These profiles represent specific proteomic biomarkers that may be useful in upfront FN risk stratification that may lead to timely interventions to decrease FN associated morbidity and mortality.

O-0098

INFECTIONS IN CHILDREN WITH DOWN SYNDROME AND ACUTE MYELOID LEUKEMIA: FROM THE CANADIAN INFECTIONS IN AML RESEARCH GROUP

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Purpose/Objective: Children with Down syndrome (DS) and acute lymphoblastic leukemia are known to be at high risk of infectious toxicities. Our objective was to determine if DS children with acute myeloid leukemia (AML) have a different risk of infection depending on treatment with a Down syndrome specific versus standard AML therapy.
Materials and Methods: We conducted a retrospective, population-based cohort study of children with DS (age $\leq$ 18 years) who had been treated for *de novo*, non-M3 AML at 15 Canadian centers between January 1995 and December 2004. All patients were monitored for infection from initiation of AML treatment until hemapoietic recovery from the last cycle of chemotherapy, start of conditioning for hematopoietic stem cell transplantation, relapse, refractory disease or death (whichever occurred first). Data was analyzed using logistic regression with generalized estimating equations.
Results: A total of 31 children with DS-AML were identified; the median age was 1.7 years (range 0.1 to 11.1 years). Eleven were treated according to a Down syndrome specific protocols and 20 were treated with standard AML therapy; 157 courses of chemotherapy were delivered. Microbiologically documented sterile site infections occurred in 11.9% and 14.3% of Down syndrome specific and standard AML treatment courses respectively. Sepsis was rare and there were no infection-related deaths. In multiple regression, treatment with a Down syndrome specific protocol was independently associated with a reduction in microbiologically documented sterile site infection (adjusted OR 0.65, 95% CI 0.42 to 0.99; P = 0.044), and clinically documented infection (adjusted OR 0.36, 95% CI 0.14 to 0.91; P = 0.031) but not bacteremia (adjusted OR 0.73, 95% CI 0.44 to 1.22; P = 0.231).
Conclusions: Our study suggests that children with DS do not experience excessive infectious toxicity during treatment for AML compared to children without DS and in particular, incorporation of treatment protocols that are Down syndrome specific has a relatively favorable infection profile.

O-0099

PEDIATRIC ONCOLOGY GROUP OF ONTARIO (POGO) GUIDELINES FOR PREVENTION OF ANTINEOPLASTIC-INDUCED NAUSEA AND VOMITING (AINV) IN CHILDREN: ACUTE AND ANTICIPATORY AINV

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Purpose/Objective: To describe the development of three supportive care guidelines: *Classification of the Acute Emetic Potential of Antineoplastic Medication; Prevention of Acute AINV*; and *Prevention and Treatment of Anticipatory AINV.*
Materials and Methods: An inter-professional, international panel of experts was convened and developed the health questions which the guidelines were to address. For the emetic classification and AINV prevention guidelines, existing adult guidelines were identified as source guidelines for adaptation to the pediatric context. Library-scientist assisted literature searches were undertaken to identify pediatric literature. Using established methods (ADAPTE, CAN-IMPLEMENT), the source guidelines were updated and reframed based on pediatric evidence. No source guideline was identified for the anticipatory AINV topic; a *de novo* guideline was developed based on systematic reviews of the adult and pediatric primary literature. The quality of evidence was assessed and the strength of each recommendation was determined using GRADE methodology. The draft guidelines underwent an extensive, two-stage external review by international experts in adult and pediatric AINV and by stakeholders (Canadian pediatric oncology physicians, nurses and pharmacists). The guidelines were revised accordingly.
Results: The emetic classification guideline released in June 2011 classifies single and combination antineoplastic agents having high, moderate, low or minimal emetic potential. The acute AINV prevention guideline released in August 2012 recommends optimal antiemetic interventions based on chemotherapy emetogenicity and antiemetic interventions for children who cannot receive corticosteroids. The guideline for prevention and treatment of anticipatory AINV will be released in September 2013. Identified research gaps included the: emetogenic potential of commonly used medications, optimal dose of many antiemetic agents and role of aprepitant.
Conclusions: These pediatric-specific guidelines provide an evidence-based approach to improving AINV control in children. Implementation of evidence-based guidelines is expected to improve AINV control and quality of life in children receiving cancer treatment. Attention to the research gaps identified is needed.

O-0100

PHARMACOGENOMICS OF VINCRISTINE-INDUCED NEUROTOXICITY IN PEDIATRIC CANCER PATIENTS

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Purpose/Objective: Vincristine is one of the most effective and widely utilized antineoplastic agents in the treatment of childhood cancer. However, its use is limited by vincristine-induced neurotoxicities (VIN) including motor neuropathies, sensory neuropathies, central nervous system toxicities such as SIADH, and autonomic neuropathies. Previous studies have reported associations of variation in candidate genes involved in the biotransformation of vincristine (CYP3A4, CYP3A5, ABCB1) with VIN, yet these results have not been consistently replicated. We investigated the association of genetic variation in these 3 genes, in addition to a broad panel of genes involved in drug absorption, metabolism, distribution, and excretion (ADME) and vincristine toxicity in pediatric cancer patients.
Materials and Methods: We genotyped 4,536 single nucleotide polymorphisms (SNPs) in over 300 key ADME genes in a cohort of 140 children with Wilms tumor and rhabdomyosarcoma (RMS). To replicate findings, known variants in CYP3A5, CYP3A4 and ABCB1 as well as variants with evidence for association ($p < 0.01$) in the pilot cohort were analyzed in a larger cohort of 422 patients with acute lymphoblastic leukemia (ALL).
Results: Preliminary results show that none of the previously associated variants in CYP3A4, CYP3A5 and ABCB1 were significantly associated with VIN in either cohort. Six novel candidate genes were identified in the RMS/Wilms cohort showing single SNP associations

with p-values < 0.01. Of these six genes, the association of variation in ABCA4 was replicated in the ALL cohort (combined cohort OR: 1.7, $p = 2.9 \times 10\text{-}4$).
Conclusions: This study was the first to broadly screen genetic variation in the context of VIN in pediatric cancer patients and has identified new candidate genes of potential relevance for VIN, whereas previously identified genes involved in the biotransformation of vincristine were not associated. These findings provide a starting point for further investigation of the genetic basis of VIN and further studies of the newly identified candidate genes are required.

O-0101

THE SYMPTOM MONITORING AND SYSTEMATIC ASSESSMENT IN YOUNG SURVIVORS (SYMON-SAYS) FOR PEDIATRIC ONCOLOGY CLINICS

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Purpose/Objective: Timely identification of symptoms related to multi-modal therapy for children with cancer is fundamental to the overall success of cancer treatment. SyMon-SAYS, a patient-oriented, technology-based symptom monitoring and reporting system, was developed to fill this need. This study evaluated the feasibility of implementing SyMon-SAYS in pediatric oncology clinics using fatigue as a prototype symptom.
Materials and Methods: Patients from the Chicago metropolitan area with a cancer diagnosis, ages 7-17 years, on- or off-treatment within 6 months, were eligible. Patients and parents completed weekly fatigue assessments over eight weeks via the internet or interactive voice response (IVR) by phone. Alert emails to clinicians were generated when pre-defined fatigue score thresholds were met. Clinicians decided how to respond based on whether or not fatigue was expected (e.g., calling families to further assess). Clinicians and parents/patients received cumulative graphic reports of fatigue scores prior to clinic visits at 4 and 8 weeks post-baseline to facilitate discussion. Parents and patients completed an exit survey at their last visit.
Results: At present, 47 patients (mean age = 11.6 yrs; 58% females; 58% white) have completed the study. An average of 6 assessments were completed (max = 9) and 54 alerts were generated. The majority of patients (92.7%) and parents (82.9%) felt it was very/extremely easy to complete SyMon-SAYS by IVR/internet, 94.3% of parents were satisfied with SyMon-SAYS, 57.6% reported SyMon-SAYS helped deal with their child's fatigue, 45.7% reported that clinicians did not discuss fatigue with them, and 79.4% were willing to use SyMon-SAYS to manage fatigue and other symptoms. Clinicians reported insufficient time to review reports, yet 64% were willing to receive the report on a monthly basis.
Conclusions: Results suggest SyMon-SAYS is feasible and acceptable to patients and parents. Future efforts should focus on better integrating SyMon-SAYS into the clinical workflow.

O-0102

THE IMPACT OF ADEQUATE SYMPTOM CONTROL AND PALLIATIVE CARE ON LONG-TERM GRIEF IN PARENTS WHO LOST A CHILD TO CANCER

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Purpose/Objective: Twenty-five per cent of children diagnosed with cancer die. Losing a child puts parents at increased risk for developing psychological problems. The aim of this study is to explore parents' perception of the quality of care and symptom management and the influence on long-term grief in parents who lost a child to cancer.
Materials and Methods: Eighty-nine parents of 57 children who died of cancer between 2000 and 2004 participated in this retrospective cross-sectional study by completing a set of questionnaires measuring grief, perception of care (communication, continuity of care and parental involvement), and the severity and level of control of their child's symptoms during the palliative phase. Care was assessed on a 5-point Likert scale (1 = disagree;5 = agree).
Results: Parents highly rated communication (4.6 ± 0.5), continuity of care (4.3 ± 0.6) and parental involvement (4.6 ± 0.7) during the palliative phase. Fatigue (75%), pain (74%), anxiety to be alone (52%) and anger (48%) were the most frequently reported physical and psychological symptoms of the child. Higher ratings of communication (β = -8.93, $p = 0.03$) and continuity of care (β = -11.71,$p = 0.01$) were associated with lower levels of long-term parental grief. The severity of the child's dyspnoea ($\beta = 3.11$,$p = 0.03$), anxiety to be alone ($\beta = 4.50$,$p < 0.01$), anxiety about the future ($\beta = 4.83$,$p < 0.01$), anger ($\beta = 4.99$,$p < 0.01$) and uncontrolled pain ($\beta = 6.52$,$p < 0.01$) were associated with higher levels of long-term parental grief. Multivariate models combining domains of care and symptoms showed a significant influence of both care and symptom management on long-term parental grief.
Conclusions: Palliative care, especially communication, continuity of care, and adequate symptom management in children dying of cancer are predictive for long-term parental grief levels.

FREE PAPER SESSION: FREE PAPER SESSION 19 - LEUKEMIA III

O-0103

SUCCESSFUL TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) WITH FIRST ISOLATED TESTICULAR RELAPSE WITH LIMITED USE OF TESTICULAR IRRADIATION: REPORT FROM CHILDREN'S ONCOLOGY GROUP (COG) AALL02P2

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Purpose/Objective: The incidence of isolated testicular relapse (ITR) of ALL has decreased with modern regimens, but outcomes are suboptimal with 58% 5-yr overall survival (OS) (Nguyen, Leukemia 2008). Subsequent bone marrow (BM) relapse and radiation related morbidity remain the causes of treatment failure and long-term sequelae, respectively. This study aimed to improve outcome using intensive systemic chemotherapy and to decrease long-term sequelae by limiting use of testicular radiation.
Materials and Methods: Forty patients in first ITR of ALL were enrolled. Induction (DEX, VCR, daunorubicin and triple intrathecal therapy-ITT) was preceded by one dose of high-dose MTX($5g/m^2$). Following induction, patients with persistent testicular enlargement ($n = 24$) underwent testicular biopsy. 11/24 had biopsy proven persistent testicular leukemia and received testicular radiation (2400 cGy). 29/40 patients were treated without irradiation. All patients received consolidation (ARAC[$3g/m^2$]/PEG-asparaginase), intensification phases (CTX/VP-16, MTX[$5g/m^2$]/6-MP, ARAC[$3g/m^2$]/PEG-asparaginase) and reinduction, plus concomitant ITT. Maintenance consisted of DEX pulses every 10 weeks and weekly MTX/6-MP alternating with CTX/VP-16. CTX total dose was capped at $6.4g/m^2$ to preserve testicular function.
Results: Overall 5-yr EFS/OS were $63 \pm 11\%/77 \pm 10\%$, with 5-yr EFS $58 \pm 15\%$ vs. $73 \pm 14\%$ for patients who did not receive XRT ($n = 29$) vs. those who did ($n = 11$), respectively ($p = 0.60$). There were 5 second BM relapses and 5 second ITRs, the latter occurred in patients who did not receive radiation. The proportion of second relapses were similar in the patients that received testicular radiation (3/11) and those who did not (7/29). However, most patients experiencing a second relapse were salvaged with chemotherapy and/or BMT resulting in 5-year OS of $77 \pm 14\%$ and $73 \pm 14\%$ for patients who did not receive XRT vs. those who did, respectively ($p = 0.62$).
Conclusions: Improved 5-yr OS rates were obtained in children with first ITR of ALL using intensive chemotherapy and limiting testicular radiation. This approach is suitable to avoid long-term toxicities associated with testicular radiation.

O-0104

THE EFFECT OF EXTRAMEDULLARY DISEASE ON OUTCOME FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANT IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: We performed a retrospective review of pediatric patients undergoing hematopoietic stem cell transplant (HSCT) for acute lymphoblastic leukemia (ALL) to determine whether history of extramedullary disease (EMD) at any point prior to HSCT influenced outcome, with particular emphasis on the impact of local radiotherapy to EMD sites immediately prior to HSCT.
Materials and Methods: Chart review identified 141 children with ALL undergoing allogeneic HSCT from 1995 through 2006 at Dana-Farber/ Children's Hospital. 54 had a history of EMD prior to HSCT while 87 did not. Demographic and treatment data were collected. Overall survival (OS) and progression-free survival (PFS) were compared using log-rank and cumulative incidences of relapse (CIR) and non-relapse mortality (CINRM) by Gray test.
Results: Median age was 8 years (range 0-20); median follow up among survivors was 9.1 years (range 0.6-16.4). Both groups had similar baseline characteristics except more patients with EMD had T cell lineage (24% vs 6%, $p = 0.005$) and HSCT in $\geq$ CR2 (83% vs 55%, $p = 0.001$). EMD and non-EMD groups had similar outcomes: 5-yr OS was 52% vs 58% ($p = 0.63$); 5 yr PFS (PFS) was 49% vs 49% ($p = 0.90$); 5-year CIR was 34% vs 33% ($p = 0.86$); and 5-year CINRM was 17% vs 19% ($p = 0.7$). Children with testicular EMD who received testicular irradiation had better PFS (89% vs 45%, $p = 0.03$) and OS (89% vs 41%, $p < 0.02$) compared to the remaining EMD cohort. For children with history of CNS

EMD (n = 30), additional CNS radiotherapy (range 150-1050 cGy, median 600) did not alter OS (44% vs 54%, p = NS) or PFS (40% vs 54%, p = NS).
Conclusions: History of EMD did not affect OS or PFS of children with ALL undergoing allogeneic HSCT. Overall, a radiotherapy boost to EMD sites prior to HSCT did not improve outcome. However, children with testicular EMD who received additional radiotherapy had a superior outcome.

O-0105

CYTOLOGICAL AND MOLECULAR REMISSIONS WITH BLINATUMOMAB TREATMENT IN SECOND OR LATER BONE MARROW RELAPSE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Purpose/Objective: Pediatric B-precursor acute lymphoblastic leukemia (ALL) in second or later relapse needs new therapeutic approaches. Blinatumomab, a bispecific T-cell engaging (BiTE®) antibody, has shown a hematological remission rate of 69% in adult patients with relapsed/refractory ALL. We initiated a phase 1 multicenter study to establish a recommended dose in pediatric patients.
Materials and Methods: Establishing the maximum tolerable dose, defined by ≤ 1 of 6 patients experiencing dose limiting toxicity (DLT) within the 1st course of treatment, is the primary endpoint. Up to 6 different dose levels of blinatumomab are being evaluated. Eligible patients are < 18 years old, have B-precursor ALL that is refractory or in second or later bone marrow relapse, or in any marrow relapse after allogeneic hematopoietic stem cell transplantation (HSCT). Blinatumomab is administered by continuous IV infusion over 28 days followed by a 14-day treatment-free interval (up to 5 cycles). To date, three dose levels have been explored with 5 $\mu g/m^2$/d, 15 $\mu g/m^2$/d, and 30 $\mu g/m^2$/d.
Results: Seventeen patients have been treated thus far; 10 patients in relapse after HSCT, three patients in $\geq 2^{nd}$ relapse without prior HSCT, and four patients refractory after 1st relapse. One DLT (gastrointestinal hemorrhage) at dose level 2 and two DLTs with 1 death at dose level 3 (both cytokine release syndrome) have occurred. Eight (47%) of the 17 patients reached a cytological complete remission in bone marrow and a molecular remission defined as MRD by PCR $< 10^{-4}$. Seven of the eight responders proceeded to allogeneic HSCT; one patient relapsed with CD19-negative ALL.
Conclusions: In this phase 1 study, blinatumomab treatment of pediatric patients with relapsed/refractory ALL resulted in hematological and molecular remissions. Cytokine release syndrome was a dose-limiting adverse event. The study continues to explore alternative dosing regimens in current cohorts to determine the recommended blinatumomab dose in this patient population.

O-0106

CHIMERIC ANTIGEN RECEPTOR FOR SPECIFIC TARGETING OF ACUTE MYELOID LEUKAEMIA

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Purpose/Objective: Despite progresses in the treatment of acute myeloid leukaemia (AML), a number of patients is still refractory to conventional regimens. Therefore novel approaches are warranted. Immunotherapy with T-cells genetically modified to express chimeric-antigen-receptors (CARs) represents a valid option. CARs are artificial T-cell receptors constituted by an antigen-binding domain and a signaling-region that leads to T-cell activation and lysis of the target. AML is an optimal target because of the over-expression of various surface antigens. Since CD33 is also expressed on normal haematopoietic-stem/progenitors-cells (HSPCs), CD123 is an attractive molecule, being overexpressed by AML and poorly expressed on HSPCs.
Materials and Methods: Here we describe the *in vivo* efficacy and safety of Cytokine-Induced-Killers (CIK) cells expressing CARs specific for the CD33/CD123 antigens.
Results: Once injected into low-level AML-engrafted NSG mice (median of $hCD45^+CD33^+$0.6% before treatment), T-cells had potent antitumour effects. The bone marrow of untreated animals or mice treated with un-manipulated CIK-cells was totally infiltrated by leukaemia, while in 7/8 anti-CD33-CD28-OX40-ζ and in 8/10 anti-CD123-CD28-OX40-ζ treated mice no AML cell was detectable. Similar results were obtained when T-cells were injected in mice with an established high-AML burden (median of $hCD45^+CD33^+$ 70% before treatment). AML engraftment was 96%, 87%, 0.35% and 0.34% for untreated mice, mice treated with un-manipulated, anti-CD33-CD28-OX40-ζ and anti-CD123-CD28-OX40-ζ transduced CIK-cells, respectively. Furthermore, the safety profile was measured against normal HSPCs. In untreated mice injected with cord blood-derived $CD34^+$cells engraftment of hCD45-compartment was 42%, whilst in mice treated with un-manipulated, anti-CD33-CD28-OX40-ζ or anti-CD123-CD28-OX40-ζ transduced CIK-cells the level of human compartment was 40%, 11.7% and 26.3%, respectively. Moreover, considering specifically the $CD34^+CD38^-$compartment, enriched in HSC, engraftment was 1.92%, 1.02%, 0.55% and 0.83%.
Conclusions: These experiments should offer relevant information concerning the efficacy and safety of the proposed strategy in the context of MRD in high-risk transplanted AML patients or for patients not eligible to standard treatments.

O-0107

EARLY DEATHS IN PEDIATRIC ACUTE LEUKEMIA: A POPULATION-BASED STUDY

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Purpose/Objective: Objectives were to describe the incidence and risk factors associated with early deaths ($\leq$ 42 days from diagnosis) among children with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) in Ontario, Canada.
Materials and Methods: The data source was Pediatric Oncology Group of Ontario Networked Information Systems (POGONIS), a population-based active cancer registry that captures all pediatric cancers in Ontario. Newly diagnosed ALL and AML patients $\leq$18 years of age diagnosed January 1997 to December 2011 were included. Secondary leukemia was excluded.
Results: 2,357 children were included: 1,954 with ALL and 403 with AML. The early death rate was 31/2,357 (1.3%); and among the 345 deaths, 9.0% occurred early. There were no early deaths in 73 children with Down syndrome. Causes of early death were unknown (25.8%), disease-related (19.4%) and treatment-related (54.8%). Among deaths that were assessed for attribution to infection, 74/297 (24.9%) of all deaths and 11/29 (37.9%) of early deaths were due to infection.

Among children, early deaths were significantly more common in AML (3.0%) compared with ALL (1.0%; P = 0.003). However, among deaths, the proportion that occurred early was similar in AML (9.4%) compared with ALL (8.8%; P = 1.0). In both the entire group and when stratified by leukemia type, age, gender, era (recent versus remote) and ethnicity were not predictive of early deaths. Anthracyclines in induction and immunophenotype were not predictive of early death in ALL.
Conclusions: Early deaths occur in 1.3% of children with acute leukemia and are more common in AML than ALL. 9% of deaths occur within 6 weeks of diagnosis. Infection continues to be an important cause of death. Further improvements in pediatric leukemia survival will need to focus on reducing the early death rate.

FREE PAPER SESSION: FREE PAPER SESSION 20 - NEUROBLASTOMA III

O-0108

REVISED EVALUATION OF IMAGE DEFINED RISK FACTORS FOR LOCALIZED NEUROBLASTOMA ACCORDING TO THE NEW GUIDELINE FROM THE INTERNATIONAL NEUROBLASTOMA RISK GROUP (INRG) PROJECT

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Purpose/Objective: Image defined risk factors (IDRFs) have been propounded for predicting surgical risks of localized neuroblastoma (NB). In 2011, the new guideline (NG) for assessing IDRFs was published (Brisse et al, Radiology). In NG, 'even if the tumor is in contact with renal vessels only', this situation should be considered IDRF present which used

to be diagnosed as IDRF not present. In this study, we re-evaluated IDRF in localized NB patients, in order to clarify the usefulness of NG.
Materials and Methods: 84 localized NBs diagnosed between 1991 and 2012 were entered in this study. Of these, 26 and 58 patients were diagnosed IDRF present (Group OP) and not present (Group ON) before NG respectively. All images at diagnoses were re-evaluated by a single radiologist.
Results: There were 59 and 25 patients who were considered IDRF present (Group NP) and not present (Group NN) according to NG respectively. Therefore, 33 patients in ON turned to be in NP by NG. Among 34 patients who underwent primary operation in NP, kidney complications (KCs) were observed in 3 patients. On the other hand, among 8 patients who underwent primary operation in OP, KC was not observed. 10 patients in OP and 12 patients in NP underwent delayed primary operation or second look operation. Of these, KCs were observed in 2 patients (20%) in OP and 3 patients (25%) in NP respectively. 8 patients in OP and 13 patients in NP had not undergone surgical resection respectively, because their tumors regressed spontaneously or by chemotherapy.
Conclusions: NG increased the ratio of patients with IDRF present from 31% to 70% improved the sensitivity of IDRF for surgical risks but less specific. The preoperative chemotherapy did not decrease KCs in patients in OP either NP. Usefulness of NG should be validated in larger population in a prospective study.

O-0109

MOLECULAR GENETIC MARKERS FOR MINIMAL RESIDUAL DISEASE (MRD) DETECTION IN PATIENTS WITH NEUROBLASTOMA

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Purpose/Objective: Investigation of RNA and DNA-based molecular markers for MRD detection in neuroblastoma patients, qualitative concordance between them and prognostic impact of obtained results.
Materials and Methods: We analyzed 331 bone marrow (BM) samples from 57 neuroblastoma patients and 26 normal BM samples for *PHOX2B* and *TH* genes expression by RQ-PCR. In 86 BM samples from 32 neuroblastoma patients and 5 samples of healthy volunteers' lymphocytes *RASSF1a* gene methylation status was evaluated by RQ-PCR. For performing of ROC-analysis BM samples were defined as positive in case of detectable *PHOX2B* expression or neuroblastoma cells presence in BM smears. Threshold levels for each gene were established by ROC-analysis and subsequently applied for overall correct prediction (OCP) calculation.
Results: *PHOX2B* and *TH* expression was not detected in normal BM samples, as well as methylated *RASSF1a* (m*RASSF1a*) was not revealed in volunteers' lymphocytes. 105 analyzed BM samples were positive for *PHOX2B* expression, while 101 for *TH*. *TH* expression was revealed in 5 out of 224 negative BM samples. OCP for *PHOX2B* and *TH* achieved 0.994 and 0.952 respectively. m*RASSF1a* was revealed in neuroblastoma cell lines (IMR-32, SH-SY5Y) and in 26 BM samples. All of them were positive for *PHOX2B* expression while in 16 of *PHOX2B*-positive BM samples m*RASSF1a* was not detected. OCP value for m*RASSF1a* assay achieved 0.814. Patients with detectable *PHOX2B* expression in BM have lower event-free survival (EFS) comparing to patients with *PHOX2B*-negative BM (0.30 ± 0.10 and 0.77 ± 0.27, $p = 0.002$), overall survival is 0.51 ± 0.11 and 0.79 ± 0.07 correspondingly, $p = 0.083$. Presence of *TH* expression in BM led to decreased EFS (0.34 ± 0.11 vs. 0.75 ± 0.26, $p = 0.019$). Detection of m*RASSF1a* in BM demonstrated negative influence on EFS of neuroblastoma patients (0.29 ± 0.16 vs. 0.74 ± 0.11, $p = 0.090$).
Conclusions: Evaluated MRD molecular markers have shown high OCP values and negative influence on survival of neuroblastoma patients.

O-0110

PET IMAGING AT DIAGNOSIS AS A PREDICTOR OF GROSS TOTAL RESECTION IN NEUROBLASTOMA

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Purpose/Objective: Gross total resection (GTR) of neuroblastoma (NB) could be predicted by imaging-defined risk factors (IDRFs) on CT/MR images present at diagnosis. This study aims to investigate the complementary role of positron emission tomography (PET) scans in predicting GTR of NB in addition to IDRFs.
Materials and Methods: From 2008 to 2012, NB patients who received diagnostic PET scans with ^{18}F-fluorodeoxyglucose (FDG) and ^{18}F-fluoro-dihydroxyphenylalanine (FDOPA) at National Taiwan University Hospital, Taipei, Taiwan, were included. The extent of tumor resections was correlated with clinical features and imaging findings.
Results: Twenty-six patients (median age, 1.8 [0.5*6.9] years; male:female, 18:8) were eligible for analysis. Six patients (23%) had stage 3 disease; 14 (54%) had stage 4 disease; and 4 (17%) had *MYCN* amplification. GTR removing more than 90% of the primary tumor was undergone at first operation in 7 (27%) and at best operation in 13 (50%) patients, while the other 6 patients (23%) only had partial resection. Based on the primary tumors' maximal standard uptake value (SUV_{max}) on PET scans, we defined a group of PET high-risk patients (PET-HR; $n = 10$) with the SUV_{max} ratio between FDG and FDOPA of 1.66 or higher. The GTR rate of these PET-HR patients was significantly lower than that of the others (50% *vs.* 94%; $P = 0.018$), and remained to be lower when only considering patients with IDRFs ($n = 17$; 38% *vs.* 90%; $P = 0.05$). GTR had no impact on event-free survival (EFS; $P = 0.46$) and overall survival (OS; $P = 0.75$); neither did IDRFs (EFS, $P = 0.15$; OS, $P = 0.89$). However, PET-HR patients had significantly worse 3-year EFS (0% *vs.* 66%; $P = 0.016$) and OS (27% *vs.* 92%; $P = 0.03$).
Conclusions: PET imaging at diagnosis may provide a complementary role to IDRFs and may help surgical planning. Primary NB tumors with FDG-high and FDOPA-low uptake were less likely to be totally resected and had a worse outcome.

O-0111

OUTCOME AND LATE EFFECTS AFTER RADIATION THERAPY FOR A HIGH RISK LOCALISED NEUROBLASTOMA. A 10 YEARS' EXPERIENCE OF THE SOCIETE FRANCAISE DES CANCERS DE L'ENFANT (SFCE).

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Purpose/Objective: To review the recurrence-free survival (RFS), overall survival (OS) and determine late toxicity of paediatric patients who received radiotherapy (RT) for a localized neuroblastoma (NBL) with macroscopical residue or MYCN amplification (MNA).
Materials and Methods: Data from patients included in NBL 90 and NBL 94 French studies were studied. From 1990 to 2000, 610 children were enrolled. Medical records for the 38 patients treated with radiotherapy were retrospectively reviewed for information on tumour, treatments, survival and late effects.
Results: There were 17 males and 21 females. Median age was 26 (2-205) months. Primary tumour was located in abdomen in 30 (78.9%), pelvis in 5 (13.1%), thorax in 3 (7.8%) and neck in 1 (2.6%). According to the International Neuroblastoma Staging System (INSS), 3 had Stage 1, 3 Stage 2, 23 Stage 3 (9 missing). Nineteen (59%) of 32 tested patients had MNA.

Twenty-six were alive five years after the diagnosis, and were analyzed to check adverse events.

Median dose of RT was 34Gy (20-60). Eight received between 20 and 27 Gy and 18 between 30 and 37Gy. 2 of them received intra-operative radiotherapy.

Median follow-up was 11.9 years (0.7-21.1).

Among the 38 children, 16 relapsed and 15 ultimately died. The 5-year RFS rate was $57\% +/- 8\%$ and the 5- and 15-year OS rates were $68\% +/- 8\%$ and $62\% +/- 8\%$.

Two patients developed secondary malignant neoplasms within radiation fields (1 uterine sarcoma and 1 thyroid papillary carcinoma.

Out of 26 long-term survivors,18 (69%) experienced at least one side effect, including musculoskeletal in 7 of the 16 patients (43.7%) having received more than 30 Gy at a median time of 6 years after diagnosis. There was no musculoskeletal late effect under 30 Gy.
Conclusions: These results suggest that RT helps to improve RFS and OS in high-risk NBL. There were no musculoskeletal late effect under the dose of 30 Gy.

O-0112

REVIEW OF SURGICAL TREATMENT IN PATIENTS ENROLLED IN THE PHASE II STUDY NB-HR07 FOR ADVANCED NEUROBLASTOMA– A REPORT FROM JAPAN NEUROBLASTOMA STUDY GROUP (JNBSG)

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Purpose/Objective: Although primary tumor resection remains a mainstay of high-risk neuroblastoma (NB) treatment, the impact of the timing and radicality of surgery on the outcome of the patients is yet to be clarified. We reviewed the surgical treatment of cases enrolled in the NB-HR07 study from this viewpoint.
Materials and Methods: Case report files and surgical records of 50 high-risk NB cases enrolled in the study were reviewed. The stages of the diseases were stage 2B in one, stage 3 in six and stage 4 in 43 cases. Three had mediastinal and 47 had abdominal tumors. Radical surgery was scheduled after 3 or 4 courses of chemotherapy on the protocol.
Results: Forty-seven primary tumors were resected, while two remained unresectable. The origin of the tumor was undetermined in one case. Surgery was performed after 3 or 4 courses of chemotherapy in 29 cases according to the protocol. Seven cases underwent upfront surgery. Surgery was performed after 2 courses of chemotherapy in one. In ten cases, surgery was postponed (after HDC: high-dose chemotherapy in eight, timing unknown in two). Within the 45 cases of which details were available, results of the surgeries were: gross total resection 32 (71.1%), subtotal resection 10 (22.2%), and partial resection 3 (6.7%). Nephrectomy was concordantly performed in 8 cases. Locoregional recurrence occurred in 11.6% of the cases. Those who underwent gross total resection were less likely to have locoregional recurrence. Radicality did not have an impact on the overall survival of the patients.
Conclusions: There were a notable number of cases in which radical surgery had been postponed until after HDC. We found that the surgeries were performed safely without affecting the overall outcomes in these cases. To verify the rationale of postponed surgical treatment, JNBSG is currently conducting a trial setting radical surgery after HDC uniformly (NB-HR11).

O-0113

INFLUENCE OF SURGICAL EXCISION ON SURVIVAL OF PATIENTS WITH HIGH RISK NEUROBLASTOMA. REPORT FROM STUDY 1 OF SIOP EUROPE (SIOPEN).

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Purpose/Objective: To evaluate the influence of operation on the survival of patients with High-Risk Neuroblastoma: International Neuroblastoma Staging System (INSS) stages 2, 3, 4, 4s with MYCN amplification and INSS stage 4 age $>$ 12 months.
Materials and Methods: All patients were offered operation after an intensive platinum based induction protocol. There-after patients received myeloablative therapy, stem cell rescue, radiation to the primary site and minimal residual disease therapy with 13 cis-retinoic acid. A small number in this cohort received immunotherapy.
The result of surgical excision was defined as: macroscopic complete (CE), macroscopic incomplete, (IE) or not attempted (0E). Data were collected on death or complication related to operation, overall and event free survival. Survival was related to the completeness of surgical excision.
Results: 969 operation data sets were analysed. Operation related mortality was 0.6%, morbidity 10%. (CE) was achieved in 76%, (IE) in 22% and 2% were inoperable (0E).

3 year Event Free Survival (EFS) for all patients was 46%; 3 year Overall Survival (OS) was 51%. 3 year EFS for 738 patients with (CE) was 50% (OS 54%) compared with 41% (OS 49%) for patients with (IE) and (0E) combined (EFS $p = 0.018$; OS $p = 0.04$).

3 year EFS for 658 Stage 4 patients with (CE) was 46% (OS 51%) compared with 38% (OS 46%) for patients with (IE) and (0E) combined (EFS $p = 0.035$; OS $p = 0.06$).

3 year EFS was 48% (OS 54%) for patients who did not suffer operative complications compared with 38% (OS 41%) for those who did (EFS $p = 0.004$; OS $p = 0.001$).
Conclusions: Macroscopic complete surgical excision of High-Risk Neuroblastoma confers a survival advantage to patients treated with intensive multi-modality therapy.

FREE PAPER SESSION: FREE PAPER SESSION 21 - RENAL AND SARCOMAS II

O-0114

RISK FACTORS FOR ABANDONMENT OF CARE FOR PATIENTS WITH WILMS TUMOR IN KENYA

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Purpose/Objective: The 4 year OS for Wilms Tumor (WT) in the United States exceeds 90%. Analysis of the Kenyan WT Registry, consisting of children with WT diagnosed at 4 hospitals in Kenya from Jan 2008- Jan 2012, revealed a 2 year OS of 52.7%. 50% of patients were lost to follow up (LTFU).
Materials and Methods: We telephoned all families possible of WT patients in the registry who were LTFU at Kenyatta National Hospital (KNH), the largest referral hospital in Kenya, to determine the status of each child. We also administered a comprehensive survey to parents of patients with WT in various stages of therapy on the inpatient wards and in clinic during a one month period. The survey included questions about families, communication, understanding and thoughts about WT and treatment plan, a Life Orientation Test (LOT-R), the child's medical history, types of support received, home environment, transportation, education, income and concerns/needs.
Results: Of 105 patients originally in the registry at KNH, 46 (43.8%) were known to have died. 6 (5.7%) continued in therapy and 24 (22.9%) completed all therapy. Of patients who completed therapy, 1 recurred, 3 are followed off therapy and 20 (83.3%) were LTFU. 11 did not have working phone numbers and 9 were alive and well. Of 29 patients who abandoned care during therapy, 12 (27.6%) did not have working numbers, 2 recurred, 6 (20.7%) died and 9 (31%) were alive and well. Financial concerns, misunderstanding of treatment, and following up at outside facilities were reasons for abandonment. 13 parents completed surveys to date. Financial constraints resulting from gaps in coverage by the National Hospital Insurance Fund, misunderstanding of treatment plans by parents and providers and treatment delays are significant barriers to care.
Conclusions: Interventions to reduce financial barriers, standardization of protocols and education for care providers are needed.

O-0115

LONG TERM ANALYSIS PROVES THE BENEFIT OF ORAL MAINTENANCE TREATMENT IN METASTATIC RHABDOMYOSARCOMA: UPDATE OF HD CWS-96 TRIAL

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Purpose/Objective: We report the follow up of the outcome in patients with metastasized rhabdomyosarcoma and rhabdomyosarcoma-like tumours treated within the Cooperative Soft Tissue Sarcoma Study HD CWS-96. The first analysis published in 2008 (Klingebiel 'T' et al, Pediatric Blood Cancer 2008; 50: 739-745) demonstrated an independent benefit of oral maintenance treatment (OMT) over high dose therapy (HDT). We have now updated the analysis after a median observation time of 11.5 years.
Materials and Methods: We prospectively studied the efficacy of HDT versus OMT in 96 patients with soft tissue sarcoma stage IV pretreated with CEVAIE combination (carboplatin, etoposide, vincristine, actinomycin D, ifosfamide, and epirubicin). HDT consisted of tandem cycles of thiotepa (600 mg/m^2) plus cyclophosphamide (4,500 mg/m^2) and melphalan (120 mg/m^2) plus etoposide (1,800 mg/m^2). This treatment was compared with OMT consisting of four cycles of trofosfamide (10 days, 2×75 mg/m^2/day) plus etoposide (10 days, 2×25 mg/m^2/day) and four cycles of trofosfamide (10 days, 2×75 mg/m^2/day) plus

idarubicin (10 days, $4 \times 5mg/m^2$/10 days) administered alternating. Eligibility criteria were diagnosis, primary stage IV, and age below 22 years.
Results: First analysis was carried out at a median follow up of 4.8 years. The follow up analysis was performed at a median time of 11.5 years. 11/45 patients in the HDT and 21/51 patients in the OMT arm were alive. Kaplan- Meier analysis demonstrated on overall survival (OS) probability at 10 years for the HDT and the OMT group of 0.24 ± 0.13 and 0.42 ± 0.14 respectively ($p = 0.04$); patients without bone/bone marrow involvement had an OS at 10 years of 0.71 ± 0.19 in the OMT and of 0.34 ± 0.16 in the HDT group ($p = 0.05$).
Conclusions: The long term results of the HD CWS-96 study are very encouraging. The role of OMT is beneficial for patients with metastases other than bone and bone marrow and allows for this group the avoidance of HDT and other risky procedures.

O-0116

REPORT OF THE CWS 2002P STUDY: TREATMENT RESULTS FOR SOFT TISSUE SARCOMAS (STS) IN CHILDHOOD AND ADOLESCENCE

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Purpose/Objective: We report the outcome in 562 patients with localized rhabdomyosarcoma (RMS) and "RMS-like" tumours (synovial sarcoma SySa, soft tissue Ewing tumors STET) treated within the fifth Cooperative Weichteilsarkom Studie CWS-2002P (Germany,Poland, Austria, Sweden, Switzerland). The CWS 2002P study was designed as pilot study for the 2002 planned joint European Study for localized RMS within the EpSSG group.
Materials and Methods: Patients were divided into a low ($n = 21$), standard ($n = 172$),and high risk ($n = 369$) group. Low risk patients were treated with VA (Vincristine and Actinomycin D), standard risk with IVA (Ifosfamide, additionaly) and high risk with VAIA (IVA plus Doxorubicine). Local therapy consisted of surgery alone and/or irradiation. An optional maintenance therapy (MT) with oral Cyclophosphamide (CYC) and Vinblastine (VBL) i.v. for 6 months was designated for high risk patients, who were in complete remission at the end of intensive therapy.
Results: After a median follow-up 4.7 [0-9.3] yrs for surviving patients, the 5 yr EFS rate was 100%, 78% and 70% and 5yr OS rate 100%, 92% and 79% for low, standard and high risk patients respectively. According to histology the 5 yr EFS was 72% for RMS, 77% for SySa and 75% for STET. 222 patients received MT, 100 did not. The 5yr EFS for patients treated with CYC/VBL was 74%, for patients who did not receive MT 59%. (p.0.01). There was no significant difference between these groups in 5 yr OS rate (80% vs. 76%). The distribution of patients and tumour characteristic was not different in patients with and without MT. Secondary malignancies occurred in 11 patients (standard risk: $n = 7$, high risk: $n = 4$).
Conclusions: All risk groups have shown improved results in comparison with the CWS-96 study despite lower cumulative chemotherapy burden. Maintenance therapy, although not randomised, seems to have positive impact on prognosis and is being studied in a randomised way in our ongoing CWS-2007HR trial.

O-0117

PRIMARY CUTANEOUS AND SUBCUTANEOUS EWING'S SARCOMA: A DESCRIPTION OF 57 CASES.

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Purpose/Objective: To describe clinical features, treatment and outcome of patients with primary cutaneous/subcutaneous Ewing sarcoma (EWS).
Materials and Methods: Retrospective study (1999-2012) on 57 patients treated in France ($n = 38$) and in two UK centres ($n = 19$).
Results: Most primary cutaneous/subcutaneous EWS occurred in late adolescent/young adult females (F/M 1.8; median age 21 years), with primary localization in the extremity (47%) and trunk (41%). Only 35/57 samples had RT-PCR or FISH analysis, 32/35 (91%) had EWS-translocation. Most of them had known good prognostic factors: localized disease in 54/57 and tumour volume $< 200mL$ in 55/57. 31 patients received chemotherapy according to Euro-Ewing99 protocol and 25 according to a shorter or less intense regimen, associated with milder toxicity. One patient did not receive chemotherapy. Surgery was performed at diagnosis in 37 patients, leading to a marginal or intra-lesional resection in 22/37; a secondary surgery was performed in 13/37. The 20 other patients had an initial biopsy, followed by chemotherapy in 18; only two patients progressed during neo-adjuvant chemotherapy and 16/18 underwent late surgery; only 4/16 had a marginal/intra-lesional resection. Overall, 26/57 received radiotherapy. Median follow-up was 6 years (1-15). All 3 patients with metastatic disease relapsed at metastatic sites. Four patients with localized disease experienced a progression/relapse (2/31 Euro-Ewing99; 2/25 others): locally in three patients, at 4, 5 and 30 months, and at metastatic site at 25 months in one case. Survival was excellent: 5y-OS and 5y-EFS were 92% (95%CI, 80-97%) and 87% (95%CI, 75-93%), respectively.
Conclusions: Initial surgery cannot be recommended. Biopsy with molecular analysis should be performed before any treatment decision. An extensive staging at diagnosis should be performed. Metastatic patients should be treated as other metastatic EWS. Further study is necessary to know whether a less-intensive chemotherapy regimen adapted to minimized acute and late toxicities could be safely used in localized disease.

O-0118

EXPRESSION OF NEURAL TISSUE-SPECIFIC INTERMEDIATE PROTEINS IN CLEAR CELL SARCOMA OF KIDNEY

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Purpose/Objective: Clear cell sarcoma of the kidney (CCSK) is the second most frequent pediatric renal tumor and is considered to be a highly malignant mesenchymal tumor. It is sometimes difficult to differentiate CCSK from other renal tumors on conventional histopathology and immunohistochemistry. Employing comparative proteomics analysis, we recently found that internexin alpha (INA), one of neural tissue*specific intermediate filament proteins (IMFs), is highly expressed in CCSK and immunohistochemical detection of INA is useful for differentiating CCSK from other pediatric renal tumors. To verify the possible neurogenic property of CCSK, we examined expression of other neural tissue-specific IMFs in CCSK.
Materials and Methods: Twenty-two CCSKs with typical histological features were collected from archives of our institutes. Immunohistochemical study for INA, neurofilament proteins (NFPs: low- medium- and high-molecular weight, NFP-L, NFP-M, NFP-H) and peripherin were performed on formalin-fixed paraffin-embedded tissue sections of each tumor. Western blotting analysis was subsequently performed to confirm the presence of the IMFs detected.
Results: On immunohistochemistry, all 22 CCSKs were INA-positive, and 19 of 22 were positive for NFP-L and /or NFP-M. No case was positive for NFP-H and peripherin. On western blotting, 3 CCSKs examined showed positive bands for INA, NFP-L and NFP-M.
Conclusions: Expression of NFP-L and/or NFP-M was confirmed in CCSK, as well as INA. INA is expressed in fetal neural tissue earlier than NFPs, and NFP-L and NFL-M are considered to appear subsequently. Expression of these three IMFs may suggest that CCSK has a character of early neurogenic differentiation. This finding would be useful not only for histopathological differential diagnosis but also for making therapeutic strategy.

O-0119

STAT3 INHIBITS WTX EXPRESSION THROUGH UP-REGULATION OF MICRORNA-370 IN WILMS TUMOR

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Purpose/Objective: Wilms tumor (WT) is a genetically heterogeneous childhood kidney tumor. Several genetic mutations have been identified in WT patients, including inactivation of WTX, somatic stabilizing CTNNB1, and p53 mutations. However, the molecular mechanisms in tumorigenesis remain largely unexplored. Therefore, it is necessary to obtain more insight into underlying mechanisms. Here, we report a functional role of Stat3 in Wilms tumor proliferation, initially identified by the observation of activation in Wilms tumor tissues.
Materials and Methods: First, we analyzed Stat3 activation in 14 Primary Wilms tumor tissues and adjacent non-tumor tissues by way of western blot. To address the functions of Stat3 in Wilms tumors, G401 cells were exposed to IL-6, a classical Stat3 agonist, and assessed using an MTT assay. Then,to explore the specific target of Stat3 in Wilms tumor cells, microRNA (miR) arrays prepared from G401 cells were performed. In order to investigate the roles of microRNA in Wilms tumors, we transfected a microRNA mimic into

G401 cells and measured cell proliferation. Finally,to predict the possible target gene of microRNA, we carried out a computational analysis on Targetscan and confirmed by luciferase reporter activity assay.
Results: We show that Stat3 is highly activated in Wilms tumor tissues compared to those in adjacent tissues. IL-6 treatment or transfection of a constitutively activated Stat3 in G401 cells promotes cell proliferation. At the molecular level, we further elucidate that Stat3 inhibits WTX expression through up-regulation of microRNA-370.
Conclusions: Stat3 activation could increase the proliferation of Wilm tumor cells, at least in part, through up-regulation of miR-370, which in turn down-regulates the tumor suppressor gene WTX. Understanding the precise roles played by Stat3/microRNA-370/WTX regulatory axis will not only advance our knowledge of Wilms tumor biology, but also will help determine if Stat3 and miR-370 has potential as a novel therapeutic target for the treatment of Wilms tumor.

FREE PAPER SESSION: FREE PAPER SESSION 22 - LYMPHOMA

O-0120

TRANSCRIPTION ACTIVATOR-LIKE EFFECTOR NUCLEASES (TALENS) MEDIATED DLEU1 GENE DISRUPTION SUPPRESSES APOPTOSIS IN PEDIATRIC BURKITT LYMPHOMA (PBL): DLEU1 MAYBE A TUMOR SUPPRESSOR GENE IN PBL

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Purpose/Objective: Pediatric Burkitt Lymphoma (PBL) is the most common histological subtype of children and adolescent Non Hodgkin Lymphoma (Cairo et al, Blood, 2007; Miles/Cairo, BJHaem, 2012). We previously identified in a subset analysis that children with BL and a 13q deletion, particularly 13q14.3 had significantly poorer outcome and inferior event free survival despite aggressive short, intensive multiagent chemotherapy (Poirel/Cairo et al, Leukemia, 2009; Nelson/Cairo/Sanger et al, BJHaem, 2009). Deleted in Lymphocytic Leukemia 1 (DLEU1) is a BL classifier gene (Dave et al, NEJM, 2006) located on chr.13q14.3. We have previously reported that Transcription Activator-Like Effector Nucleases (TALENs) mediated down-regulation of DLEU1in Raji and decreased the spontaneous apoptotic rate (Lee/Cairo et al, ASH, 2012). We hypothesize that DLEU1 may act as a tumor suppressor and therefore investigated whether the loss of DLEU1in BL result in changes in programmed cell death and associated signaling pathways.
Materials and Methods: TALENs induced DLEU1 gene disruption in Raji (BL). Caspase 3/7 and MTS assays were performed for BL proliferation and apoptosis analysis, respectively. qRT-PCR and immune-blotting were performed for mRNA and protein levels and statistical significance was determined by Student t-test.
Results: DLEU1 knockout (dleu1$^{+/-}$) in Raji (BL) exhibited significantly reduced mRNA reduction (80%. p$^{+/-}$ Raji cells.
Conclusions: TALENs mediated DLEU1 gene disruption resulted in down regulation of DLEU1 mRNA and consequently, inhibition of BL apoptosis and caspase 3/7 activities. We hypothesize that deletion of DLEU1 in childhood BL may result in chemotherapy resistance secondarily to a loss of a tumor suppressor gene.

O-0121

EVALUATATION OF THE EXPRESSION OF NPM-ALK FUSION TRANSCRIPT IN PERIPHERAL BLOOD AND BONE MARROW IN CHILDREN WITH ALCL.

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Purpose/Objective: The risk of relapse and disease progression in children with Anaplastic Large-Cell Lymphoma (ALCL) is still very high. The aim of this trial was improvement of diagnosis, monitoring and evaluation of response in patients(pts) with ALCL. From 2009 to 2012 in a molecular study making use of RT/RQ-PCR assay we evaluated the expression of NPM-ALK fusion transcript (NPM-ALK) in children with ALCL in peripheral blood(PB) and bone marrow(BM).
Materials and Methods: 19 pts were enrolled with ALCL (9/M,10/F), aged 22-217months (average:126), in stage II-1,III-10,IV-5,NA-3, in the risk group:HR-16 NA-3, with follow-up 6-65months (average:23.7). In total 90 samples of RNA were analyzed (33/BM, 57/PB).

Molecular tests were performed: at the beginning and the end of treatment, at the time of relapse/progression, before and after Hematopoietic Stem Cell Transplantation(HSCT), and lastly upon achieving complete remission(CR) of the disease.
Results: Of the RNA samples analyzed, NPM-ALK was confirmed in: 19/33 BM (57.6%) and 19/57 PB (33%). The level of the NPM/ALK varied in BM: 0.03-693.00(average:99.6) and in PB:0.11* 4365.45(average:151.97). It was hypothesized that the level of expression of NMP-ALK/10,000 fusion transcript should be a confirmation of activity of the disease on the molecular level. 7of 9pts with relapsed ALCL were confirmed to have a high level of the NPM-ALK at the beginning of treatment, which increased under chemotheraphy to reach an undetected level. At the moment of relapse/progression there was a significant increase in the level of the NPM-ALK in PB and/or BM, with higher level in PB than BM (45:0; 1533:201; 99:25).
Conclusions: Preliminary results show that during progression of disease the expression level of NPM-ALK transcript was remarkably higher in PB as compared to BM.
In summary, a systematic examination of the NPM-ALK fusion transcript in PB is recommended in pts with ALCL, especially for pts with an initially high level of NPM/ALK (indicating a high risk of relapse).

O-0122

FDG-PET AFTER TWO CYCLES OF CHEMOTHERAPY PREDICTS TREATMENT FAILURE AND PROGRESSION-FREE SURVIVAL IN ADVANCED PEDIATRIC HODGKIN LYMPHOMA

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Purpose/Objective: Risk-adapted Hodgkin lymphoma treatment in children requires early and precise assessment of prognosis. Starting from January 2005, newly diagnosed children with advanced Hodgkin's lymphoma (HL) were enrolled to assess the prognostic role of an early interim 2-[18 F] Fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scan and the other prognostic factors in advanced HL, treated with conventional ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) therapy.
Materials and Methods: 112 newly diagnosed children underwent FDG-PET at staging, after two-three cycles (PET-2), and completion of chemotherapy. No treatment change was allowed on the basis of the PET-2 results.
Results: The median age was 9 years and median follow-up was 40 months. After two cycles of chemo- therapy, 70 (69%) patients had negative FDG-PET scans and 32(31%) patients had positive scans. Twelve of 32 FDG-PET*positive patients progressed and seven of 70 FDG-PET*negative patients progressed. Survival analyses showed strong associations between interim FDG-PET and PFS ($P < .002$) and OS ($P < .006$). The OS and PFS was 93% and 91% for patients with negative PET-2 whereas OS and PFS was 72% and 68% respectively for slow early responders. None of the patients with stage II or stage III without B symptoms or bulky disease and negative PET-2 relapsed. For prediction of PFS, PET-2 was as accurate as post completion PET and superior to computerized tomography (CT) at all times. No patient in metabolic CR after 2 cycles showed progression at the end of therapy. In regression analyses, early interim FDG-PET was stronger than the established prognostic factors.
Conclusions: Early interim FDG-PET is a strong and independent predictor of PFS in advanced HL in children. After demonstration of CR on interim PET, there is no incremental value of repeating the scan after completion of therapy.

O-0123

IMPROVED TREATMENT OUTCOME IN CHINESE CHILDREN AND ADOLESCENTS WITH ANAPLASTIC LARGE T-CELL LYMPHOMA BY USING A MODIFIED B-NHL-BFM-90 PROTOCOL

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Purpose/Objective: Anaplastic large T-cell lymphoma (ALCL) is an aggressive malignance disease in children and adolescents. Different protocols have been adopted in the treatment of ALCL including the short-pulse therapy such as B-NHL-BFM 90 protocol and leukemia-like protocols. This study was designed to evaluate the efficacy and toxicity of the modified B-NHL-BFM 90 protocol in Chinese children and adolescents with ALCL
Materials and Methods: From October 2002 to March 2011, 38 untreated patients with ALCL from a single institution were enrolled. The patients were stratified into three groups according to risk factors (a modified St Jude stage and chemotherapy response).Low risk group (R1) was defined as patients with I/II disease, intermediate risk group (R2) was defined as stages III disease, high risk group (R3) was defined as stage IV disease and R2 patients with partial remission (PR) after AA and BB courses. All patients were treated with the

modified B-NHL-BFM 90 protocol. The patients in group R1 received four courses(A-B-A-B), group R2 received six courses(v-AA-BB-AA-BB-AA-BB)and Group R3 received six courses(v-AA-BB-CC-AA-BB-CC).
Results: Of the 38 patients, with a median age at diagnosis of 10 yr (range 2*16 yr). Thirty-one cases (81.6%) were ALK positive, 3 cases (7.9%) were ALK negative, and 4 cases (10.5%) were not done. Four patients (10.5%) had assigned into group R1, 13(34.2%) in group R2 and 21(55.3%) in group R3. About 89.5% of patients were stage III/IV. At a median follow up of 42 months, the 5-year event free survival (EFS) for all patients were 83.7% ± 6.1% with 100% for group R1, 84.6% ± 10% for group R2 and 80.7% ± 8.7% for group R3. The major toxicity complications were myelosuppression and mucositis, but these conditions were tolerated and manageable.
Conclusions: Our study showed that the modified B-NHL-BFM-90 protocol is highly effective and improves the survival for Chinese children and adolescents with ALCL.

O-0124

TREATMENT OF CHILDREN WITH ADVANCED-STAGE LYMPHOBLASTIC LYMPHOMA WITH PEGASPARGASE

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Purpose/Objective: The objective is to evaluate the feasibility of pegaspargase(PEG-asparaginase) taking place of L-asparaginase to treat children with advanced-stage LBL on the Non-Hodgkin's Lymphoma-Berlin-Frankfurt- Munster 95 regimen.
Materials and Methods: Between 2000 and 2006, 54 newly diagnosed patients with stage ? or ? LBL(30 stage ? and 24 stage ?) and without any treatment before were enrolled in this study. PEG-asparaginase took place of L-asparaginase in NHL-BFM95. The complications and treatment responses of patients treated on the modified NHL-BFM-95 protocol and BFM-95 protocol were then evaluated respectively.
Results: Patients' treatment responses were evaluated on day33 of induction and at the end of chemotherapy. The CR rate was 97% in the modified NHL-BFM-95 group and 94% in the NHL-BFM-95 group. The 5-year overall survival rates were 91% with NHL-BFM-95 versus 90% with modified NHL-BFM-95, and the event-free survival rates were 83% with NHL-BFM-95 versus 87% with modified NHL-BFM-95. During induction, stage 4 myelosuppression was the most common complication in two groups of patients. Among 31 patients receiving pegaspargase during induction and reinduction phases, five patients(16%) experienced grade 3 coagulation defects, one(3%) developed grade 3 anaphylactic reaction. Five(16%) developed mild liver dysfunction. In addition, there was another grade 2 complication in one(3%) patient, who developed mild pancreatitis. The other 23 patients had receivied BFM-95 protocol. Ten(43.5%) of 23 patients experienced grade 3 allergic reaction during the later period of chemotherapy. One(4.3%) had a sever allergic shock. 7(30.4%) of them experienced grade 2 pancreatitis.
Conclusions: For patients with LBL, compared NHL-BFM 95 protocol with modified NHL-BFM 95 protocol, the CR rate, EFS, OS were similar but the kinds of complications were different. PEG-asparaginase can reduce the incidence of allergic reaction and increase patient's compliance to chemotherapy. However, dysfunction of liver and coagulation system was apparent with PEG-asparaginase.

O-0125

COMPARISON OF PRESENTATION AND OUTCOME IN 100 PEDIATRIC PATIENTS WITH HODGKIN LYMPHOMA TREATED AT CHILDREN HOSPITAL, LAHORE, PAKISTAN AND ROYAL MARSDEN HOSPITAL, UK

M. Faizan[1], M. Taj[2], S. Anwar[1], N. Asghar[1], A. Ahmad[1], D. Lancaster[2], A. Atra[2], G. Hanif[3], N. Abbas[1], S. Mahmood[1], A. Shabbir Ali[1]

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Purpose/Objective: Hodgkins lymphoma (HL) exhibits distinct characteristics in the developing and developed world. A retrospective study was conducted to compare differences in demographics and outcome in childhood HL presenting at the Children's Hospital, Lahore and Royal Marsden, UK. Once basic presentation is known, further studies can tell whether differences are due to environmental/ social circumstances or indicate racial/ genetic variation
Materials and Methods: Hundred consecutive patients of HL, 50 each from Children's Hospital and Royal Marsden were evaluated retrospectively. Data regarding age, gender, staging, histopathology, and outcome were analyzed. Clinical and pathological staging done according to Ann-Arbor and new world health organization classification respectively.
Results: Patients presenting to Children's Hospital were younger (mean 8years) with male predominance 42(84%). Histopathology showed mixed cellularity (MC) 32(64%), nodular sclerosis (NS) 5(10%), lymphocyte rich 4(8%), lymphocyte depleted 1(2%), nodular lymphocyte predominant (NLP) 1(2%) and unspecified in 7(14%) patients. Presentation was stage IV 25(50%), stage III 20(40%), and stage II in 4(8%) patients. Constitutional B symptoms were present in 37(74%). Bone marrow involvement 23(46%) was common. Total 42(84%) patients completed treatment and are in remission, 1(2%) relapsed, 5(10%) expired and 2(4%) left against medical advice. In contrast Royal Marsden Patients were older (mean 12 yrs.) with 30(60%) males. NS 40 (80%) and NLP 6 (12%) were predominant and 1(2%) had MC disease. Presentation was Stage I 2(4%), Stage II 27(54%), Stage III 12(24%) and Stage IV 9(18%). Only 14(28%) had B symptoms. No patient had bone marrow disease. Event free survival was 46(92%).Four (8%) patients relapsed. Three responded to second line therapy and one relapsed post autologous transplant.
Conclusions: Our study confirms varied presentation. Delayed diagnosis could account for advanced stage but difference in pathological subtype needs further study. Of interest is bone marrow involvement in stage IV patients in Pakistan. Further research is required in this regard.

FREE PAPER SESSION: FREE PAPER SESSION 23 - BRAIN TUMOURS III

O-0126

ACNS0831: A CHILDREN'S ONCOLOGY GROUP PHASE III RANDOMIZED TRIAL OF POST-RADIATION CHEMOTHERAPY IN PATIENTS WITH NEWLY DIAGNOSED EPENDYMOMA AGES 1 TO 21 YEARS

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Purpose/Objective: Primary aim: to determine event free survival (EFS) and overall survival (OS) of children with completely resected ependymoma treated with post-operative conformal radiation therapy (cRT) then randomized to either receive four cycles of post radiation maintenance chemotherapy (VCEC) or RT only. Secondary aims: 2a) estimate EFS and OS of children with incompletely resected ependymoma unable to achieve a complete response (CR) by either post-operative induction chemotherapy or second surgery, 2b) evaluate EFS and OS of children with supratentorial classic ependymoma who achieve complete resection or CR to induction chemotherapy, 2c) determine neurologic, neuropsychological and endocrine sequelae compared to ACNS0121 2d) determine biologic prognostic factors of childhood ependymoma.
Materials and Methods: Completely resected (GTR1) classic (WHO Grade II) supratentorial tumors(ST) will be observed only. Patients with classic ST tumors (GTR2/NTR), anaplastic ST tumors and infratentorial tumors grade II or III with GTR1/2/NTR will be randomized. All patients with sub-total resection (STR) will undergo induction chemotherapy and be evaluated for response and considered for second look surgery. ST classic ependymoma who achieve a CR following induction or GTR1 at second surgery will be observed. All patients with STR who cannot achieve CR after induction chemotherapy or at least NTR after second surgery will be non-randomly assigned to receive maintenance chemotherapy. Target accrual: 400 total; 320 randomized.
Results: Study opened to accrual 3/29/2010. As of 9/30/12, 119 eligible patients enrolled. Eighty (80) randomized, 41 post cRT maintenance chemotherapy, 39 cRT only. Forty-one (41) (34%) supratentorial and 78(66%) infratentorial tumors. Fifteen(15) assigned to observation; 14 assigned to maintenance chemotherapy. COG sites with current IRB approval: 137/212.
Conclusions: Study continues to accrue. Routine adverse event collection on this study includes grade 4 or higher non-hematologic AE. As of 9/30/2012 no AdEERS reports filed and no unexpected toxicities reported.

O-0127

PRIMARY SPINAL CORD EPENDYMOMA WHO GRADE II AND III: A MULTI-INSTITUTIONAL EUROPEAN SERIES OF 40 PATIENTS

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Purpose/Objective: Purpose: The aim of this multi-institutional retrospective study is to collect clinical data of children and adolescents with primary spinal cord ependymoma WHO grade II and III within the SIOP Europe Brain Tumour Group.
Materials and Methods: Methods: Forty patients with spinal cord ependymoma WHO grade II (n = 29) or III (n = 11) were included (male, n = 22). Median age at diagnosis was 13.7 years. Median duration of symptoms was 2 months (data missing, n = 5).
Results: Results: A complete resection was achieved in 23 patients (58%). Seventeen patients (42%) underwent an incomplete resection. Twenty-two patients (55%) received postoperative radiotherapy and 10 (25%) chemotherapy. With a median follow-up of 4.2 years 36 patients (90%) were alive. Three patient died due to progressive disease (WHO grade II, n = 1; WHO grade III, n = 2; data missing, n = 1). Twenty-five patients (62.5%) were in complete remission at last follow-up. Eleven patients (27.5%) were alive with stable (n = 9) or progressive (n = 2) residual tumors. Estimated progression-free (PFS) and overall survival (OS) at 5 years are 81% and 97% for the entire cohort (89% after complete and 70% after incomplete resection [p = 0.26]). Estimated 5-year PFS and OS for WHO grade II tumors are 85% and 100% (100% after complete, 77% after incomplete resection [p = 0.59]). For spinal cord ependymoma WHO grade III 5-year PFS and OS are 71% and 89% (86% after complete, 50% after incomplete resection [p = 0.33]).
Conclusions: Conclusions: Overall survival in patients with spinal cord ependymoma WHO grade II and III is favorable both after complete and incomplete resection. Progression-free survival is inferior in WHO grade III tumors. Patients undergoing complete resection have a non-significant trend towards better PFS compared to patients in whom an incomplete resection was achieved. Follow-up is too short to sufficiently identify late relapses. A higher number of patients is essential for a meaningful statistical analysis.

O-0128

MOLECULAR TARGETED THERAPIES OF CHILDHOOD CHOROID PLEXUS CARCINOMA

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Purpose/Objective: The overall objective is to identify novel, effective and relatively non-toxic lead compounds for the treatment of choroid plexus carcinoma (CPC)
Materials and Methods: We have generated a mouse model of CPC that develops in the hindbrain of Rb-/-; p53 -/-; Pten -/- conditional mice electroporated in utero with Cre recombinase. CPC cells isolated from these mice, transduced with luciferin and injected stereotactically into the IV ventricle of immunocompromised mice robustly form CPC in vivo, generating an orthotopic allograft model for in vivo efficacy studies. Isolated CPC cells were adapted to grow in stem cell culture conditions in 384 well plates amenable to unbiased, high throughput screen (HTS). Following 72 hrs of compound exposure, cell viability was measured using CellTiter-Glo reagent (Promega). Over 500,000 compounds were screened with a target screening complement of >1 million chemical entities consisting of various libraries.
Results: Of the first library that consisted of 6546 compounds, 691 demonstrated $>$ 80% activity against CPC cells and were taken forward from primary screen (single point screen of 10uM) to a secondary screen (dose response). A total of 64 unique active compounds were identified of which 29 were FDA approved. Two FDA approved compounds Gemcitabine (GEM) and Pemetrexed (PEM) showed penetration into the brain and tumor parenchyma and were tested in vivo using our CPC orthotopic allograft model as single agents and in combination. The median survival of vehicle (n = 31) and PEM (n = 9) was not significantly different (p = 0.6095) while GEM (n = 15) and GEM/PEM combination (n = 14) increase survival significantly (p = 0.0108 and p = 0.0059 respectively).
Conclusions: The methodology we describe here, from screening large numbers of compounds to preclinical testing using our mouse CPC model provides a promising approach that should significantly advance the efficiency and speed with which we discover and translate active compounds for clinical testing.

O-0129

EFFECTIVE THERAPEUTIC TARGETS IN METASTATIC MEDULLOBLASTOMA

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Purpose/Objective: Tumor metastases are a poor prognostic sign at presentation, and often lethal at recurrence. Medulloblastoma (MB), the most common malignant pediatric brain tumour, disseminates by shedding cells into the cerebrospinal fluid and forming secondary tumors at the surface of the frontal brain and spinal cord. Due to lack of animal models and limited availability of human samples, studies on metastatic MB are minimal, which is in striking contrast to remarkable progresses in understanding primary MB biology. Mechanisms driving MB dissemination have been largely assumed similar to the primary tumor.

This study's goals included: 1. Establish a novel metastatic MB mouse model; 2. Identify genes/pathways important for primary MB and metastases. 3. Uncover mechanism(s) of MB dissemination.
Materials and Methods: Using *Sleeping Beauty* (SB) transposon-based forward mutagenesis to create a novel mouse model; Using 454-deep sequencing to identify SB tansposon insertion sites; Using microarrays and exome sequencing for genomic and epigenomic profiling of human MB; Multiple molecular genetics approaches were used for validation studies.
Results: 1. Established a novel highly penetrant metastatic Shh MB mouse model *Math1SB11/SB transposon/Ptch*$^{+/-}$; 2. Identified 359 and 285 genes significantly associated with SB insertions, potentially important for the primary tumors and matched metastases, respectively, including known human MB genes and other cancer genes; 3. Illustrated that in both mouse and human, multiple metastases from a single animal are similar to each other, but are genetically highly divergent from their primary tumor due to clonal selection, revealing that both common and distinct biological pathways exist in primary MB and its metastases.
Conclusions: Clonal selection drives genetic divergence of metastases from the primary tumors; Failure to target both primary MB and its metastases may be responsible for current ineffective treatments on metastatic MB patients; Common genes/pathways shared by primary MB and matched metastases should be prioritized as therapeutic molecular targets for metastatic MB.

O-0130

MOLECULAR GENETIC ALTERATIONS IN CNS-PNETS SUGGEST SIGNIFICANT OVERLAP WITH VARIOUS WELL-DEFINED ENTITIES

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Purpose/Objective: Childhood CNS primitive neuro-ectodermal tumors (CNS-PNETs; WHO IV) are classified as poorly differentiated embryonal tumors with early onset and aggressive clinical behavior. Absence of a clear histomorphological pattern and divergent differentiation along neuronal, astrocytic, or ependymal lines render histologic diagnosis complicated. We recently identified molecular subgroups of CNS-PNETs with biological characteristics similar to other childhood CNS tumors. This study further investigates the molecular heterogeneity of CNS-PNETs in relation to other childhood brain tumors.
Materials and Methods: A cohort of 147 tumor samples with an institutional diagnosis 'CNS-PNET' was investigated for genome-wide DNA methylation patterns and copy-number aberrations, complemented by transcriptional profiling of a subset of tumors (n = 45). Sequencing of *H3F3A* and *IDH1*, immunostaining for INI1, LIN28A, and OLIG2, and Fluorescence *In Situ* Hybridization for 19q13.42 was performed for selected cases. CNS-PNET characteristics were compared to the genetic make-up of >500 other childhood brain tumors including medulloblastomas, pilocytic astrocytomas, ependymomas, glioblastomas, AT/RTs, and ETMRs.
Results: Pediatric brain tumor samples could be segregated by histologic entity and molecular subgroup using unsupervised clustering methods of DNA methylation and gene expression profiles. However, CNS-PNETs did not form a separate cluster, but were scattered across the entire spectrum of entities. Genome-wide profiles and molecular aberrations of CNS-PNETs frequently resembled those of ETMRs (focal amplification of 19q13.42 and high expression of LIN28A), AT/RTs (loss of 22q and absence of INI1 expression), and glioblastomas (mutations in *H3F3A* or *IDH1*).
Conclusions: The correct classification of CNS-PNET remains contentious. Using molecular diagnostic tools, many cases could reliably be re-classified as ETMRs, AT/RTs, or glioblastomas based on recurrent genetic aberrations. Genome-wide profiling further indicates misdiagnosed medulloblastomas or supratentorial ependymomas, suggesting that a significant proportion of CNS-PNETs may comprise a variety of other tumor subtypes. These findings warrant deeper molecular analysis and central histopathological re-evaluation of this group of tumors.

O-0131

BET BROMODOMAIN INHIBITION OF MYC-AMPLIFIED MEDULLOBLASTOMA

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Purpose/Objective: Group 3 medulloblastomas are highly lethal tumors characterized by *MYC*-amplification. It was recently discovered that drugs targeting bromodomain-containing proteins effectively shut down MYC-associated transcriptional activity. JQ1 is a compound that inhibits BRD4, a BET bromodomain-containing protein expressed in Group 3 medulloblastomas. Here, we investigate BET bromodomain targeting for the treatment of Group 3 medulloblastoma.
Materials and Methods: We tested the efficacy of JQ1 in established and newly generated patient- and GEMM-derived Group 3 medulloblastoma cell lines and xenografts, in vitro and in vivo. Non-*MYC*-amplified cell lines and normal human SVZ-derived neural stem cells were tested as controls. We performed cell cycle profiling and analyzed markers for apoptosis, senescence and differentiation after treatment with JQ1 versus control. The effect of JQ1 on MYC expression and global MYC-associated transcriptional activity was assessed by quantitative real time PCR and gene expression microarray profiling, respectively. *In vivo* efficacy of JQ1 was assessed in orthotopic xenografts established in immunocompromised mice.
Results: Treatment of *MYC*-amplified medulloblastoma cells with the active isomer of JQ1 (JQ1-S) resulted in decreased cell viability compared to treatment with the inactive enantiomer (JQ1-R). This corresponded with the down-regulation of MYC expression and MYC-associated transcriptional activity. JQ1-S treatment also resulted in a decrease in the percentage of cells transitioning through S phase compared to cells treated with JQ1-R. In contrast, no effect was observed with JQ1 on neural stem cells derived from the subventricular zone. JQ1 significantly prolonged survival of xenograft models of MYC amplified medulloblastoma ($p < 0.001$).
Conclusions: JQ1 represses MYC expression and MYC-associated transcriptional activity in Group 3 medulloblastomas, resulting in an overall decrease in medulloblastoma cell viability. These preclinical findings highlight the promise of BET bromodomain inhibitors as novel agents for MYC-driven medulloblastomas.

FREE PAPER SESSION: FREE PAPER SESSION 24 - RENAL AND SARCOMAS III

O-0132

NON PARAMENINGEAL HEAD-AND-NECK RHABDOMYOSARCOMA IN CHILDREN AND ADOLESCENT: A VERY LONG TERM EXPERIENCE OF THE INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY MALIGNANT MESENCHYMAL TUMOR (SIOP-MMT) COMMITTEE.

D. Orbach[1], V. Mosseri[2], M. Stevens[3], A. Rey[4], S. Gallelo[5], A. Kelsey[6], D. Christine[7], B. Brenann[8], M. Van Noesel[9], M. Gaze[10], V. Minard-Collin[11], H. Merks[12], C. Bergeron[13], C. Rechnitzer[14], M. Jenney[15], J. Chisholm[16], M. Scopinaro[17], H. Martelli[18], O. Oberlin[19]

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Purpose/Objective: Around 10% of all rhabdomyosarcomas (RMS) occur at non-parameningeal head and neck sites (NPM-HN). This study was set up to analyze risk factors and long term outcome in NPM-HN RMS in children and adolescents.
Materials and Methods: In the SIOP-MMT 84, 89 and 95 studies in total 140 children with localized NPM-HN RMS were prospectively enrolled (9.3%). After primary surgery or biopsy, all children received ifosfamide/actinomycin/vincristine-based chemotherapy. Radiotherapy and surgery were administered in patients failing to achieve complete remission.
Results: Median age at diagnosis was 5 years (ranges: 0-18). Superficial facial primary represents 46% of all tumors, oral cavity 21.5%, cervical 19.5% and salivary glands 13.5%. In 73% the tumors were small (Outcome: Local control was achieved in 96% of patients but 49% relapsed, mainly loco-regionally (92%). Five patients develop a secondary osteosarcoma. After a median follow-up of 10 years [0.1-25 years], 10-year overall survival (10Y-OS) was 70.2% (95%CI: 62.3%-78.1%) and disease free survival (10Y-DFS) 47.1% (95%CI: 38.7%-55.5%). In univariate analysis, age, gender, histology, size or specific HN locations, does neither influence DFS nor OS. The 10Y-OS was dependent on nodal involvement (N0: 75.4% vs. N1: 52.2%, p
Conclusions: Prolonged control is critical in NPM-HN RMS with frequent loco-regional relapses. Systematic use of radiotherapy avoidance in selected case in this location does not influence overall survival. Survival is better with recent protocol.

O-0133

INTERSTITIAL BRACHYTHERAPY FOR CHILDHOOD SOFT TISSUE SARCOMAS: LONG TERM DISEASE OUTCOME & LATE EFFECTS

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Purpose/Objective: To evaluate the clinical outcome & long term adverse effects of interstitial brachytherapy (BRT) for children with soft tissue sarcomas (STS).
Materials and Methods: From September 1984 to Dec 2012, 76 children (median age 15 years, range 1 to 18) with STS who received BRT as part of loco-regional treatment were included. There were 45 males and 31 females. Majority (74%) had primary lesions. Synovial sarcoma (30%) was the most common histological type, and 44% had high-grade lesions. Treatment included wide local excision and BRT with or without external beam radiotherapy (EBRT). Forty children (66%) received BRT alone.
Results: After a median follow-up of 68 months, the local control (LC), disease-free survival (DFS), and overall survival (OS) were 85%, 74%, and 77%, respectively. LC was superior in patients with tumor size $\leq$5 cm versus $>$5 cm (96% vs. 78%, $p = 0.08$), symptom duration $<$2 months versus $>$2 months (100% vs. 81%, $p = 0.06$), and Grade I versus Grade II versus Grade III tumors (100% vs. 95% vs. 70%, $p = 0.02$). Children receiving a combination of BRT and EBRT had comparable LC to those receiving BRT alone (76% vs. 89%, $p = 0.28$). There was no significant difference in LC for patients receiving LDR versus HDR BRT (84% vs. 95%, $p = 0.31$, for BRT alone; and 73% vs. 83%, $p = 0.60$, for BRT + EBRT). Surgical wound healing complications was seen in 8% patients. Subcutaneous fibrosis (31%) was the commonest late complication followed by distal limb edema (5%), joint stiffness (3.3%), & bone growth abnormality (1.6%). There was no neuropathy, non-healing ulcer or second malignancy.
Conclusions: Interstitial BRT with or without EBRT result in excellent outcome in children with STS. Radical BRT alone, when used judiciously in select groups of children, results in excellent local control and functional outcome with reduced treatment-related morbidity.

O-0134

KAPOSI SARCOMA: IS THE PROFILE CHANGING?

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Purpose/Objective: Kaposi Sarcoma (KS) is an Aids defining malignancy. The aim was to describe two different cohorts of patients with KS, the 1st that started ARVs at diagnosis or never received ARVs and the 2nd on ARVs when diagnosed.
Materials and Methods: Retrospective study of HIV positive patients with KS who were seen between 1990 and 2011.
Results: A total of 33 patients were seen, of whom 57% were male, male to female ratio for 1st cohort was 1:1; while in the second cohort it was 4:1. The average age for the whole group was 81 months with the second cohort almost 30 months older than the 1st cohort. Presentation was varied and the pattern changed from a predominance of visceral disease in the 1st cohort to skin and face or nodes in the second cohort. The number of severely immune supressed children was very similar in both cohorts. Only 4 patients received no treatment while the remainder had chemotherapy with or without ARVs depending on the cohort. Of the twenty nine patients who commenced chemotherapy only 12 patients are currently alive.
Conclusions: Yes, the profile has changed. In the 2nd cohort there were more males and their average age older. Clinical presentation seems to be more skin and face involvement and less visceral disease in the 2nd cohort. Patients with isolated skin lesions appear to have a worse outcome than other forms of KS. The percentage immune suppressed chilren is similar. The overall survival rate is 32%. Intent to cure survival rates are better with the 1st cohort doing better than the second cohort.

O-0135

METRONOMIC APPLICATION OF CYCLOPHOSPHAMIDE AND VINORELBINE FOR TREATMENT OF SOFT-TISSUE SARCOMA IN CHILDREN

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Purpose/Objective: Recent studies have demonstrated that maintenance therapy of children with soft-tissue sarcoma produces the treatment outcomes which are non-inferior and, according to some authors, even better than those of consolidating high-dose chemotherapy with peripheral blood stem cell transplantation. Protocol EpSSG RMS 2005 specified a combination of low dose cyclophosphamide and vinorelbine as maintenance chemotherapy for high and very high risk groups. The objective of this study was to evaluate the efficiency of metronomic chemotherapy in treatment of adult-type soft-tissue sarcoma in children.
Materials and Methods: In 2007*2012, metronomic chemotherapy was administered to 37 children with rhabdomyosarcoma in high and very high risk groups and 24 children with adult-type soft-tissue sarcoma. All patients received 24-week low dose metronomic maintenance therapy: vinorelbine 25 mg/m^2 (Days 1, 8, 15) intravenously, cyclophosphamide 25 mg/m^2 (Days 1*28) perorally. Direct side effects of vinorelbine administration were seen in 5 patients as vascular response (dizziness, slightly lower arterial blood pressure) and required no medicinal correction. The only further side effect in 50% of patients was non-febrile neutropenia III*IV that required vinorelbine dose adjustment in further administration (dose reduction to 66%).
Results: The overall survival in the group of patients with RMS was 66.7%. 15 of 27 patients, (55.5%) are now alive in prolonged remission with 11*48-month follow-up periods. 8 of 24 patients without rhabdomyosarcoma (31.2%) completed the treatment and are in remission with 15*37-month follow-up period. The overall survival in the group was 54.1%.
Conclusions: The above results demonstrate sufficient efficiency of maintenance low-dose metronomic chemotherapy for treatment of soft-tissue sarcoma in children.

O-0136

EVALUATION OF OUTCOME AND PROGNOSTIC FACTORS IN EXTRAOSSEOUS PRIMTIVE NEUROECTODERMAL TUMOR: A SINGLE INSTITUTIONAL EXPERIENCE OF 60 CASES WITH UNIFORM CHEMOTHERAPY PROTOCOL

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Purpose/Objective: Data on outcome and prognostic factors of extraosseous primitive neuroectodermal tumor (PNET) with uniform chemotherapy protocol is minimal.
Materials and Methods: This is single institutional data review of extraosseous PNET patients treated between June 2003 and November 2011 with uniform chemotherapy protocol and evaluated on intent-to-treat analysis. All patients received neoadjuvant chemotherapy (NACT), surgery and/or radiotherapy as local treatment followed by ACT.
Results: Of 374 patients with PNET, 60 (16%) were extraosseous PNET with median age 16 years (range: 0.1*48) and male:female of 7:3; 20 (33%) had metastases. Thirty patients underwent surgery; 15 patients received radical radiotherapy following NACT. After median follow up of 21.7 months (range: 1.7-97.8), 5-year EFS, OS and local control rate were 47.1 $\pm$ 8.1%, 61.6 $\pm$ 8.1% and 77.2 $\pm$ 8.9%, respectively for extraosseous PNET cohort. On multivariate analysis, hemoglobin $\leq$10 g/dl ($p = 0.02$) and white blood cell count (WBC) $>11 \times 10^9$/L ($p = 0.004$) predicted inferior EFS for entire cohort; whereas hemoglobin $\leq$10 g/dl ($p = 0.02$) and high lactate dehydrogenase (LDH) ($p = 0.02$) predicted inferior EFS for localized disease. Tumor size $>$8 cm ($p = 0.05$) and high LDH ($p = 0.01$) predicted inferior OS for entire cohort on multivariate analysis, whereas hemoglobin $\leq$10 g/dl ($p = 0.02$) predicted OS for localized disease. As compared to skeletal primary ($n = 314$), higher proportion of patients underwent surgical reception in extraosseous PNET ($p = 0.003$); EFS ($p = 0.006$) and OS ($p = 0.08$) were superior for extraosseous PNET than skeletal PNET.
Conclusions: Extraosseous PNET constituted 16% of the whole cohort and 33% had metastatic disease. We identified novel prognostic factors like low hemoglobin and high WBC count other than high LDH and tumor size. Overall outcome was significantly better for extraosseous PNET than skeletal primary, though clinicopathological features were almost similar in both the groups.

O-0137

HIGH SERUM MIR-206 EXPRESSION LEVELS DEFINE AN AGGRESSIVE RHABDOMYOSARCOMA SUBTYPE.

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Purpose/Objective: We previously showed that the absolute serum *miR-206* expression levels were higher in patients with ARMS than in patients with ERMS. However, it is unclear whether serum *miR-206* values are correlated with characteristics of tumors, such as tumor size, fusion gene status and metastatic status. Here, we analyzed the correlation using 22 RMS and 28 non-RMS serum specimens.
Materials and Methods: Total RNA was extracted from serum samples (200 μL) from 49 patients (13 alveolar RMS (ARMS), 8 embryonal RMS (ERMS), 28 non-RMS) and quantified by real-time quantitative RT-PCR. Absolute microRNA expression levels were determined by using a dilution series of synthetic *miR-206*. Expression levels of microRNAs were compared using the Mann*Whitney U test. Receiver-operating characteristics (ROC) curves were established to evaluate the diagnostic value of *miR-206*. The Spearman rank order correlation test was used to examine correlation relationships. A p-value of less than 0.05 was considered statistically significant.
Results: Serum *miR-206* expression levels were higher in RMS patients than in non-RMS patients ($p < 0.001$) with a sensitivity of 0.809 and a specificity of 0.893. The absolute serum *miR-206* expression levels were higher in patients with fusion gene positive RMS than in patients with fusion gene negative RMS ($p = 0.045$). The serum *miR-206* value was not correlated with tumor size ($p = 0.719$) or tumor *miR-206* expression level ($p = 0.45$). The absolute serum *miR-206* expression levels were higher in patients with metastatic RMS (distant metastasis or regional lymph node positive) than in patients with localized RMS ($p = 0.01$).
Conclusions: Serum *miR-206* is a reliable diagnostic biomarker for RMS. Our results show that serum *miR-206* expression level is correlated with metastatic status and fusion gene status, suggesting that high serum *miR-206* value is an indicator of a poor prognosis. Our next goal is to test this hypothesis in large cohort studies.

NURSES: NURSES - NURSE EDUCATION IN COUNTRIES WITH LIMITED RESOURCES

O-0138

THE DEVELOPMENT OF A PAEDIATRIC ONCOLOGY NURSING CURRICULUM FOR LOW AND MIDDLE-INCOME COUNTRIES

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Purpose/Objective: To create a forum for nurses caring for children and adolescents with cancer in low and middle-income countries (LMIC) to foster communication, interaction, mutual learning and collaboration with nurses from resource-rich countries.
To develop a paediatric oncology nursing curriculum adaptable to local settings in each country.
Materials and Methods: An initial questionnaire (needs survey) asked nurses in LMIC to identify areas of strength in their practice, and aspects of care requiring additional training. It was distributed to participants across Africa, Asia and Latin America. The results were used to develop a two-round 'Delphi survey' sent to nurses in resource-rich countries who had experience working in LMIC (principally in 'twinning projects) with the aim of identifying curricular strategies to build on the strengths of nurses working in LMIC, and elicit teaching solutions to the identified challenges. The results of both surveys formed the basis of a two-day nursing workshop attended by 16 nurses (8 from LMIC and 8 resource-rich countries).
Results: The results of both the 'Needs Survey' and the Delphi Survey showed a high degree of consensus in identifying the strengths and challenges of nurses working in LMIC.

During the two-day Workshop, key topic areas required in the development of the curriculum framework were identified, agreed and refined.

'Volunteer' partnerships were identified, a LMIC nurse with a nurse from a resource-rich country, to work on core modules. A module development template was created to support this pilot work.

LMIC nurses positively evaluated the Workshop mentioning areas of specific learning, personal growth, and empowered practice.
Conclusions: The diversity of participants from a range of geographical and cultural settings, and the mix of nurses from LMIC and resource-rich countries enabled nurses to work together and learn from each other. The final outcome, the curriculum framework, will be flexible and adaptable to a range of settings.

O-0139

DEVELOPMENT OF NURSES' TEACHING MODULE FOR INFECTION CONTROL AND VIDEOS FOR EDUCATING PARENTS IN LOCAL LANGUAGES AT KORLE-BU TEACHING HOSPITAL, GHANA

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Purpose/Objective: To develop a teaching module for nurses on infection control and to produce locally relevant educational material for parents that would help improve care for children with cancer in Ghana.
Materials and Methods: A pre-conference nurses' meeting was held in London just before SIOP 2012. Areas of need in childhood cancer care in resource limited countries were identified with particular emphasis on giving supportive care. Nurses from resource limited countries were paired with those from resource rich countries. A nurse from Korle Bu Teaching Hospital, Ghana was paired with a nurse from Royal Hospital for Sick Children, Edinburgh. This pairing was made because a World Child Cancer/Africa Oxford Cancer Foundation twinning programme between the two hospitals is already in place. We were tasked to develop a teaching module for nurses on infection control. A video camera was also given to be used in developing educational material in the local languages for parents and new nurses on the paediatric oncology ward.
Results: An infection control teaching module for nurses has been developed and is awaiting approval by the SIOP nurses' group. Areas covered include but are not limited to hand washing, isolation/barrier nursing and observing sterile procedures. Educational videos are also being developed for parents in local languages and in English for new nurses.
Conclusions: The pre-conference nurses' workshop gave us the opportunity to be able to work alongside nurses from resource rich countries to develop various curricula. The module on infection control will help us as nurses reduce deaths from infection.

The video for educating parents will lessen the burden of having to spend time talking to each parent. New nurses to the ward will learn a lot from the information in the videos.

This program has imparted more skills and new experience to those of us from resource poor countries.

O-0140

TEACHING PAIN ASSESSMENT AND CONTROL TO NURSES WORKING WITH CHILDREN WITH CANCER IN ETHIOPIA

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Purpose/Objective: Purpose - Improve pain control in children with cancer in Ethiopia. Tikur Anbessa Specialized General Hospital (TASGH) in Addis Ababa, is the only center in Ethiopia for cancer care. There are 91 million people, 83% of whom live in rural areas, and almost half live below the poverty line in the country. There are 40 available beds for children with cancer on two separate wards (0-4 and 5-12 years old) and generally on each ward three nurses work day shift and two on evening and night shifts.
Materials and Methods: The shortage of nurses makes pain assessment difficult; however, nurses are acutely aware of the children's pain and this causes them significant distress. The nurses asked a physician (a palliative care and pain specialist) to present an introduction to pain control. Paracetamol (suppository, syrup, and tablets), Diclofenac (injection), Tramadol (IM or IV), and morphine (syrup) are available. The use of morphine is new at the hospital and residents are not trained in pain control. The nurses, together with two visiting US nurses, created a pain module for nurses including: a repeat of the physician's presentation and a pain problem story with a critical thinking exercise. The nurses' learning was measured with a pre and post-test on pain beliefs and myths.
Results: Seven pediatric nurses participated in the class on nursing issues of children with cancer and pain. Pre- and post-test results were mixed and a new evaluation criteria is being considered.
Conclusions: Led by one experienced local nurse, the pediatric nurses are trying to increase all rotating nurses' awareness about nursing children with cancer in pain. The nurses are encouraged to advocate for the child with physicians (particularly the residents) and ensure that no child suffers. This objective is not without challenges in a local culture of strict physician and nurse hierarchies.

O-0141

PEDIATRIC ONCOLOGY NURSING CURRICULUM FOR DEVELOPING COUNTRIES: A COLLABORATIVE APPROACH

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Purpose/Objective: Through previous meetings of SIOP, the medical and nursing community in Africa expressed their need and desire for the assistance in developing a pediatric oncology nursing curriculum. Over the past three years nurses from British Columbia Children's Hospital (BCCH) and Johannesburg General Hospital (JGH) have been working collaboratively to develop pediatric oncology nursing curriculum that is currently being utilized at JGH and Chris Hani-Baragwanath Hospital (CHBH).
Materials and Methods: An initial site visit by BCCH nurse educator and pediatric oncologist allowed for an assessment of learning needs and infrastructure resources on the oncology units at JGH and CHBH. A resource nurse from JGH and CHBH was identified and a framework for the nursing curriculum was developed. Learning modules have been distributed at both sites over the last three years. Ongoing evaluations and subsequent adaptations of educational material and method of delivery have occurred with each module.
Results: Along with the acquisition of new knowledge, nurses from JGH have become empowered to share this knowledge with other medical professionals in primary health care facilities in Gauteng (Johannesburg). A workshop created and delivered by these nurses was very well received. The Childhood Cancer Foundation of South Africa (CHOC) therefore decided to fund a contract nursing position to provide pediatric oncology nursing education at primary health care facilities in Gauteng (Johannesburg) as a pilot study using the curriculum that has been developed. This allows for this standardized curriculum to be distributed in a more efficient manner. This position also allows for increasing awareness in these communities about pediatric oncology in hopes signs and symptoms are recognized sooner by all medical professionals
Conclusions: A collaborative approach to developing nursing curriculum in developing countries is crucial. International partnerships build capacity, share best practices, and build relationships for sustainable outcomes as demonstrated by the development of an education coordinator position in Johannesburg.

NURSES: NURSES - TALKING AND WORKING WITH CHILDREN AND TEENAGERS

O-0142

TALKING WITH CHILDREN WITH CANCER ABOUT THEIR DISEASE AND TREATMENT: AN ETHNOGRAPHIC STUDY OF EVERYDAY PRACTICE

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Purpose/Objective: Bluebond-Langner's highly influential ethnographic study in the 1970 s was the first of its kind to detail the everyday experiences of patients and their families during childhood cancer. The landscape of care and treatment is now very different, with families having a realistic expectation of cure, despite the continuing arduous nature of the treatment: our current study takes place in a very different medical and cultural context. As part of our on-going research programme to explore communication patterns, this study looks at the work of newly diagnosed children with leukaemia. We sought to enrich our understanding of the complicated context-related factors facilitating or barring successful communication.
Materials and Methods: An ethnographic approach using child-centred participatory methods (e.g. drawings, ratings games, play) was employed to allow children to tell their stories. Observations of children's communicative interactions with parents and health professionals were undertaken. Data collection took place across three inpatient and one outpatient wards at a large tertiary hospital in the UK over 12 months. The researcher spent 2-3 days in the field each week.
Results: Seven children and their families aged between 4 and 11 years participated. Nine themes concerning the 'work' of newly diagnosed children were identified. Formal and informal forms of communication were observed between health professionals and families. Communication focused mainly on treatment and disease updates. Less evidence existed of emotional and psycho-social support. Children took on multiple and often conflicting management roles (of the body, self, others and space), where they learnt very quickly the social norms and the language of cancer required to help them to grasp what they needed to know.
Conclusions: This presentation will focus briefly on the method of data collection to support findings shared. Comparisons will be drawn with Bluebond-Langner's previous work. Using these methods there is much we can learn to inform best practice in communication.

O-0143

PROCEDURE OF INFORMED ASSENT/CONSENT FOR CLINICAL TRIALS IN PEDIATRIC HEMATO-ONCOLOGY: THE ADOLESCENTS' AND PARENTS' POINT OF VIEW

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Purpose/Objective: Clinical trials require an assent by the adolescents to participate. Few literature data are available on the experiences expressed by adolescents. A study has been conducted to explore the personal views of adolescents and their parents in order to optimize this consent procedure.
Materials and Methods: Adolescents (n = 10) and their parents (n = 15) completed a questionnaire and were interviewed. Qualitative data were coded using NVIVO 8. Quantitative data were analyzed by the statistic program SPSS.
Results: All adolescents (> 13 years) want to be informed about the trial.

The majority of them want to co-decide. They want this from an average of 10 years (SD = 2,88) while parents indicate an average of 12,5 years (SD = 2,30).

Adolescents believe that their decision should be taken in consultation with parents and physicians. Parents are in favour of a unilateral decision only made by themselves (significant difference between adolescents and mothers, p = 0,008) or by a physician.

Adolescents and parents experience mostly positive emotions. Important preconditions for the adolescents were: presence of their parents and structured and clear approach by the physician during the informed consent (IC) interview.

The majority of the adolescents wanted information: as much as possible, adapted to their developmental level. There was a significant difference regarding the amount of information: males wanted more information than females (p = 0,033).

Both adolescents and parents are positive about participating in clinical trials: it's important to improve cancer treatment and it may help others.

Reported suggestions for improvement: no coincidence between IC and the diagnostic interview, more written/oral information for adolescents.
Conclusions: Despite this small sample, the results give us an insight into the adolescents' and parents' point of view.

These results are a first step towards the adaptation and the improvement of the departmental guidelines and towards the adjustment of the written information for adolescents about their participation in clinical trials.

O-0144

THE EVALUATION OF AN INTERNET-BASED TV CONFERENCE SYSTEM (TVCS) TO LINK CHILDREN UNDERGOING CHEMOTHERAPY IN HOSPITAL CLASS AND THEIR REGULAR SCHOOL CLASS

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Purpose/Objective: The aim of this study was to evaluate an internet-based TV Conference System (TVCS) to link children undergoing chemotherapy, who were enrolled in the hospital class, and their classmates in regular school, and to evaluate relationship of class development through the TVCS.
Materials and Methods: Research period: March 2009 to Jan. 2013. The 2 classes in the regular school and in the hospital were linked by optical broadband network on the TVCS over period of 3 to 5 months. We conducted 30-minutes interviews with 5 children, their mothers and teachers.
Results: The participants were 6 to 9-year-old children who were undergoing chemotherapy for solid tumors or leukemia. The intervention began when they transitioned from bedside learning to participation in a hospital classroom. The TVCS linked them with their home classmates, allowing them to talk via the TV screen. Sessions focused on informal conversation and recorder playing. In total, 3 to 9 sessions were held. The evaluation by parents revealed that initially, they were worried about when and how to contact with school, but they were happy their children could see their friends in the class. After leaving the hospital, they had no problems in relations with friends, and enjoyed playing and participating in other activities with classmates. The evaluation by their teachers revealed that none of the teachers had ever experienced taking care of children with cancer. After used TVCS, they were pleased very much, and the operation of the machine was very easy.
Conclusions: The establishment of bidirectional system strengthened communication between the school and hospital. Parents and teachers evaluated the TVCS with satisfaction. Children were able to participate in classes in their regular school via the system which facilitated friendships and reduced psychological isolation from the school, and enabled them to prepare to return to school after leaving the hospital.

O-0145

HOW EFFECTIVE IS PREPARATION IN PAEDIATRIC RADIOTHERAPY TO HELP REDUCE THE NEED FOR A GENERAL ANAESTHETIC (GA)?

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Purpose/Objective: A review of the efficacy of preparation methods used in Paediatric Radiotherapy in reducing the need for a General Anaesthetic (GA) when treating young children (3 * 7 years).
Materials and Methods: The creation the Paediatric Radiographer post in 2010 gave an opportunity to review preparation methods used for young children requiring treatment with the aim of reducing a GA need.

Following the review of practice, a process of preparation has been developed and implemented.

Families are invited to the department at an early stage so preparation began at the earliest opportunity.

Children are assessed by a Play Specialist who works to provide activities and a 'reward' system.

The Paediatric Radiographer has facilitated access to play sessions with the complex Linear Accelerators used to deliver treatment. Furthermore, a miniature replica model of a Linear Accelerator ('Baby Linac') has been built to support this.A 'buddy' system was set up in 2012, to widen the number of radiographers with knowledge and skills to provide support to families.
Results: Reviewing activity from the last 3 years demonstrated a steady decrease in the number of GAs required.

8/10 children required a GA in 2010 (80%).
10/14 children required a GA in 2011 (71%).
4/12 children required a GA in 2012 (33%).
Conclusions: The results demonstrate that the preparation methods used, in addition to collaborative working between members of the multidisciplinary team have been effective in reducing a GA need.

This has led to decreased risks to patients from daily GA, improved patient experience, as children do not need to fast for extended periods or spend time recovering from a GA, and shows significant cost benefits in releasing staff time.

There are still some children who require GA; reasons include positioning, language barriers, separation from parents and behavioural issues, which the team will continue to communicate, co-operate and address.

NURSES: NURSES - SHARING NURSING PRACTICE

O-0146

REVIEW OF SIOP ABSTRACTS 2003-2012: WHAT DOES THIS TELL US ABOUT OUR SPECIALTY?

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Purpose/Objective: Nurses have been regular participants at the SIOP congress since Jerusalem in 1987. Over the years the nursing programme has become more established, increasing in number of days as the quality and number of abstracts increased. Presentations have changed over the years with a predominate focus on reporting clinical practice being replaced by participants presenting research. The characteristics and focus of these presentations can offer a reflection on the changing landscape of our specialty: important for identifying trends, uncovering gaps, and providing new directions for research.
Materials and Methods: A retrospective review of abstracts submitted to SIOP between 2003-2012 is being undertaken utilizing the congress database of abstracts. A data extraction sheet is being used to ensure consistency of data retrieved, with paired researchers assessing each abstract prior to item review to promote reliability by multiple reviewers. One further member will check data sheets for consistency of recording, and resolve missing data. The review items allow extraction of data that relates to authorship, country of origin, focus, and population, area of inquiry, and methodology. Data will be entered into a bespoke database and summarized descriptively. Author's names are being used to identify subsequent publications that relate to the abstract.
Results: Ten years abstracts accepted for oral and poster abstracts will be reviewed. The data extraction is underway and will be completed by the summer.
Conclusions: Our specialty continues to develop in parallel to advances in medicine that requires new approaches to treatment and care. Nurses are constantly challenged to think differently about how they work, and how they can continue to deliver high quality care that is responsive to patient and family need, and evidence-based. We anticipate this presentation will provide examples of how practice has changed, and illuminate the importance of audit, service evaluation and research in informing change.

NURSES: NURSES - NUTRITION MATTERS

O-0147

ADEQUACY OF ENERGY INTAKE IN CHILDHOOD CANCER PATIENTS

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Purpose/Objective: Despite a widespread belief that adequate energy intake is needed to maintain weight during childhood cancer treatment, consensus on how to define adequate energy intake is lacking, and the impact of energy intake on weight has never been tested. Therefore, the objective of this study was: to evaluate which criterion is the best to determine the adequacy of energy intake during treatment within a heterogeneous childhood cancer population.
Materials and Methods: We conducted a prospective cohort study of 115 newly diagnosed cancer patients and assessed energy intake at diagnosis, 3, 6, and 12 months. Intake was compared to recommended daily allowances (RDA), healthy controls, individual energy requirements (IR) based on Schofield formula, and weight changes.
Results: Energy intake was lower than RDA and lower than in healthy Dutch children (according to a food consumption survey 2008/2011) (FCS) at all measurement points. About 41-56% of the patients had insufficient intake ($< 80\%$) according to RDA or FCS. Energy intake matched IR at diagnosis and 6 months. However, energy intake was higher than IR at 3 months ($P = 0.020$) and lower at 12 months after diagnosis ($P = 0.044$). According to IR, intake was insufficient in 13-30% of the patients.

During the study period, weight-for-age (WFA) increased from .01 SDS to .34 SDS ($P = 0.001$). Energy intake was not associated with increase of weight.
Conclusions: Despite energy intake being lower than RDA and FCS, weight increased. Obviously, childhood cancer patients need less energy than RDA or than healthy children. Instead of using RDA or FCS, adequacy of energy intake can better be evaluated with IR.

O-0148

DEVELOPMENT OF A MODIFIABLE NUTRITION ALGORITHM ADDRESSING NUTRITION GUIDELINES IN PAEDIATRIC ONCOLOGY: A REPORT FROM THE INTERNATIONAL PEDIATRIC ONCOLOGY NUTRITION GROUP

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Purpose/Objective: Despite advances in paediatric oncology, malnutrition is still a major concern across paediatric oncology sites in both High Income Countries (HIC) and Low Income Countries (LIC). Nutrition therapy is often neglected, despite studies demonstrating that the duration of malnutrition is strongly associated with poorer outcomes and that remediation of poor nutritional status results in survival comparable to that of children with optimal nutrition status. The International Paediatric Oncology Nutrition Group (IPONG) aims to develop a modifiable nutrition treatment algorithm to improve nutritional care in pediatric oncology patients.
Materials and Methods: The algorithm was designed utilizing an interdisciplinary process with evidence to serve as its guide when available. Review of algorithm was obtained by internal and external reviewers.
Results: *Phase 1 Consultation with the international community*: IPONG group members from both HIC and LIC were asked to provide nutrition algorithms/guidelines currently used in their hospital. *Phase 2 Review of the literature*: An extensive literature search was conducted across four electronic databases regarding: current standards of nutritional care and intervention in paediatric oncology. *Phase 3 Draft algorithm development*: A draft algorithm was developed from Group feedback and literature search. *Phase 4 Algorithm feedback*: Algorithm was presented at ANZCHOG (Aus 2012), SIOP (UK 2012), AHOPCA (El Salvador 2013) and to group members for feedback and discussion. *Phase 5 Consultation with LIC*: Feedback sort from LIC dieticians to identify additional options for oral supplements when limited nutrition supplements available. *Phase 6 Final review by expert panel*: A review panel of dieticians/nutritionists, nurses, and physicians from both HIC and LIC was established for final consultation of the algorithm.
Conclusions: IPONG have developed a nutrition treatment algorithm to improve nutritional care in paediatric oncology patients. The next step is to test the feasibility and effectiveness of the algorithm across international sites.

O-0149

THE EFFECT OF NUTRITION IN CANCER MANAGEMENT

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Purpose/Objective: To ensure how simple changes in diet availability, preparation and provision can make nutritional intake bearable, through giving appropriate education and information guidelines to nurses, care-givers patients and their families about nutritional needs of oncology patients
Materials and Methods: A prospective observational and cross sectional survey of 14 nurses, 26 patients,20 family members and 2 dieticians was done on a day to day basis; regarding environment, attitude, presentation and serving of meals in the unit

Cultural background was analyzed in relation to food handling, preparation, eating patterns, served portions especially for teenagers

Socio-economic issues were considered in relation to affordability when patients were discharged
Results: 85% nurses verbalized the challenges of having to serve standardized meals even if the patients' needs were different, 90% needed time and educational information on nutrition to educate and evaluate individual needs

Hospital stores supplies have a limited range which affects the kitchen's ability to provide food in the wards

80% of patient's nutritional status remained compromised by the effects of cancer, treatment, cultural and socio-economic issues when at home
Conclusions: Adequate nutrition is a cornerstone for improving chances of recovery as treatment effects are minimized, immunity and response to treatment is improved which enhances quality of life. Empowering nurses with skills and knowledge is a way forward because nurses are responsible in ensuring nutritional support

NURSES: NURSES/PARENTS SESSION - "EAT UP YOUR GREENS!" – THE IMPORTANCE OF NUTRITION IN CHILDHOOD CANCER DURING AND AFTER TREATMENT

O-0150

CHANGES IN NUTRITIONAL STATUS AND BODY COMPOSITION IN CHILDHOOD CANCER PATIENTS: A PROSPECTIVE COHORT STUDY

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Purpose/Objective: Since malnutrition and obesity have adverse outcomes during and after childhood cancer treatment, it is essential to gain insight in timing of weight loss and weight gain and in contributing factors. Therefore, the objectives of this study were to determine (1) in which period of treatment changes in nutritional status and body composition occurred, and (2) which factors contributed to these changes.
Materials and Methods: We performed a prospective cohort study of 133 newly diagnosed cancer patients with hematological, solid, and brain malignancies. Anthropometric data and related factors were assessed at 0, 3, 6 and 12 months after diagnosis.
Results: Despite initial weight loss in the first weeks after diagnosis in patients with hematological and solid malignancies, body mass index (BMI) and fat mass (FM) increased within 3 months with 0.13 standard deviation scores (SDS) ($P < 0.001$) and 0.05 SDS ($P = 0.021$) respectively. Increase continued during the next 9 months, and resulted in doubling of the number obese patients. Fat free mass (FFM), already low at diagnosis, remained low. During the whole study period about 17% of the patients were malnourished according to low FFM. Tube feeding and diminished activity level were related to increase in respectively BMI and %FM SDS. No relationship was found between energy intake or corticosteroids and increase in BMI or %FM.
Conclusions: Alarming increase of BMI and FM SDS already started within the period of intensive treatment and continued thereafter, while FFM SDS remained low. Improvement of nutritional status and body composition might be accomplished by prevention of overfeeding and improvement of physical activity in children on treatment.

NURSES: NURSES - SUPPORTING FAMILIES ON THEIR JOURNEY

O-0151

NAVIGATION, EDUCATION AND ELECTRONIC INFORMATION FOR ADOLESCENTS AND YOUNG ADULTS WITH CANCER: CHEMOTHERAPY, CALENDARS, FLASH DRIVES, AND WEBSITE RESOURCES TO SHOW YOU SHARE AND CARE

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Purpose/Objective: LOTS of information is shared with patients with childhood cancers and their families, friends, and caregivers. Oral information may lack sufficient detail and often is poorly remembered. Written information can become a 'really big book'. Personal computers with internet access and flash drives have made patient education and navigation easier and quantity and quality of information better.
Materials and Methods: We will share both electronic and internet resources as well as some strategies for navigation and education that our families have found useful.
Results: During work-up and therapy we commonly update and share a summary containing contact and clinical information including a problem list/action plan. Our patients have electronic access to their schedule using My MD Anderson. The treatment plan is often explained using a roadmap or a 5 week calendar that is available as an Adobe professional editable pdf document. This helps families, oncologists, and nurses 'at a glance' coordinate therapy, family events, and follow-up. Articles, chemotherapy drug information, calendars, images (e.g. powerpoint or pdf), radiation treatment plans and pdf of order sets can be placed on a flash drive. Families can then review this material and share information with their primary physician or others with the same rare cancer (e.g. via acor.org). A website useful for letting family and friends know of progress and events during therapy is caringbridge.org. A website with a calendar for families to organize their lives (e.g. making meals, transportation needs, child sitting, etc.) is lotsahelpinghands.org. A website which can send messages, photos and video clips to an email address on a FUTURE date is zarpz.com (to create a legacy).
Conclusions: Since most families of patients with childhood cancer have a personal computer with internet access, the quality and quantity of information provided by physicians, nursing educators and navigators is becoming better and better!

O-0152

PARENTAL SATISFACTION FOR CHEMOTHERAPY ADMINISTRATION FOR HEMATOLOGIC MALIGNANCY AT PROVINCIAL HOSPITALS; DATA FROM SOUTHERN CHILDHOOD CANCER NETWORK THAILAND

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Purpose/Objective: The Southern Childhood Cancer Network has been established to increase treatment adherence for patients who live far from cancer treatment center. Chemotherapeutic agents were prescribed and carried to provincial hospitals by parents. The chemotherapy schedules and guidelines were distributed to 13 network hospitals. Pediatric oncologists are available for consultation by phone.

To evaluate parental satisfaction for childhood cancer network, parents were asked to fill questionnaire during routine visit at treatment center.
Materials and Methods: Parents of 64 children who entered network program from October 2011- September 2012 were asked to filled questionnaire during routine visit at treatment center.
Results: Sixty four patients (43.8%) of total 146 hematologic malignancy patients entered network program. Of 64 families from 10 provinces in southern region, 51(80%) responded the questionnaire. Satisfaction scores (total = 5) for service process, medical equipments & provincial hospitals and health care personnel were 3.6 ± 0.9, 3.6 ± 1.0 and 3.6 ± 1.1, respectively. The scores for parental trust and convenience for service were 3.5 ± 1.1 and 3.7 ± 1.0 respectively. Overall satisfaction score for the service was 3.8 ± 1.1. 77% of parents scored the benefit of the network from good to very good. No major chemotherapy-related complication or drug error has been reported among the network hospitals.
Conclusions: The Southern Childhood Cancer Network decreased travel cost & time and improved quality of life for children with hematologic cancers in southern Thailand. The parents satisfied with the chemotherapy network program. The cancer network improved treatment adherence in resource limiting area.
Acknowledgements: Our network has made possible by support from Union International Cancer Control (UICC) under 'My Childs Matters' program and National Health Security Office (NHSO) Thailand.

O-0153

EFFECTIVE COMMUNICATION: IMPACT OF PAEDIATRIC ONCOLOGY NURSES WITH PARENTS AND CHILDREN IN PREVENTION & EARLY DETECTION OF FEBRILE NEUTROPENIA.

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Purpose/Objective: To reduce the risk and consequences of febrile neutropenia with good communication and family counselling by paediatric oncology nurses with children with cancer and their parents. Communication is a key component of palliative care.
Materials and Methods: Study of data generated last two years for 100 children newly diagnosed with febrile neutropeniaa in a paediatric oncology unit at a tertiary care children hospital in India. A questionnaire was created by communicating and observing the patients and parents during cancer treatment and was tested in the field for clarity and information. Parents and patients were interviewed. Data was analysed and compared. A needs analysis identified areas of weakness and barriers in communication and aspects of care requiring additional training for oncology nurses.
Results: The majority of our patients and their relatives have a low education level and do not understand the importance of observing simple measures of cleanliness, follow-up treatment and nutrition. However, if efforts are made to teach them, the rate of infection and other complications is decreased. Generally there is little communication between the doctor,nurse and patient. This results in abandonment of treatment or refusal of various curative modalities to increased perceived risk or lack of perceived benefit.
Conclusions: Good communication skills and knowledge can make a significant difference in a cancer patient's management, thus reducing the risk and consequences of febrile neutropenia, relapse and abandonment of treatment.

Training programs in communication skills should teach doctors and nurses how to elicit patients' preferences for information. Systematic training programs with feedback can decrease physicians and nurses' stress and burnout. More research for understanding a culturally appropriate communication framework is needed.

O-0154

NURSING CARE FOR CHILDREN WITH DOWN SYNDROME (DS) AND LEUKEMIA

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Purpose/Objective: To clarify nursing care issues required for children with DS and Leukemia
Materials and Methods: Ten children with DS who were consecutively diagnosed with leukemia (7 acute myeloid leukemia and 3 acute lymphoblastic leukemia) at St. Luke's International Hospital between January 2005 and November 2012 were evaluated in this retrospective analysis.
Results: Median age at diagnosis was 2.5 years (range. 1.0 - 7.2). Median developmental quotient (DQ) at admission was 39 (range, 26 - 63) and had no significant difference compared at the end of hospitalization (median duration was 10 months). Eight patients had DS-associated complications including congenital heart disease, hypothyroidism and laryngomalacia, but none of them interfered starting chemotherapy. All patients suffered from treatment-related complication such as infection and mucositis, but no treatment-related mortality was observed. Nursing care issues, specifically required for patients with DS and leukemia, are divided into 4 categories:safety management (self-removal of central venous catheter (CVC) and falling), infection control (skin care, oral care and management of respiratory infection), difficulties in daily nursing care (oral medication and toilet support) and psychosocial problems (anxiety and stress among family). The risk of self-removal of CVC was significantly correlated with only lower age. However there was no correlation between other problems and variables (DQ, type of leukemia and presence of autism). All issues were addressed collaboratively with multi-disciplinary team including child life specialist, nursery teacher, and medical social worker.
Conclusions: Since children with DS and leukemia have developmental disabilities and increased susceptibility to infection, special considerations in nursing care are needed. Taking into account physical and cognitive abilities of each patient, nursing care should be individualized. Multi-disciplinary approach is important to promote development of these patients and to support their families. Lastly, in order to implement optimal nursing care, sufficient staffing and child-friendly environment should be maintained.

NURSES: NURSES - SYMPTOMS AND SIDE EFFECTS

O-0155

PATIENT-REPORTED OUTCOMES COLLECTED VIA SMARTPHONE: ADOLESCENT CANCER PATIENTS' NAUSEA TRAJECTORIES

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Purpose/Objective: Nausea is commonly associated with cancer treatment. However, the trajectories of patients' daily experiences with nausea have not been well characterized, particularly during adolescence. Therefore, the purpose of this investigation was to describe adolescents' daily reports of nausea over a 3-week period.
Materials and Methods: In this study, 58 cancer patients aged 13-21 years (on therapy, n = 22; off-therapy, n = 36) completed an electronic symptom diary on a smartphone platform daily for 21 days. Nausea was measured on the Pediatric Nausea Assessment Tool

(PeNAT, potential range: 1-4) and a visual analog scale (potential range: 0-100). Higher scores on both instruments indicate more severe nausea.
Results: Adherence to daily symptom reporting exceeded 80%. The correlation of scores on the PeNAT and the nausea visual analog scale were strong and positive ($\rho = 0.75$, $p < 0.001$). Nausea severity did not vary by gender or ethnicity and did not correlate significantly with age. As expected, nausea severity was significantly higher among patients who were on-therapy (mean PeNat = 1.55) than those who had completed treatment (mean PeNat = 1.24, $p = 0.011$). Although among patients receiving chemotherapy nausea severity scores were fairly low when averaged among a typical 21-day treatment course, considerable inter-patient and intra-patient variability was noted. While some patients reported no nausea, others reported high levels of nausea throughout the chemotherapy cycle. In addition, the relationship of nausea to other symptoms (i.e., pain, sleep quality, fatigue), mood, and to quality of life will be presented.
Conclusions: Despite the common use of multi-agent anti-emetic therapy, some patients remain burdened by nausea. Additional research of the etiology and treatment of chemotherapy-induced nausea is needed.

O-0156

PATIENT TAILORED MOTOR PERFORMANCE PROGRAMME DURING TREATMENT FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A NOVEL APPROACH

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Purpose/Objective: Impaired motor performance as a result of chemotherapy for acute lymphoblastic leukemia (ALL) is well-documented, but there is great variation in similarly treated patients. Meanwhile, several studies have shown the benefit of physical activity and exercise during ALL treatment. However, a preventative exercise programme throughout the chemotherapy treatment period proved ineffective, most likely due to adherence problems. We hypothesised that adherence may improve if we monitor motor performance at standardised time points and modify the level of exercise when motor problems occur, in a patient-tailored manner.
Materials and Methods: Based on the phases of the ALL protocol of the Dutch Childhood Oncology Group we defined four time points for evaluation: immediately after diagnosis (T0,week 1), after completion of induction therapy (T1,week 12), halfway during treatment (T2,week 52) and at cessation of treatment (T3,week 104). Standardised tests are used (Lansky Scale, Movement Assessment Battery for children, Six Minute Walk Test); ankle mobility is measured using a goniometer. Cut off points for motor performance and ankle mobility determine which intensity of exercise is required. The exercise programme is based on the Stop Light Physical Therapy Programme (Tanner and Hooke, unpublished), which has three versions with ascending levels of intensity. The first and second levels are managed by hospital-based physiotherapist and parents; the treatment frequency in the third level needs involvement of a community-based physiotherapist.
Results: Twenty-five patients have been diagnosed with ALL since the motor performance programme became operational, twelve have reached T3 evaluation. An update on this cohort will be presented.
Conclusions: The purpose of this programme was to identify early impairment of motor performance and ankle mobility, from the start of treatment for ALL, in order to start early intervention. In due course we will report whether the programme is beneficial in maintenance of motor performance during treatment for ALL.

O-0157

PHYSICAL CONDITION AND ITS RELATIONSHIP TO UNCERTAINTY OF SURVIVORS OF CHILDHOOD AND ADOLESCENCE WITH LOWER EXTREMITY BONE TUMOR IN JAPAN

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Purpose/Objective: This study aimed to determine the current physical condition, including physical function, limb pain, and self-care for the limb, of survivors of childhood and adolescence with lower extremity bone tumor, and identify factors related to uncertainty.
Materials and Methods: Self-administered questionnaires were distributed at two cancer hospitals in Japan. Forty-two participants who had been diagnosed with osteosarcoma (n = 33) or Ewing's sarcoma (n = 3) before the age of 19 were recruited. Physical function was measured using the Toronto Extremity Salvage Score translated in Japanese. Correlation analysis and multiple regression analysis were performed to examine the relationships between uncertainty and physical condition.
Results: The most common surgical procedure was total knee replacement (n = 23). The prevalence of limb pain was 42% and three participants had phantom limb pain. Seventy-five percent of participants responded that they could perform self-care for the limb and specific examples given in free descriptions included skin care for the amputation surface, requesting repairs for equipment failures, and control of limb pain. The results of a correlation analysis revealed that physical function ($r = -0.47$, $p < 0.01$), limb pain ($r = 0.56$, $p < 0.01$) and self-care for the limb ($r = -0.58$, $p < 0.01$) were factors related to uncertainty. Multiple regression analysis (adjusted $R^2 = 0.41$) indicated that uncertainty is affected by physical function ($\beta = -0.36$) and self-care for the limb ($\beta = -0.46$).
Conclusions: Previous studies assumed that the psychological state of survivors of childhood and adolescence with lower extremity bone tumor is not affected by their physical function. However, this study clarified the correlation between survivors' uncertainty and their physical condition. Maintaining good self-care for the limb improves survivors' ability to cope with uncertainty. Moreover, those who underwent total knee replacement were likely to experience limb pain. Therefore, it is important for medical staff to assess the degree of limb pain and support pain control.

O-0158

RESTROSPECTIVE ANALYSIS ON THE USE OF LAXATIVES IN CHILDREN IN PALLIATIVE CARE

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Purpose/Objective: Constipation is a common problem in pediatric oncology, mainly due to use of vinca alkaloids and/or opioids and lifestyle changes secondary to treatment. Few articles describe the impact on constipation in pediatric oncology and even less is known in pediatric palliative care.
Materials and Methods: Retrospective drug use evaluation on patients receiving laxatives during palliative care (January 2009-February 2012).
Results: Fifteen patients (5 females; 10 males; median age 9 years) on a total of 53 palliative patients (28.3%) were receiving laxatives. Diagnoses included brain tumors (n = 9), acute myeloid leukemia (n = 2), Wilms tumor (n = 2), osteosarcoma (n = 1) and hematological disorders (n = 1). Of the 15 eligible patients, 13 (86.7%) suffered from constipation. In 7 out of 15 patients receiving opioids (46.7%), laxatives are not timely started in relation to the use of opioids.

Osmotic laxatives were most commonly prescribed (48.7%), followed by rectal laxatives (phosphate klysma and glycerin) (43.2%) and contact laxatives (8.1%).

Causes of constipation were divided in pharmacological and non-pharmacological causes. Pharmacological causes (45.1%) were related to use of opioids (n = 11), anti-epileptics (n = 4), anti-emetics (n = 8), diuretics (n = 3), sedatives (n = 9) and corticosteroids (n = 9) or a combination of them. Non-pharmacological causes (54.9%) were related to nutrition and intake of fluids (n = 14), mobility (n = 12), fatigue (n = 9) and nausea (n = 12).
Conclusions: Prevention and treatment of constipation is an important issue in palliative care. If constipation is not adequately treated, this can have a negative impact on the comfort of the patients and the quality of life. The results of this study indicate that more attention should be paid on the appropriate prevention and treatment of constipation, especially during treatment periods under opioids. Nurses in palliative care are in a key position to assist in the prevention and management of constipation as many strategies are in the scope of nursing practice.

NURSES: NURSES - FAMILY AND FRIENDS

O-0159

PARENTS' PERCEPTIONS OF THEIR CHILD'S SYMPTOM BURDEN DURING AND AFTER CANCER TREATMENT.

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Purpose/Objective: The aim is to describe parents' perceptions of their child's symptom burden during and after cancer treatment and to investigate whether parents' perceptions vary with child characteristics and parent gender.
Materials and Methods: One hundred sixty parents (49% fathers) of 89 children answered a modified version of the Memorial Assessment Symptom Scale (MSAS) 10-18 at six different time points from one week after the child's diagnosis (T1) to 12-18 months after the end of successful treatment (T6).
Results: Feeling drowsy, pain, and lack of energy are initially the most prevalent symptoms. During treatment, the most prevalent symptom is less hair than usual. Pain, feeling sad, and nausea are initially the most distressing symptoms. Pain is both prevalent and distressing throughout treatment. The child's symptom burden decreases over time. There is no difference with regard to reported symptom burden between parents of a daughter or a son, or parents of a child over or under 7 years of age. Mothers' and fathers' assessments of the symptom number, total MSAS, and the subscales are associated, but mothers' assessments are often higher than fathers' assessments.

Conclusions: The prevalence and distress of symptoms and symptom burden decrease over time. However, even though the cancer is cured, feeling sad is reported as being prevalent and psychological distress is an issue. A dialogue between staff and the family about distressing symptoms and when they can be expected may increase acceptance and adaptation in children and parents during the disease trajectory.

O-0160

FACTORS RELATED TO PARENTS' RESILIENCE WHEN THEIR CHILD IS SUFFERING FROM CANCER

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Purpose/Objective: Childhood cancer has an enormously stressful impact on families. Such stressful events are generally of unparalleled importance to people facing them.Thus, interventions that promote healthy and effective coping skills could help parents adapt to their new lifestyles. The purpose of this study is to explore the factors that influence resilience and positivity in Japanese parents experiencing the hardships resulting from their child's cancer diagnosis.
Materials and Methods: Data were obtained through semi-structured, face-to-face, in-depth interviews and analyzed using a qualitative approach. All interviews were conducted between 2012 and 2013. Codes were extracted from transcribed data, and then classified into categories. Participants were recruited from a university hospital in Japan. The study was approved by the local ethics committee.
Results: Ten parents (9 women and 1 man) were interviewed. This study focused on the use of positive views in coping with stressful events. Furthermore, it seemed useful to apply the concept of resilience; therefore, we classified the categories according to factors named in Grotberg's theory of resilience. These factors include (1) 'I am,' relating to inner strengths that develop over time and sustain those who are dealing with adversities; (2) 'I can,' relating to interpersonal and problem-solving skills that deal with actual adversity; and (3) 'I have,' relating to external supports that promote resilience. The results suggest that the degree of recovery in their child's illness and their relationships with health care professionals are two of the most important factors in minimizing stress responses. Thus, parents require adequate information concerning the illness and must ensure that their contact with health care professionals does not end after the child has been discharged.
Conclusions: Using an empirical approach, we have identified several factors relating to parents' resilience in the face of their child's suffering from cancer. While the three factors that we derived are independent, they all appear to work together to enhance resilience.

O-0161

CHALLENGES FACED BY PARENTS WITH CHILDREN UNDERGOING CANCER TREATMENT AT KORLE BU TEACHING HOSPITAL, ACCRA, GHANA

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Purpose/Objective: To identify the challenges, including psychosocial issues, faced by parents of children undergoing cancer treatment at Korle Bu Hospital, Accra, Ghana
Materials and Methods: A cross-sectional descriptive survey was undertaken at the Paediatric Oncology unit of the Korle Bu Teaching Hospital in Accra, Ghana in January 2013. A questionnaire was administered to 50 parents of children with cancer who were undergoing treatment. Consent was obtained from parents beforehand.
Results: Females comprised 68% of those interviewed. Financial distress was high. 66% were unemployed as they had to move to Accra for treatment and 74% faced accommodation difficulties. Only 4% could afford treatment. Relationship problems with spouses were reported in 75% as a result of child's illness. For 57% it had affected relationship with their other children. 94% were satisfied with the way the child's condition was explained to them although 36% stated the information was inadequate. 88% felt worried something awful would happen to the child. Most of the parents stated they felt sad or depressed.
Conclusions: Parents of children undergoing cancer treatment face significant psychosocial challenges. Attending to psychosocial needs and other identified challenges faced by parents should be an integral part of quality paediatric oncology care particularly in developing countries.

O-0162

'GIVE AS MUCH HELP AS YOU CAN, BUT TREAD CAREFULLY': GRANDPARENTING ACROSS THE GENERATIONS WHEN A GRANDCHILD IS DIAGNOSED WITH CANCER.

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Purpose/Objective: During a child's cancer treatment, grandparents are often relied upon for the provision of practical and emotional support. Most grandparents last raised a child several decades earlier and have no experience in children's oncology. This study explored grandparents' experiences of grandparenting in the paediatric oncology context, focussing on the perceived impact of cancer on grandparent-parent, -patient, and *sibling relationships.
Materials and Methods: Grandparents of children with cancer (treated at three paediatric oncology hospitals) completed a self-report questionnaire. Open-ended responses regarding their grandparenting experiences were coded line-by-line and categorised using *QSRv8*.
Results: Eighty-seven grandparents participated (mean age 65 years [range 46-81]; 31% male). Many described improved relationships with the ill child (n = 27), their siblings (n = 10) and the children's parents (n = 25). Grandparents reported increased feelings of anxiety and protectiveness for all family members. Grandparents described being challenged by parents' emotional outbursts (including encountering anger directed toward them). They also experienced uncertainty about how to provide support and advice without over-stepping parents' authority. Several reported being more forgiving of the ill child and their siblings' disobedient behaviour, and described their role as one of providing a 'link' between the affected child and the extended family (e.g. cousins).
Conclusions: The impact of paediatric cancer on grandparents is under-studied. Grandparents are often called on to provide co-parenting support for the family in crisis, often without benefit of the knowledge imparted by the treating team to the child's parents. The unique context of grandparenting during childhood cancer treatment places a considerable burden on this aging group.

O-0163

FRIENDSHIP FROM THE PERSPECTIVE OF CHILDREN WITH EXPERIENCE OF CANCER: A FOCUS GROUP STUDY

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Purpose/Objective: Friendship is a significant contributor to the experience of health. Disease and treatment can end contact with friends and it has been found that children treated for cancer often have fewer close friends and consult less often with their friends compared to healthy children. Children with cancer identify friends as one of the main sources of support but also that friends that do not share experiences of cancer have less abilities to support them. Support programs for those who share similar experiences (peer support) have been recognised as an important contributor to health and well-being but empirical evidence that could guide development of peer support programs involving children is limited. The purpose of this study was to explore perceptions of friendship from the perspective of children with experience of cancer.
Materials and Methods: Fifteen children with experience of treatment of cancer participated in focus groups with 3 children in each group. A mixture of informative and creative techniques assisted the children in talking and expressing themselves. The focus group discussions were analysed using qualitative content analysis.
Results: Children described friendship in terms of having common interests and experiences, to respect and help each other, and to build common trust and understanding. They also described that friendship is a process that develops over time and that interaction takes place both face-to-face and digitally.
Conclusions: These insights are now used in an iterative and participatory development of a digital service for peer support for children with cancer. The knowledge based on this study may contribute to interventions designed to promote children's social networks.

IPSO: IPSO - SESSION 1: GASTROINTESTINAL TUMOURS

O-0164

TREATMENT OUTCOME OF RECURRENT HEPATOBLASTOMA: ROLE OF IRRINOTECAN

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Purpose/Objective: To evaluate the outcome in patients with recurrent HB treated with Irinotecan
Materials and Methods: Retrospective review from the records of all children with recurrent HB enrolled from 1999 through 2012. Treatment of recurrence after 2008 was with Irinotecan. Prior to 2008 they were mainly treated with different chemotherapies(super PLADO, ICE, etc). Kaplan Meir analysis was done for 2-year overall survival (OS) and 2*year event free survival(EFS) [events being death/progression] and it was compared between these two groups.

Results: Of the 90 HB treated in this time period, 13(14%) children with recurrence were enrolled. The age range 6-72 months(mean 24.5). Two(15%) patients had recurrence even before completion of chemotherapy. The time to recurrence was 4-33 months (Mean11.9).The site of recurrence was local 7(54%), lungs 3(23%), scalp and bone 1, while 2(15%) presented with increasing AFP with no site discernible. Eleven were treated with chemotherapy for recurrence (1 died prior to treatment, 1 refused). Re-operation was done for 4 of 13 (31%) patients (1 caudate lobe resection, 3 pulmonary metastectomy).Over all 5(38%) died, and 4(31%) progressed, 1(8%) has stable disease and 2(15%) were in CR. The time to event was 4-25 months(mean10). The 2-year OS was 73%(95CI 37-90) and the 2-year EFS was 31%(95CI 9-55). Six(46%) recurrences were before 2008 and 7(54%) were after 2008. For those treated with irrinotecan, the OS was57%(95CI 7-87) and the EFS was 43%(95CI 10-73). While for those treated prior to 2008 the OS was 0% and the EFS was 17% (95CI 1-51). This difference in OS and EFS is not significant ($p = 0.26$ and 0.23).
Conclusions: The outcome of recurrent HB is poor (OS 73% and EFS 31%). Treatment with Irrinotecan resulted in better OS (56% vs 0%) and EFS (43%vs 17%). However, this was not significant ($p = 0.26$ and 0.23).

O-0165

VASCULAR INVASION IS A MAJOR RISK FACTOR OF RECURRENCE IN FRANTZ TUMOR: RESULTS OF A NATIONWIDE RETROSPECTIVE STUDY.

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Purpose/Objective: Solid pseudopapillary tumors of the pancreas (Frantz tumor) are rare and usually occur in the second decade of life. We aimed to collect all cases in a nationwide basis to analyze overall and disease-free survival, delineate factors of recurrence and get an overview of treatment employed.
Materials and Methods: A questionnaire was sent to all pediatric oncologists and pediatric surgeons involved in oncology and also to adult pancreatic surgeons in order to retrieve late recurrences that had occurred at adult age.
Results: Over the last 20 years thirty-six patients (28 females) were collected with a median age at diagnosis of 13 years [8.7-20.8]. Abdominal pain was the commonest symptom (64%). Location of the tumor was in the pancreatic head in 45%. Preoperative biopsy or cytology was performed in 13/36 (36%) patients. All patients were operated on within a median delay from diagnosis of 17 days [0-124]. Postoperative morbidity was 27.8%. Median follow up was 5.8 years [0.7-18.3]. Six (17%) patients recurred with a median delay of 5.2 years after the initial surgery [0.75-9.9]. One patient beyond any treatment was still alive at last news. The other five patients were treated either by surgery alone ($n = 1$), or by pre or postoperative chemotherapy ($n = 2$), or by surgery associated to HIPEC ($n = 2$). The only identified risk factor of recurrence was the presence of vascular invasion on the specimen ($p = 0.01$). Tumor rupture ($p = 0.35$), preoperative biopsy ($p = 0.17$) and positives surgical margins ($p = 0.21$) did not reach statistical significance.
Conclusions: Our paediatric series is the most important ever published and confirmed that overall survival is very good despite recurrences. Treatment of recurrence was not standardized but complete surgical removal seems the best option. Histological aggressiveness appeared as the most important risk factor of recurrence prior to the classical tumor rupture.

O-0166

TREATMENT OF CARCINOMATOSIS USING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN ADOLESCENTS AND YOUNG ADULTS WITH COLON CARCINOMA

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Purpose/Objective: Background: United States cancer incidence data (SEER) show approximately 200 adolescents and young adults/year have stage IV colon cancer, with a 5 year overall survival of 11.9%. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) is used in adults with colon cancer and confers a superior survival compared to standard chemotherapy, but the applicability of adult therapies to AYA colon carcinoma patients is unknown. We applied an algorithim of standard adult chemotherapy followed by cytoreductive surgery and HIPEC, to AYA colon carcinoma patients.
Materials and Methods: Methods: Five AYA patients age 11-19 years were referred to our institution between 2010 - 2012 for cytoreductive surgery and HIPEC with Stage IIIC-IV colon carcinoma. All underwent FOLFOX (5-FU, leukovorin, Oxaliplatin) and/or FOLFIRI (Irinotecan) +/− Avastin after diagnosis and prior to HIPEC with Mitomycin C. Outcomes were recorded.
Results: Results: All patients had signet ring/poorly differentiated pathology. One patient progressed rapidly on chemotherapy and died before completing chemotherapy. One patient progressed slowly and was unable to be completely cytoreduced and therefore did not undergo HIPEC. Three patients underwent HIPEC. One recurred at 8 weeks after HIPEC and at 12 weeks died. One recurred at 32 weeks and underwent a second HIPEC with Oxaliplatin. One patient has not recurred. The two patients who are alive, had no evidence of disease at the time of surgery and HIPEC.
Conclusions: Conclusions: Peritoneal carcinomatosis secondary to colon cancer in AYA patients carries a poor prognosis, and better treatment options are needed. Pending the results of ongoing adult studies delineating the efficacy of HIPEC in different histologies and scenarios, consideration should be given to doing HIPEC in AYAs at the time peritoneal implants are removed, or when minimal disease is evident.

O-0167

SURGICAL MANAGEMENT OF CARCINOID TUMORS OF THE APPENDIX IN CHILDREN AND ADOLESCENTS: RESULTS OF A FRENCH MULTICENTER STUDY.

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Purpose/Objective: Carcinoid tumors of the appendix (CTA) in children and adolescents are rare and usually an incidental finding on pathology after appendectomy for acute appendicitis. The aim of this study was to define evidence for secondary right hemicolectomy or ileocecal resection in children or adolescents with CTA.
Materials and Methods: We contacted all French pediatric surgeons and oncologists by mail and reviewed the records of patients under 18 with CTA from 1988 until 2012. Analyzed data were demographics, pathology of the appendix, complementary exams and treatment after CTA finding, pathology findings after further surgery, survival and follow up.
Results: A total of 108 patients were recorded. Nine patients (8.3%) had a tumor of 2 or more cm. Twelve patients (11.1%) had a tumor at the base of the appendix amongst whom 3 with positive margins. An infiltration of the mesoappendix was found in 18 patients (16.6%). Invasion of blood or lymph vessels was found in 6 patients (5.5%) and a high proliferation index was found in 1 patient (0.9%). Nine patients (8.3%) had secondary right hemicolectomy and 1 had ileocecal resection. Nineteen patients (17.6%) were candidates to hemicolectomy but the indication was not validated by the medical teams. Eighty-two patients (76%) had follow-up. Median follow-up was 6 months [1 month - 10 years]. Outcome was uneventful for all patients except one who had recurrence 6 years after hemicolectomy.
Conclusions: Infiltration of the mesoappendix, invasion of blood or lymph vessels and high proliferation index are not indications to secondary right hemicolectomy in children and adolescents with CTA. We no longer consider right hemicolectomy in children or adolescents with CTA completely removed after appendectomy. The size of the tumor being the best prognosis factor, risk-adapted follow-up is required for patients with tumors of 2 or more cm.

IPSO: IPSO - SESSION 2: SARCOMA

O-0168

INTERNAL HEMIPELVECTOMY FOR EWING SARCOMA – A STUDY BASED ON A NATIONAL REFERENCE CENTRE EXPERIENCE

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Purpose/Objective: The analysis aims to evaluate the impact of hemipelvectomy on the outcomes in patients with Ewing Sarcoma there located.

Materials and Methods: Twenty-four patients aged from 2.3 to 19.6 years were treated according to EE99 and EE2008 (2000-2012) for pelvic Ewing Sarcoma. Tumors were located in the hip-joint in 16 pts, in pubic bone in 3, in ischium in 3 and in pubic&ischium in 2. Twelve patients had distant metastasis at initial diagnosis. Follow-up ranged from 9 months to 9.1 years. After neoadjuvant chemotherapy, all patients underwent internal hemipelvectomy with following reconstructions: allogenic bone graft/14, endoprosthesis/6, non-absorbable mesh to restore the hip-joint/4. Postoperatively, chemotherapy was continued and in 13/24 patients consolidated with aBMT. Local radiotherapy was used in 15 patients.
Results: Perioperative period was uneventful, however late complications occurred in 8 (surgery-related infections/2 and wound necrosis and/or dehiscences/6). In one case, the complications led to external hemipelvectomy 2 years after primary treatment. Four patients had local and two distant relapses and died; only one of them had microscopically incomplete surgery. Remaining 3 patients after microscopically incomplete resections are alive. 5-year EFS was 67% and OS 72%. Functionally, all patients were ambulant: 14 without crutches, 4 with one crutch and 6 with 2 crutches.
Conclusions: Internal hemipelvectomy offers similar chance for cure as more mutilating procedures with reasonable rate of complications and better function.

O-0169

PEDIATRIC CHEST WALL EWING SARCOMA/PNET: SURGICAL TREATMENT AND OUTCOMES

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Purpose/Objective: To evaluate the clinical presentation, management and outcome of children with chest wall Ewings sarcoma/PNET and correlate the outcome with the site of disease, presence of metastatic disease and treatment strategy.
Materials and Methods: All children (< 14 years) with chest wall PNET registered in our oncology clinic from March 2001 through November 2011 were included. All received neoadjuvant chemotherapy(NACT) [vincristine + doxorubicin +cisplatin + ifosphamide + etoposide] and either radical radiotherapy(RRT) or surgical resection or both surgery + RT(S + RT). Kaplan Meier survival estimates for overall survival(OS) and event free survival(EFS; events being progression/recurrence/death) were done in relation to localized or metastatic disease and based on the management options (surgery/surgery + RT/RRT) using statistical program STATA 9.
Results: Thirty-three children in the age range 3-14 years (mean 8.9 years) were enrolled. Skeletal involvement was present in 27(82%) and soft tissue disease in 6(18%). The primary site was rib in 14(42%), scapula 10(30%) and clavicle 3(9%). Twenty-one(63%) had localized disease while in 12(27%) it was metastatic at presentation. All received NACT for a median duration of 6 months(3-11m). Post NACT, 5 patients underwent surgery,12 RRT and 9 S + RT. Of the remaining 7, 4 died and 3 were lost to FU. The 4-year OS for the whole group was 51.2%(median 30.5 months; range 2.1-104.6). For localized disease OS was 70.2% and for metastatic disease 48%. The 4-years OS for children who underwent surgical resection was 80%, RRT 33.3% and both(S + RT)66.7%. The 4-year EFS was 32.3%(median FU 21.5 months). The 4 year EFS with surgery was 80%, with RRT 10% and both(S + RT)42.9%. On multivariate analysis, metastatic disease was recognized as a single independent prognostic factor for EFS($HR = 4.1$, $p < 0.01$) and also for OS($HR = 8.04$, $p < 0.01$).
Conclusions: Metastatic chest wall PNET has a significantly poorer OS and EFS. Surgical resection, after neoadjuvant chemotherapy has a significantly better OS and EFS as compared to RRT alone

O-0170

SURGERY OF NON METASTATIC RHABDOMYOSARCOMA (RMS) OF THE EXTREMITIES

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Purpose/Objective: We have reviewed data prospectively collected of patients with localized RMS of extremities registered in three consecutive Italian Protocols to assess their clinical characteristics and outcome.
Materials and Methods: 66 evaluable patients enrolled between 1979-2005 (32 males,34 females; age:2 weeks-16 years, median 7y.) were analyzed. Surgical guidelines did not change during the years: initial complete excision was recommended when complete, otherwise a biopsy was suggested. Patients were subsequently treated with chemotherapy with/without radiotherapy according to the risk group.
Results: Histotype was alveolar in 43/66 cases; age was < 10 years in 48/66. Upper and lower extremities were equally represented (31,35 respectively), distal localization was more frequent in upper-limbs (61.3%), proximal in lower-limbs (65.7%). Nodal involvement was present in 14 cases. Initial excision (IE) was performed in 31/66 cases, but completeness was reached in 15 (all T1); micro-residuals were left in 13, macro-residuals in 3. Initial biopsy was performed in 35: most of them (24/35) had tumors > 5cm. No demolitive excision was done in initial surgery, while one amputation was performed at delayed surgery (DE). Completeness was reached in 18/29 DE. Radiotherapy was delivered to 37 patients: 5 after complete IE, 13 after IE with residuals, 8 after complete DE, 6 after DE with residuals, 5 after biopsy.

37 patients are alive, 10 after loco-regional relapse. 29 died, mainly due to metastatic relapse (12/29). No statistical difference were noticed in the overall-survival comparing patients with different age, sex, histotype, dimensions, T-status, IRS-group, nodal involvement, localization.
Conclusions: Patients treated with initial/delayed complete surgery + RT had the best outcome (5y-OS:75%). The worst prognosis was registered in those who relapsed with distant metastases. Metastatic relapse was more frequent in patients with more invasive tumors (T2 and/or N1) who did not receive a good local control (incomplete DE and/or no-radiotherapy administered). Adequate local treatment including complete IE/DE and RT is essential for prognosis.

O-0171

THE SOFT TISSUE SARCOMAS LOCATED IN THE LIMBS: AN ATTEMPT FOR RESECTABILITY ASSESSMENT.

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Purpose/Objective: Soft tissue sarcomas (STS) located in the limbs create specific difficulties if complete and not mutilating resection is planned.
Aim: to assess the classical risk factors (RF) for incomplete surgery in STS located in the limbs.
Materials and Methods: Seventeen children treated consecutively (2000-2009) for STS (aRMS/5; eRMS/4, Synovial Sarcoma/6, Triton Tumour/1, MPNST/1) located in the upper (9) or lower (8) limb. Following RF were compared to the quality of resection and the outcome: encasement of brachial (upper limb) or femoral/popliteal artery/vein (lower limb), encasement of the median, radial, ulnar (upper limb) or ischiadic, tibial or peronealnerves (lower), encasement of the bones and infiltration of the joint capsules. All ptsbut 3 submitted to early re-excision following incomplete surgery performed elswhere, were operated on after chemotherapy (CWS2002/2006). The postoperative ChT +/− XRT also followed the above schedules. F-u > 36 months.
Results: Encasements of the vessels and nerves were observed in 3 pts, all had R1 resection, 1 relapsed and died. Encasement ofthe femoral bone (1 eRMS) was not circular (270°) and R0 resection was possible;despite circular encasement of the fibula in another case (aRMS), tumour was resected intogether with the bone (R0); both are in CR. Infiltration of the joint capsule was observed in 4 (2/R0, 2/R1), 3 of them relapsed and died(compared to 1/13 remaining; Fisher, $p = 0.0223$). Five pts (3 joint capsule infiltration, 2 nerves/vessels encasement) had R1 resection, 3 relapsed and died (compared to 1/12 ptsfollowing R0; Fisher, $p = 0.0525$). Outcome by site (upper or lower limb) or pathology were not significant. In total - 4/17 pts relapsed.
Conclusions: Summary: The vessel/nerve encasement and joint capsule infiltration nearly imply R1 at conservative approach (5/7; $p = 0{,}00339$). Infiltration of the joint capsule seems to influence the outcome ($p = 0.0223$) even more than R1 vs. R0 ($p = 0.052$). General results look satisfactory.

O-0172

IN-TRANSIT METASTASES IN RHABDOMYOSARCOMA PATIENTS, NOT A RARE TUMOR LOCATION

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Purpose/Objective: In transit metastases (ITM) are tumor emboli trapped within the lymphatics between the primary tumor and the regional lymph node basin. In distal extremity tumors those ITM are located in the sulcus bicipitalis and popliteal region. In a report from the children's oncology group ITM in pediatric rhabdomyosarcoma (RMS) patients were recognized in 4% of patients. Our aim was to evaluate the involvement of and relapses in ITM in a national cohort of RMS patients.
Materials and Methods: In one of our hospitals we diagnosed a patient with a RMS in the calf. A suspicious popliteal ITM was detected by pet-scan and biopsied. With a sentinel node biopsy we harvested an inguinal lymph node. The ITM was positive for tumor, the sentinel node negative. Additionally we evaluated a Dutch national database of RMS patients between 0-18 years, diagnosed between 1990 and 2012. We reviewed radiology and pathology reports at diagnosis and at a relapse.
Results: We identified 25 non metastatic (M0) patients with a RMS in the extremities of which 16/25 (64%) in the distal extremities. There were 12 alveolar and 4 embryonal RMS. In 5/16 patients no radiological evaluation was performed of the ITM. In 5/8 (62,5%) N1 patients with regional lymph nodes at presentation ITM were also involved. Two of those patients relapsed in the in-transit location. One patient with only inguinal node metastases relapsed in an ITM. In 2/8 (25%) N0 patients, a relapse occurred in an ITM location.
Conclusions: The in-transit metastasis is an important regional lymphatic location in RMS patients and more dedicated search for those metastases is necessary. A sentinel node biopsy can falsely underdiagnose a tumor loaded ITM so radiological or nuclear (PET) evaluation of the whole extremity must be performed to detect the in- transit metastases.

IPSO: IPSO - SESSION 3: MEDIASTINAL TUMOURS/ SURGICAL APPROACHES AND TECHNIQUES

O-0173

CLINICAL FEATURES AND SURGICAL INTERVENTION OF PRIMARY MEDIASTINAL TUMORS IN CHILDREN: A 25-YEAR SINGLE INSTITUTION EXPERIENCE

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Purpose/Objective: Primary mediastinal tumors are relatively rare in children, many of which are malignant and life-threating. For treatment of these tumors, the role of pediatric surgeons includes the perioperative intensive care, biopsy for accurate diagnosis, and resection with minimal morbidity if indicated. In this study, we reviewed the clinical features and surgical intervention strategy of these tumors in our institute.
Materials and Methods: 37 mediastinal tumors were treated from 1988 to 2013, and medical charts were retrospectively reviewed.
Results: Their median age was 34 month (2 - 201). Dyspnea was seen in 6, 3 of whom required tracheal intubation before surgical intervention. The site of tumors was 9 in the anterior mediastinum, 26 in posterior, and 2 in superior. Pathological diagnosis was neuroblastoma in 19, ganglioneuroma in 6, lymphoma in 5, germ cell tumor (GCT) in 3, schwannoma in 2, Langerhans cell histiocytosis in 1, and hemangioma in 1. Complete or partial resection of the tumor was performed in 30. Postero-lateral thoracotomy was indicated before 1997. Video-assisted thoracic surgery (VATS) was conducted since 1998 except early infants and giant tumor. Suprasternal approach was used in 1. A patient with giant malignant GCT was operated by median sternotomy with cardiopulmonary support. Biopsy was undertaken in 7 patients via thoracentesis or mini-thoracotomy with or without VATS. The perioperative mortality was none, and the postoperative complications were Horner syndrome in 5, and progressive scoliosis in 4 with a residual intra-spinal tumor.
Conclusions: It is important to select surgical intervention for pediatric mediastinal tumors based on the clinical features and biology of tumors. The short-term surgical outcomes were excellent with prompt perioperative intensive support and the appropriate surgical procedure. The indication of VATS should be more extended and long-term follow-up is necessary in terms of cosmetic and functional results.

O-0174

A MULTIDISCIPLINARY APPROACH TO THE MANAGEMENT OF ANTERIOR MEDIASTINAL MASSES IN CHILDREN

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Purpose/Objective: Pediatric anterior mediastinal masses (AMM) pose a diagnostic challenge to surgeons, oncologists, and anesthesiologists as induction of general anesthesia (GA) can cause airway obstruction and cardiovascular collapse. We hypothesize that standardizing a multidisciplinary preoperative evaluation minimizes anesthetic risks.
Materials and Methods: Our protocol divides patients with AMM into four groups based on radiographic findings and clinical symptoms: 1) no airway compromise, 2) minor airway compromise 3) large tumor burden posing a prohibitive risk to anesthesia, and 4) those who required emergent intubation at presentation. Group 1 can be managed with GA, group 2 with sedation and local anesthesia, group 3 undergo radiation and steroid therapy prior to operative intervention. Group four patients may undergo GA because the airway is already secured. To evaluate the protocol validity, a retrospective review was performed for all patients with AMM from 2002 to 2012.
Results: We identified 72 patients with AMM (mean age 12.4 $\pm$ 4.4 years, range 1-20, 63% male) secondary to Hodgkin lymphoma (36), Non-Hodgkin lymphoma (27), and other diagnoses (9). Anesthetic planning for tissue biopsy was performed per group status. There were 45 patients in group one, 12 in two, 11 in three, and four in group four. Only three patients suffered respiratory complications. One had minor right upper lobe collapse that resolved with bronchoscopy (group 1), one needed to be intubated secondary to lung collapse (group 2), and one developed superior vena cava syndrome requiring abortion of the procedure and emergent intubation (group 3). In 78% of patients, diagnosis was made based on tissue sampled outside the AMM. There were no deaths.
Conclusions: A standardized protocol for pediatric patients with AMM can be utilized to determine the optimal management for diagnosis. This multidisciplinary approach leads to decreased anesthetic risks.

O-0175

SURGICAL INTERVENTION IN MALIGNANT SOLID TUMORS IN CHILDREN – COMPARATIVE ANALYSIS OF 2 DECADES FROM A HOSPITAL BASED REGISTRY

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Purpose/Objective: In developing countries, malignant solid tumors in children are still a major cause of childhood mortality. Worldwide, even though the incidence of malignancies in children is rising, the 5 year survival has dramatically improved. The aim of this study was to evaluate the pattern and frequency of malignant solid tumors who underwent surgery and compare the trend between two decades with regards to outcome.
Materials and Methods: Retrospective analysis of all cases registered in the department of Pediatric Oncology and Pediatric Surgery between 1992 to 2012. 2 groups were created, the first group (first decade) between 1992 to 2001 and the second group (decade) between 2002-2011. All demographic, staging, treatment and surgical details were analysed.
Results: Male: female was 2.5:1, mean age 4.6 years overall. Analysis of type of tumor showed a similar trend with Neuroblastoma as the most common tumor followed by Wilms' tumor, Lymphoma, Hepatoblastoma, Soft tissue sarcoma, malignant teratomas and rare tumors, the non-hodgkins lymphoma being less common in second group. First decade had total of 295 registrations, versus 224 in the second decade. Staging distribution revealed more patients in stage 3 and 4 in the first decade versus the second, and 32% more patients undergoing complete treatment including surgical procedures in the second decade. R1 resection was feasible in 27% versus 42% between the 2 groups, though Re-excision rates were similar. Chemotherapy related complications did seem to show a significant improvement between the 2 decades from 34% to 23%. The abandonment rate decreased from 48% to 36% from the first to second decade. The overall survival rate improved marginally from 52% to 60%.
Conclusions: This study indicates that there is a dire need to reformulate the policies and management schedules for treatment of malignant solid tumors in developing countries and improve the outcomes over decades. Surgical policies have to be more stringently applied.

O-0176

SIMULTANEOUS RESECTION OF SOLID PEDIATRIC TUMORS AND LUNG METASTASES IN CHILDREN

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Purpose/Objective: Treatment of children suffering from metastatic solid pediatric tumors remains difficult. Besides the advantages in chemotherapy and immunotherapy, surgery plays a key role for an improved survival of these children depending on the tumor entity. Simultaneous resections of abdominal tumors and lung metastases might have a beneficial influence on the tumor biology. The aim of this study was to evaluate the efficacy of combined resections of abdominal tumors and lung metastases as single stage approach in a retrospective analysis.
Materials and Methods: Seventeen patients suffering from hepatoblastoma (n = 6), hepatocellular carcinoma (n = 1), nephroblastoma (n = 5), rhabdomyosarcoma (n = 2), osteosarcoma (n = 2), and epitheloid sarcoma (n = 1) underwent combined tumor resection of the abdominal tumors and lung nodules.
Results: Patients consisted of 9 females and 8 males. The median age was 6 years [range: 1-18 y]. Viable lung metastases were found in 16 patients. In one patient, no viable metastases were found during histological work-up. A total number of 107 metastases were resected using sternotomy (n = 11), lateral thoracotomy (n = 3), thoracoscopy (n = 2), and one

transdiaphragmatic approach. Chest tubes were removed after a median of 5 days on the right and after 6 days on the left. Patients were discharged after a median of 14 days [range: 5 * 35 d]. Postoperative chemotherapy was initiated after a median of 20 days [range: 14 * 30 d]. 10/17 patients are currently alive after a median follow-up of 41 months. Complications occurred in 7/18 patients (bilioma: n = 3, pneumothorax: n = 2, pericardial tamponade: n = 1, mechanical ileus: n = 1).
Conclusions: Simultaneous resections of abdominal tumors and lung metastases are feasible and safe in children with metastatic solid tumors. Postoperative chemotherapy can be initiated early and there are no delays due to staged approaches.

O-0177

MINIMALLY INVASIVE SURGICAL TECHNIQUES ARE SAFE IN THE DIAGNOSIS AND TREATMENT OF PEDIATRIC MALIGNANCIES

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Purpose/Objective: Minimally invasive surgical (MIS) techniques have an expanding role in the diagnosis and treatment of pediatric malignancies. We hypothesize that MIS techniques can be used to provide safe and reliable care to pediatric surgical oncology patients.
Materials and Methods: A retrospective review of all patients who underwent a minimally invasive operation for diagnosis or treatment of a solid tumor from 2002-2012 was performed.
Results: A total of 106 minimally invasive procedures were performed in 98 patients (60% male; 78 thoracoscopic, 28 laparoscopic; mean age 10.2 ± 6.4 years). Median follow up was 2.5 ± 2.7 years. Twenty-two (28%) thoracoscopic procedures were performed for complete resection of primary tumor or metastases. Two cases were converted to open thoracotomy (9%), secondary to an inability to completely resect the mass thoracoscopically, and the large size of the tumor obscuring the aorta. Tumors that were successfully removed thoracoscopically include neuroblastomas (n = 8), metastatic disease (n = 6), and others (2). The remaining 56 (72%) thoracoscopic cases were biopsies performed to diagnose primary, metastatic, or recurrent disease; two cases were converted to open (4%). These conversions resulted from an inability to definitively identify the nodule and to avoid significant bleeding complications. Of the 28 laparoscopic procedures, nine were performed for tumor resection with one case converted to open. Tumors that were successfully removed laparoscopically include 6 adrenal neuroblastomas and one pseudopapillary pancreatic tumor. The remaining 19 (68%) laparoscopic procedures were biopsies performed for diagnosis of primary, metastatic, or recurrent disease. Only one surgical specimen was insufficient for pathologic diagnosis. This patient underwent repeat thoracoscopic biopsy with adequate sample for diagnosis. There were no major surgical complications. No port site or surgical site recurrences were reported.
Conclusions: MIS techniques can be used safely for the diagnosis and resection of pediatric malignancies and treatment decisions can be made accurately based on tissue obtained.

O-0178

AN AUGMENTED REALITY NAVIGATION SYSTEM FOR PEDIATRIC SURGERY FOR TUMORS.

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Purpose/Objective: In pediatric endoscopic surgery, limited views and a lack of tactile sensation restrict the surgeon's abilities. Moreover, in cases of pediatric oncological surgery, it is sometimes difficult to detect and resect tumors because of adhesion to the surrounding organs due to previous surgery and the effects of preoperative chemotherapy and radiotherapy. We developed an augmented reality (AR) navigation system based on preoperative CT or MRI imaging for endoscopic surgery for pediatric tumors.
Materials and Methods: The patients underwent CT or MRI with body surface markers preoperatively. We used an optical tracking system for registration between the reconstructed three-dimensional (3D) images and body surface markers during the operation. The AR visualization was superimposed with the preoperative 3D images projected onto captured endoscopic live images. Six patients underwent surgery using this system.
Results: The median age of the patients was 3.5 years old (1∼12 year old). Two of the six patients underwent laparoscopic surgery, Two patients underwent thoracoscopic surgery and two patients underwent laparotomy using this system. The indications of operation were a local recurrence of Wilm's tumor, metastasis of rhabdomyosarcoma at the chest wall, undifferentiated sarcoma of the pelvis, a bronchogenic cyst of the mediastinum, bronchogenic cyst of the stomach and hepatoblastoma, respectively. The average tumor size was 22.0 ± 14.2 mm (6∼40 mm). Four malignant tumors were treated with chemotherapy and three were treated radiotherapy before surgery. Four out of six operations were re-operations. All six tumors were detected using this AR navigation system and successfully resected without any complications.
Conclusions: This AR navigation system is considered to be very useful for pediatric endoscopic surgery, especially for resecting malignant tumors.

IPSO: IPSO - SESSION 5: PBC - SESSION: BEST OF IPSO

O-0179

LONG TERM RENAL FUNCTION AND BLOOD PRESSURE AFTER UNILATERAL NEPHRECTOMY FOR THE TREATMENT OF UNILATERAL WILMS' TUMOUR

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Purpose/Objective: The treatment of unilateral Wilms' tumour (uWT) is highly successful with an overall survival for localised disease of over 90%. Long-term side effects of treatment are estimated at around 75%. The aim of this cross-sectional study is to examine the influence of unilateral nephrectomy (UN) in uWT survivors on the long-term renal function.
Materials and Methods: From our childhood cancer survivors registry (established in 1966), 186 uWT patients could be identified with a minimum survival of 5 years. All patients underwent UN and were treated according to SIOP guidelines. 70 patients (38%) received additional radiotherapy (uWT + RT). 544 survivors, treated for a non-WT malignancy and who received no nephrotoxic therapy were included as controls. The glomerular filtration rate (GFR) was estimated using the Schwartz and the CKD-EPI formulas whenever relevant. Urine dipsticks for albuminuria were considered normal only if negative. Adults with a systolic blood pressure > 140 mmHg and/or a diastolic blood pressure > 90 mmHg and children with a systolic and/or diastolic blood pressure ≥2 the standard deviation corrected for gender, age and height were considered hypertensive. The median follow-up was 15 years.
Results: The GFR was significantly lower (p
Conclusions: Lifelong follow-up of renal function and blood pressure is warranted in all uWT as early detection of adverse effects may prevent additional damage if timely therapy is initiated.

O-0180

PATTERNS OF RELAPSE IN MALES WITH NON METASTATIC PARATESTICULAR RHABDOMYOSARCOMA (RMS) TREATED IN SIOP MMT 84,89,95 STUDIES UTILISING A NON-SURGICAL APPROACH TO LYMPH NODE STAGING.

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Purpose/Objective: To report patterns of relapse in non metastatic paratesticular RMS from studies which utilised a non surgical approach to lymph node staging.
Materials and Methods: Patients were treated from 1984-2003. Radical inguinal orchidectomy was recommended, but retroperitoneal lymph node assessment was based on imaging alone. Treatment was stratified by stage, size, age and histological subtype. 10 year overall(OS) and event-free(EFS) survival were analysed with attention to patterns of relapse.
Results: 190 patients, median age 5.5years(0.3-19yrs); 44(23%) aged > 10 years; 42(22%) alveolar; 53/174(30%) tumours ^{3} cm. Larger tumours were more frequent in older(^{3} years) males (24/41;58% vs. 30/133;22%: p < 0.001). 13/187(7%) had regional node involvement(N1) at diagnosis

For the whole cohort, 10 year OS and EFS were 92% and 82%. Survival was superior in males aged < 10yr (OS 96%, EFS 88% vs 79% and 61% in those ^{3}10yrs: p = 0.005 and p < 0.001).

31/190(16%) patients relapsed of whom 14/31(45%) died. Relapse was local in 7(22%), in nodes 21(68% including one with concurrent local relapse), and distant metastatic in 3(10%). Amongst those without nodal involvement at diagnosis (N0 = 174), nodal relapse occurred in 20(11%) -of whom 9 died- and was more common in older (^{3}10yrs) males (11/38;29% vs. 9/136;7%: p < 0.0001). Tumour size strongly correlated with age and had no independent

impact, nor did histology. 10 year OS was 92%(CI95%:87-95%) in N0 and 90%(CI95%:60%-98%) in N1 patients.
Conclusions: Large collaborative studies confirm an excellent prognosis for paratesticular RMS, except in older patients and those with larger tumours. There is an unresolved controversy about the optimal approach to lymph node staging. Nodal relapse occurred in 11% (20/174) of clinical N0 patients of whom 9 died, indicating the need for more accurate staging. New technologies available since the era of these studies include PET and/or laparoscopic techniques which need prospective evaluation in future studies.

O-0181

INTRAOPERATIVE IN VIVO VISUALIZATION OF PEDIATRIC RHABDOMYOSARCOMA USING FLUORESCENCE LAPAROSCOPY

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Purpose/Objective: Surgical treatment of children suffering from rhabdomyosarcoma is often challenging especially in difficult anatomical regions such as the pelvis and mutilating surgery is sometimes necessary. Procedures are complicated due to a lack of possible visualization of these tumors and their margins in vivo. The aim of the study was to establish fluorescence laparoscopy in mice for optimized in vivo tumor visualization and possible photodynamic therapy.
Materials and Methods: We used our recently described model of disseminated human RMS. Therefore, alveolar human RMS cells were transfected with Gaussia Luciferase and mCherry and injected i.p. into 21 NOD/LtSz-scid Il2Rγnull-mice. Intraperitoneal tumor growth was monitored for 4 weeks using serum luciferase activity. Fluorescence labeled Cetuximab and the photodynamic active substance Hypericin were injected i.v. into the animals (100 µg/25 g body weight). 24 hours later, fluorescence laparoscopy using the Storz D-Light system was carried out. Tumors were resected under fluorescence guidance and specimens were evaluated histologically.
Results: Successful tumor growth was found in 80% of animals. A significant clear discrimination between tumors and surrounding tissue was possible by their fluorescending properties since tumors expressed the fluorescent protein mCherry and Hypericin was accumulated in the tumors. Targeted resection of the lesions was feasible using fluorescence laparoscopy. Histological work-up confirmed alveolar RMS in all fluorescence-guided, resected specimens in contrast to standard laparoscopy.
Conclusions: Improved intraoperative visualization of pediatric RMS was feasible using hypericin-based fluorescence laparoscopy in mice. Besides intraoperative visualization, the system can also be used for photodynamic therapy as a novel treatment option and can be transferred into humans in near future.

O-0182

QUALITY OF LIFE (QOL) OF LONG-TERM SURVIVORS OF BLADDER-PROSTATE RHABDOMYOSARCOMA (BPRMS), LOCALLY TREATED WITH CONSERVATIVE SURGERY AND BRACHYTHERAPY (BT). A SINGLE TEAM EXPERIENCE.

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Purpose/Objective: To analyse QoL and long-term sequelae of males treated with conservative local treatment (surgery and brachytherapy) for a BPRMS within the framework of SIOP studies.
Materials and Methods: From April 1991 to December 2007, 23 males were treated by conservative surgery (partial cystectomy or partial prostatectomy or both) and post-operative low-dose rate interstitial BT using iridium 192 and were in first complete remission with more than 5 years of follow-up. Twenty-two males, who retained their bladder, were sent a QoL questionnaire (similar to that used by the International workshop in 2006). One patient underwent a cystectomy for a non functioning bladder and was not included in the study. Median age at operation was 24 months (range:14 months-11years). Median age at time of questionnaire was 13 years (range: 7-25years). Median follow-up was 9 years (range: 5-21years).
Results: Seventeen males/parents (77%) completed the questionnaire. Twelve patients (71%) considered themselves as having a normal QoL, with normal urinary continence (9 patients) or very rare diurnal dribbling without impact on their QoL (3 patients). Among them, 3 still had enuresis (age:7-9-10years). Four males had frequent diurnal dribbling, requiring protection for 3 and causing difficulties for social life and/or sports for 3 of them. They have no nighttime incontinence. All underwent urodynamic studies.- One patient developed a neurogenic bladder with dysuria, pollakiuria and urgency and was submitted to intermittent catheterism after urodynamic study. Other patients complained rarely of these symptoms (pollakiuria (3 patients), urgency (2 patients), dysuria (1 patient)). Fifteen patients had normal erections. For 2 males (9-11years), the parents did not answer the question.
Conclusions: 71% of long-term surviving males after conservative local treatment of BPRMS, combining limited surgery and BT consider themselves as having a normal QoL. All but 2 have normal erections. These long-term results encourage to develop this treatment in other institutions/countries.

IPSO: IPSO - SESSION 6: NEUROBLASTOMA

O-0183

CHYLE LEAK COMPLICATING ABDOMINAL NEUROBLASTOMA SURGERY: SURGICAL MANAGEMENT AND PREVENTION

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Purpose/Objective: Chyle leak is a known complication in abdominal neuroblastoma surgery due to the tumors' proximity to the chylous drainage channels. We reviewed our management strategy with the aim to avoid unnecessary delays in subsequent adjuvant therapy.
Materials and Methods: All patients who underwent resection of abdominal neuroblastoma between 2002-2013 were included. A change in surgical strategy commenced from August 2010 when routine meticulous mesenteric lymphatic ligation (MLL) before abdominal closure was included in the primary surgery, thereby forming 2 study groups (Group A: before routine MLL; Group B: after routine MLL). Patients' demographics, disease characteristics, operative techniques, and postoperative management were reviewed.
Results: There were 64 patients in Group A and 31 patients in Group B. 10 (15.6%) patients in Group A developed chyle leak that required additional nonsurgical management that included parenteral nutrition with medium chain triglyceride diet or bowel rest, prolonged abdominal drainage and delay in adjuvant chemotherapy. Duration of chyle leak was 32 days (ranged 6 * 60 days). Of these, 1 patient's chyle leak (1000 mls/day) persisted on postoperative day (POD)60 and underwent laparotomy with MLL, whilst another patient drained 900 mls/day by POD6 and was similarly operated. Both patients' resolution of abdominal chyle leak was evident by POD2. None in Group B developed chyle leak.
Conclusions: Chyle leak complicating abdominal neuroblastoma surgery disrupts neuroblastoma treatment. Besides conservative measures, surgical management with meticulous MLL should be considered when chyle leak occurs. Meticulous MLL can be preventative if performed routinely before abdominal closure in the primary surgery.

O-0184

STAGE 4S NEUROBLASTOMA: A TALE FROM TWO CENTERS – A 27 YEAR EXPERIENCE

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Purpose/Objective: Stage 4S neuroblastoma is widely considered a 'special' disease with good prognosis despite the presence of disseminated metastases. This study therefore examines outcomes for stage 4S neuroblastoma patients treated over a 27 year period at two major centers.
Materials and Methods: Patients presenting with stage 4S neuroblastoma were identified from ICD10 codes during the period, 1985-2012. Data analyzed included * (1) site of primary tumour, (2) age at diagnosis, (3) management strategies and (4) clinical outcomes including treatment-related morbidity with late effects.
Results: Thirty-eight stage 4S infants; median age at diagnosis = 124 days (IQR 50-91days). Urinary catecholamine profiles were elevated in 17/29 patients. Primary tumours were located - abdominal cavity / pelvis (n = 7, survival 71%), adrenal gland (n = 20, survival 70%), thorax (n = 7, survival 100%), neck region (n = 1, survival 100%), site unknown (n = 3, survival 100%). MYCN amplification was recorded in 3/19 (16%) patients; 1p36deletion in 4/21 (19% cases.

Five infants had supportive care with 'watchful waiting', 16 patients required chemotherapy alone and 9 babies surgery including - biopsy or resection of the primary tumour only. Seven children received chemotherapy along with surgery including an additional single case that had chemotherapy, surgery and radiotherapy. Overall survival at 10 years was 79% with an event-free survival - 61%. Causes of death were * progressive hepatomegaly (n = 6), intracranial bleed (n = 1) and tumour relapse (n = 1). Among survivors adverse events included * (a) severe sepsis following chemotherapy (n = 5), (b) renal impairement (n = 1) and two 'new early cancers' - retinoblastoma (n = 1) - 22 months and Burkitt lymphoma (n = 1) * 21 months.
Conclusions: Stage 4S neuroblastoma was associated with a favourable outcome for the majority of young infants treated at these two centers. Morbidity including the onset of new malignancies can occur even in the early years after treatment. Mortality was linked with adverse tumour biology (MCYN, 1p deletion) and hepatomegaly.

O-0185

STAGE 4S NEUROBLASTOMA – WHAT ARE THE OUTCOMES? A SYSTEMATIC REVIEW OF PUBLISHED STUDIES

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Purpose/Objective: The prognosis of Stage 4S neuroblastoma has traditionally been reported as excellent yet conflicting treatment protocols exist for this enigmatic disease. To critically address this question we have undertaken a systematic review of published studies to accurately determine outcomes for infants with Stage 4S neuroblastoma.
Materials and Methods: Studies were identified using Medline (1950-), Embase (1980-) and Cochrane database(s) using the relevant search terms. Literature reviews, case reports (<3 patients) and adult studies (age >18 years) were excluded. Data were extracted independently following paper selection by 2 authors and reviewed by the senior author. Biologic factors, treatment modalities and mortality were reviewed.
Results: The original search retrieved 1320 articles. Following application of exclusion criteria and removing duplicate data - 23 studies (617 patients) were included for final review. The published studies covered the period 1971-2012. The most common site of primary tumour was the adrenal gland with metastasis observed in the liver. Overall patient survival was 85%. Only 10 studies (323 patients) recorded MYCN status. Mortality in MYCN amplified tumours was 70%. 1p status was reported in only 4 studies (133 patients). 1p deletion carried a 40% fatality rate. Management included - observation only (114 patients - 3.5% mortality), surgical resection of primary tumour only (77 patients - 8% mortality), chemotherapy only (76 patients - 16% mortality), radiotherapy (5 deaths - 33% mortality), chemotherapy with surgery (128 patients - 11% mortality), surgery with radiotherapy (18 patients - 22% mortality), radiotherapy with chemotherapy (42 patients - 29% mortality), surgery with chemotherapy and radiotherapy (18 patients - 39% mortality).
Conclusions: There is a significant mortality observed in Stage 4S neuroblastoma infants with a dismal outcome observed in those patients with MYCN amplification and 1p deletion. Those patients amenable for conservative management carry the best prognosis.

O-0186

TUMOR ASSOCIATED CACHEXIA (TAC) IN CHILDREN: HUMAN HEPATOBLASTOMA AND NEUROBLASTOMA CELLS ALTER THE GLUCOSE METABOLISM AND LEVELS OF GHRELIN, GLP-1 AND PYY IN NUDE RATS

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Purpose/Objective: Recent evidence in adulthood cancer suggests that tumor associated cachexia (TAC) may be caused by specific interferences of the tumor with the hosts neuroendocrine regulation of appetite and energy balance. For children such mechanisms remain rather unclear. The present study investigates the glucose metabolism and gastrointestinal hormones such as Ghrelin (stimulates hunger), GLP-1 (glucagon-like peptide-1, stimulates satiety) and PYY (peptide tyrosine-tyrosine) in nude rats diseased with human hepatoblastoma (HB) and neuroblastoma (NB).
Materials and Methods: In a prospective, randomized study human HB (HuH6) and NB (MHH-NB11) cells (3×10^6) were transplanted into the abdominal wall of immuno-incompetent (nu/nu) rats (ethic committee approval Nr.: TVV43/11). Sham operated animals received cell culture medium only. Tumor growth was allowed for 8 weeks. Then all animals were investigated by an oGTT (oral glucose tolerance test) and assessed for serum levels of Ghrelin, GLP-1 and PYY. Finally all tumor masses and adipose tissues were excised and calculated.
Results: Total body weight (ex tumor masses) differed between the groups (HB $=$ 330g, NB $=$ 350g, Sham 370g). Subcutaneous adipose tissue was significantly decreased for both tumor groups (HB $=$ 2.6g, NB $=$ 2.1g, Sham $=$ 3.5g). During the oGTT glucose levels (calculated as area under the curve) were significantly decreased for HB (104 ± 10) and NB (102 ± 13) compared to Sham (84 ± 3), but insulin levels remained similar for either group. Total and active Ghrelin were significantly increased for HB (102 ± 15) and NB (111 ± 10) compared to Sham (84 ± 8). Vice versa total and active GLP-1 were statistically decreased in HB (92 ± 7) and NB (88 ± 12) compared to Sham (127 ± 13). Finally, total PYY showed equal kinetics to GLP-1 (HB 117 ± 5, NB 120 ± 4, Sham146 ± 12).
Conclusions: Human HB and NB altered the glucose metabolism and levels of Ghrelin, GLP-1and PYY in nude rats. Further studies must reveal the underlying metabolic pathways and possibly discover therapeutic options.

IPSO: IPSO - SESSION 7: RENAL TUMOURS/ RARE TUMOURS

O-0187

WHEN IS THE BEST TIME TO RESECT WILMS TUMOUR WITH INTRAVASCULAR EXTENSION? LESSONS FROM THE LITERATURE.

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Purpose/Objective: Preoperative chemotherapy is recommended for children with Wilms tumour and intravascular extension. Chemotherapy may increase tumour adherence to vascular endothelium, precluding complete resection. To evaluate the optimal length of preoperative treatment we report a systematic review of the literature.
Materials and Methods: Studies were identified using Medline and Embase databases from 1996 to present. Search terms were 'atrial', 'atrium', 'caval', 'intraatrial', 'intracaval', 'intravascular', 'nephroblastoma', 'vascular', 'vena cava' and 'Wilms'. English language titles reporting management of intravascular Wilms tumour were analysed.
Results: The search retrieved 32 articles meeting the inclusion criteria; 25 case reports (62 children) and 7 case series (355 children). The pre-treatment tumour extent was cardiac in 115 and caval in 288; 70% received neoadjuvant chemotherapy. Course duration was reported in 157: 8 received a short course (<4 weeks, SC); 83 standard course (4-6 weeks, StC); 66 extended course (>6 weeks, EC). Post-chemotherapy regression, surgical details and mortality data were reported for 74, 63 and 115 patients respectively. Regression of intravascular tumour occurred in 80% SC, 95% StC and 78% EC patients; complete resection was possible in 33%, 83% and 67%; mortality (non-standardised) was 38%, 12% and 40%. Of 21 patients with intracardiac extension who completed treatment, 5 received SC, 9 StC, 4 EC, 3 unknown. In 8 the tumour regressed into the vena cava, but 3 still required cardiac bypass, and 2 others were incompletely resected. Of 13 with persistent atrial extension 9 were completely resected, 8 on bypass. Statistical comparison was not possible, but the data suggest that extended chemotherapy may increase tumour regression into the IVC, and resectability without bypass, but without improved survival.
Conclusions: Published data is too limited to allow conclusions to be drawn, but suggests that there is enough uncertainty to merit larger studies, particularly to evaluate optimal treatment length for patients with intracardiac tumour extension.

O-0188

DOES WILMS TUMOUR IN OLDER CHILDREN HAVE A WORSE PROGNOSIS?

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Purpose/Objective: There is scant literature available regarding age as a prognostic factor in Wilms tumour. For stage 1 favorable histology (FH) prognosis is best for ages <4 yrs. Above age 10 yrs a worse outcome was reported associated with a higher prevalence of diffuse anaplasia.
Aim: to analyse if patients with Wilms tumors >8yrs of age (stage II-V) have a worse prognosis than to <8yrs or <4 yrs
Materials and Methods: Nineteen patients >8 yrs with Wilms tumour stages II-V were identified from a cohort of 192 new patients (2002-2012). For each patient two controls were chosen matched for stage and histology, one 0-3 yrs and one 4-7 yrs. In all patients pretreatment biopsies were obtained. Neo-adjuvant chemotherapy was offered to all, combined with nutritional resuscitation, TB-prophylaxis, anti-helminthics, anti-retrovirals and anti-hypertensives as indicated. Postoperative treatment was determined by local stage and histology. Survival of the >8yrs age group was compared with <8yrs, and with 0-3 and 4-7 yrs using Kaplan-Meier curves for OS and EFS.
Results: All three age groups ($n = 19$) contained 6 patients with stage II tumours, 3 stage III, 8 stage IV and 2 stage V. Histology was IR in 17 and HR in 2. OS at 5 years was 80.8% and EFS was 79.2% for the whole group. Survival of the >8 yrs group was equal to the <8 yrs group. No difference could be shown between the three age groups, although the 0-3yrs group showed a trend to better survival. Loss to follow up was 6/57 (11%).
Conclusions: Age <4yrs as a positive prognostic factor as shown in stage I, FH could not be reproduced in higher stages. Older patients as defined as >8yrs of age had a similar prognosis to younger children, although a trend to better outcome was seen in children <4yrs.

O-0189

LOSS OF IMPRINTING AND LOSS OF HETEROZYGOSITY AT 11P15 LOCUS IN INDIAN PATIENTS OF WILMS TUMOR

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Purpose/Objective: To evaluate the incidence of loss of imprinting (LOI) and loss of heterozygosity (LOH) of 11p15 in Wilms tumor (WT) in the Indian population and its correlation with outcome.
Materials and Methods: This was a prospective study for WT over a period of 4.5 years. Fresh tumor and adjacent uninvolved kidney tissue (control) were snap frozen and

refrigerated at minus 80°C. Tumor and germline DNA were extracted and treated with EZ DNA Methylation-Gold TM Kit for bisulphite conversion. PCR products for both tumor and germline control were studied for LOH (ten different microsatellite markers) and LOI. LOH and LOI were correlated with 2year Overall survival (OS) and relapse free survival (RFS) by Kaplan Meir analysis and correlated using Cox regression analysis.
Results: Forty-seven nephrectomy specimens were studied. LOH were seen in 16/47(34%) and LOI 14/47 (29.8%) cases and either LOH or LOI 18 (38%). There were 6 (12.7%) deaths and 7 (14.9%) recurrences giving a 2-year OS of 82.8% (95CI 64.9-92) and 2-year RFS of 78.6% (95CI 59.7-89.3). All 6 deaths were among those without LOH. The OS was 100% for those with LOH and 45.9% (95CI 45.9-87) for those without ($p = 0.04$;HR 9.9).The RFS for those with LOH was 92% (95CI 56.6-98.9) and 69% (95CI 42-85) for those without ($p = 0.14$;HR0.23). The OS was 87.5% (95CI 38.7-98) for those with LOI and 81.6% (95CI 60.7-92) for those without ($p = 0.75$;HR 0.7). The RFS for those with LOI was 64% (95CI 22.6-87.5) and 83% (95CI 61-93.5) for those without ($p = 0.1$;HR 3.3).
Conclusions: The incidence of LOI and LOH at 11p15 region in WT is low in Indian population as compared to that reported from the west. The OS among those without LOH is significantly lower ($p = 0.04$) while the presence of LOI significantly increases the risk of relapse (HR = 3.3).

O-0190

THE IMPORTANCE OF SIZE AND LOCATION IN PEDIATRIC DESMOID TUMORS

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Purpose/Objective: Pediatric desmoid tumors are benign, non-metastasizing fibrous tumors with an unpredictable course. Since predictors of survival and relapse are challenging, we performed an institutional review of pediatric desmoid tumors.
Materials and Methods: Following IRB approval, we conducted a retrospective review of all pediatric desmoid tumor patients (< 18 yrs) from September 1966 to August 2010 and identified 61 patients. Variables analyzed for predictors of survival included tumor size, site, age at diagnosis, sex, margins following resection, recurrences, and adjuvant radiation or chemotherapy.
Results: Tumor size and location were significant predictors for survival in patients with desmoid tumors ($p = 0.002$ and $p = 0.03$, respectively). Patients with tumors $\geq$ 5cm ($n = 35$) had improved survival (97 $\pm$ 5% at 10 years), compared to 84 $\pm$ 13% for patients with tumors $<$ 5 cm ($n = 26$). No patients with trunk tumors ($n = 8$) died. Only 1 of the 23 patients with extremity tumors died. The 10-year survival for patients with head/neck tumors ($n = 15$) was 82 $\pm$ 14%; the survival at 8 years for intracavity tumors ($n = 15$) was estimated to be 83 $\pm$ 35%. There was a significant association between tumor size and site ($p = 0.001$). Two-thirds of the intracavity tumors were $\geq$ 5 cm (10/15) and 75% of trunk tumors were large (6/8). Most of the upper extremity tumors (14/18; 78%) were $\geq$5 cm. Most head or neck tumors were small (87%). Only 3 of the 5 lower extremity tumors were $\geq$ 5 cm. Adjuvant chemotherapy, radiation therapy, treatment with Tamoxifen, Sulindac, and NSAIDS were not significant for survival.
Conclusions: Tumors $\geq$ 5 cm and location were the only predictors of survival. We feel that tumors $<$ 5 cm have decreased survival because of proximity to vital structures and consequently incomplete resection. Since significance in survival is not associated with other therapies, we advocate an aggressive surgical approach whenever feasible.

O-0191

SURGICAL TREATMENT OF PEDIATRIC PRIMARY CARDIAC TUMORS: A SINGLE CENTER EXPERIENCE

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Purpose/Objective: Primary cardiac tumors in infants and children are rare and mostly benign, surgical intervention is advocated when clinical symptoms or hemodynamic obstruction is present. This study summarizes our surgical experience with pediatric primary cardiac tumors.
Materials and Methods: Between January 2000 and September 2010, 13 children (7 males and 6 females, median age 87 days, ranging from 1 day to 12.3 years) with primary cardiac tumors were surgically treated in our institution. Diagnosis was made by prenatal echocardiography in 5 patients and by 2-dimensional Doppler echocardiography in 8 patients.
Results: Surgical resection of primary cardiac tumors was feasible in all patients. Histologic examination revealed rhabdomyoma in 4 patients, myxoma in 3 patients, papillary fibroelastoma in 3 patients (multiple in 1), fibroma in 2 patients and hemangioma in 1 patient. One patient with a huge rhabdomyoma, died in the third day after surgery because of severe ventricular fibrillation and subsequent low cardiac output. The operative mortality was low (7.7%). At a mean follow-up period of 57.7 months (ranged 12 months to 85months), all the remaining 12 patients are in good clinical condition with no tumor-related symptoms. Two-dimensional echocardiography reveals good ventricular function and no tumor recurrence.
Conclusions: Surgical resection of primary cardiac tumors in infancy and children is safe and feasible. The operative mortality was low. Heart transplantation or a less complete resection may be a good therapeutic choice when the tumor invades the myocardium extensively. Echocardiography is still the current primary diagnostic modality, whereas computerized tomography and magnetic resonance imaging provide complementary information about intra- and pericardiac masses. A definite diagnosis of tumor types depends on an accurate histopathologic characterization.

O-0192

TREATMENT STRATEGY OF VAGINAL ENDODERMAL SINUS TUMOR, THE LIMITED EXPERIENCE OF ONE SINGLE CENTER.

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Purpose/Objective: To evaluate the treatment modality for vaginal endodermal sinus tumor, exclusively with chemotherapy or combined with surgery?
Materials and Methods: From October 2001 to October 2011, 18 cases of vaginal endodermal sinus tumor were enrolled in our department. The age on diagnosis ranged from 6 months to 21 months. The most common symptoms were bloody excretion in vagina. All cases showed elevated alpha fetal protein and mass in vaginal tract. The diagnosis was determined by pathology in 16 cases and by clinical features in 2 cases. There was no metastasis to lung but to retroperitoneal lymph nodes in one case. The treatment and outcome were retrospectively analyzed.
Results: The primary chemotherapy protocol was VAC in one case and PEB in 17. After 4 cycles of chemotherapy, 8 cases reached CR and 10 cases PR. The 8 cases with CR finished consistent chemotherapy for 8 to 10 cycles. They were followed up for 6 months to 8 years and without recurrence. 8 of the 10 cases with PR underwent surgical removal, followed by adjuvant chemotherapy for 6 to 8 cycles. 2 of 10 cases with PR went on chemotherapy and reached CR after 6 and 8 cycles of chemotherapy. However, they found recurrence 5 months and 17 months respectively after finishing treatment. Later on they accept surgery to remove the tumor tissue and followed by chemotherapy for 6 to 8cycles. For follow-up of 3 months to 10 years, 2 case showed recurrence and died, 8 cases on event free survival.
Conclusions: Chemotherapy should be the primary treatment to preserve vagina and uterus. Cases reached CR on 4 cycles of chemotherapy could avoid surgery. Cases reached PR on 4 cycles of chemotherapy should accept surgery and followed by further chemotherapy. CR could be reached on 5 to 8 cycles of chemotherapy, but longer chemotherapy regimen may be needed to prevent recurrence.

IPSO: ISPO - SESSION 8: GERM CELL TUMOURS

O-0193

RECURRENT TESTICULAR MALIGNANT GERM CELL TUMORS

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Purpose/Objective: To evaluate the presentation, management and outcome of children with recurrent testicular malignant germ cell tumors (MGCT).
Materials and Methods: All recurrent testicular MGCT children treated at our hospital, with chemotherapy (PEB) and surgery, between 1994 and 2012, were evaluated for presentation, initial stage and treatment, time to recurrence, sites of recurrence, management and outcome. Kaplan Meier survival analysis was done for overall survival (OS).
Results: Seventeen children in the age range 8-54 months (Mean 30) were enrolled. At initial diagnosis of MGCT, 15 (88%) were stage 1 disease, 1 stage 3 and 4 each (6% each). All stage 1 patients had not received any chemotherapy previously. Fourteen (82.5%) had been treated elsewhere as stage 1 disease and presented to us with recurrence while 3(17.5%) had undergone initial treatment at our institution (stages 1, 3 and 4) all of whom had received appropriate chemotherapy. Histology was endodermal sinus tumor in 15 (88%), gonadoblastoma & embryonal carcinoma in 1(6%) each. Time to recurrence ranged from 1-27 months (Mean 8.35) with 14 (82%) recurrences within 12 months of initial treatment. The site of recurrence was retroperitoneal lymph nodes in 11(65%), lungs 7(41%), liver 3(18%), inguinal LN 2(12%), local recurrence 1(6%), mediastinum 1(6%) and bone marrow 1(6%). Six (35%) had single site recurrence while 8 (47%) had multiple sites of recurrence and in 3 (18%) there was only increase in αFP. On treatment for recurrence 7 (41%) did not achieve CR (2 died, 5 discontinued treatment) while 10 (59%) achieved CR

and were alive at last FU. Overall there were 2(12%) deaths giving a 5-year OS of 74.7% (95%CI 24.6-94.1).
Conclusions: Most recurrences (82%) were within 12 months and at multiple sites (47%). 30% had progressive disease leading to abandonment of therapy. Only 60% patients could achieve disease free long term survival on treatment for recurrence.

O-0194

REVIEW ON PAEDIATRIC TESTICULAR TUMOURS IN A TERTIARY CENTRE AND THE ROLE OF TESTICULAR SPARING SURGERY

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Purpose/Objective: To review our own experience in the management of testicular tumours in the local paediatric population. Among those benign tumours with orchidectomy performed, further retrospective evaluation was made to determine the possibility of testicular sparing surgery (TSS).
Materials and Methods: From 2002 to 2012, 36 patients (mean age: 5.50 years, range 0 day * 17 year old) with testicular tumours were treated in our unit. Operations were performed in 34 of them. TSS was only considered as an alternative to orchidectomy since 2010.
Results: Among the 34 patients who had operations done, 24 were confirmed to be benign lesions. Twenty-two patients (91.67%), including one with bilateral teratoma, had orchidectomy performed. Only five out of 24 patients had attempted TSS and 2 of the five patients had successful TSS done. Among the 19 benign lesions who had not attempted TSS, sonographic & pathology reports showed that the tumours might have been removed completely by TSS in nine patients (mean size 21.17% of the testicular volume).
Conclusions: In retrospect, TSS might be done in up to 45.8% (11 out of 24) of the benign testicular tumours. However, only 2 (8.33%) was performed in reality. We therefore propose that TSS should more be considered in small testicular tumours, as an alternative surgery to orchidectomy.

O-0195

OVARIAN SPARING SURGERY IN BILATERAL TERATOMAS: RESULTS FROM GCTM 2004.

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Purpose/Objective: Germ cell tumors represent about 70% of all ovarian masses in females and young women. Among them, ovarian teratomas are the most frequent lesions: 65% are mature teratomas (MT), 5% immature (IT). In 5-15% of cases, synchronous or metachronous lesions are present.
Materials and Methods: Italian AIEOP GCTM 2004 protocol includes 65 patients affected by ovarian MT or IM. In 9 (age 6-17 years, mean 12.5), a contralateral tumor occurred: metachronous in 7 and synchronous in 2.
Results: Metachronous lesions (7/9): contralateral lesions were observed 1 to 6 years after the first operation (mean 4). At first operation 3 lesions were localized in the right ovary, 4 in the left, and tumor size ranged from 5 to 16 cm. In all cases surgery consisted in a complete excision of the ovary (3 ovarosalpingectomies, 4 ovariectomies). At the time of relapse, a conservative excision was possible in 6/7; the only patient who had a mutilating procedure is following treatment with hormone replacement therapy. Histology was MT either at diagnosis and at relapse.

Synchronous lesions (2/9). Both patients underwent ovarian sparing surgery: in 1 case a MT was diagnosed in both gonads, in other MT occurred in one gonad and a functional cyst in the other.
Conclusions: Surgery is the mainstay of treatment of ovarian teratomas and, in most cases, ovarectomy is the usual approach for monolateral tumors at diagnosis due to their size. Although very rare, metachronous or synchronous tumors are possible and imply the risk of a mutilating procedure. A strict follow-up, extended up to at least 7 years after the first operation, is stressed, to make it feasible an early diagnosis, which allows removing small metachronous tumors, preserving ovarian tissue. The conservative approach may also limit the possible occurrence of fertility failures, reported even in some cases of monolateral ovariectomy.

O-0196

SACROCOCCYGEAL TERATOMA-10 YEAR EXPERIENCE OF TERTIARY CARE HOSPITAL IN NEW DELHI

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Purpose/Objective: To evaluate the presentation, treatment and long term outcome of children with sacrococcygeal teratoma.
Materials and Methods: Retrospective analysis of consecutive cases of sacrococcygeal teratoma presenting at VMMC and Safdarjang Hospital, New Delhi from2003 through 2012 was carried out. The age at presentation, mode of delivery, significant pelvic extension (upper margin of tumour not reachable on rectal examination), treatment, histology, early complication, recurrence and long term outcome were reviewed.
Results: Thirty-one patients (24 female, 7 male) were identified. Median age of presentation was 30 days (range1-4320 days). Twenty-four (77%) patients were delivered vaginally. Twenty-four (77%) presented with external mass, 4 (13%) with urinary problem, 2 (7%) with faecal obstruction and 1 (3%) with perineal fistula. Significant pelvic extension was found in 10(32%). Pre-operative chemotherapy (PEB regimen) was given in 2. Posterior sacral 20(64%), combined abdominal and sacral 8(26%), and posterior saggital 3 (10%) approaches were used for excision. Histologically 22 (71%) were mature teratoma(MT), 1 immature teratoma(IMT), 8 yolk sac tumor(YST) (5 only intra-pelvic mass; 3 both external and intra-pelvic). All underwent complete excision. Four (13%) developed wound infection (3 managed conservatively, 1 required diverting colostomy). Four (13%) had early urinary dribbling and 3 (10%) had early fecal incontinence (which resolved). Recurrence (in pelvis) developed in 3 (10%) [2 YST and 1 MT at initial diagnosis]. Histology of recurrences were 2 YST and 1 IMT. Mean follow-up was 48 months (range 10-110 months). In the long term, 3 (10%) had persistent urinary dribbling, none had fecal incontinence. Overall there were 2 deaths (both recurrent YST) giving an overall survival of 93.5%.
Conclusions: Sacrococcygeal teratoma have varied presentation. Rectal evaluation is important for deciding appropriate operative approach. Overall survival (93.5%) is good with a recurrence rate of 10%. Long term sequelae are minimal (10%) and manageable.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS

O-0197

A CHILDHOOD CANCER PARENT ROUNDTABLE; OPPORTUNITIES FOR ENGAGEMENT AND EMPATHY

D. Mornar

British Columbia Children's Hospital, Paediatric Oncology, Vancouver, Canada

Purpose/Objective: To provide parents and other stakeholders the opportunity to exchange ideas and strategies for coping with and managing the many facets of a childhood cancer diagnosis and its treatment.
Materials and Methods: at the request of parents and health care professionals involved in pediatric cancer control in british columbia, canada we held several parent/family retreats and town hall meetings. In this session we prpose a similar set of roundtable discusiions with 6-10 tables able to seat 6-8 people each. Participants select fron a range of topics identified by parents like; relationships, finances, beyond cancer, advocacy, late effects and stress busters. Leading questions are provided to get the discussion going. .each group selelcts its own secretary. Later on a report is made to the entire group. A document is then compiled and shared with other stakeholders. Sessons require 60-90 minutes. In that timeframe groups can take part in as many as two topics.
Results: Improved parent to parent communication. Improvved parent to health care porfessional communication. Improved clinical care for patients. Increased rappor and solidarity amongst all stakeholders involved. Increased and more effective positive useuse of social media like facebook,twitter and you tube. Excellent feedback from all participants with ongoing requests to hold more sessions. Reduced stress in parent and health care provider communities.
Conclusions: Delegates or stakeholders come to these congresses to improve the outcomes of a childhood or aya cancer diagnosis. More opportunties must be available for delegates to meet in sessiions other than a lecture format. Sessions that also acknowledge the many social and economic realities of the world we live in.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS

O-0198

THE ROLE OF A PARENT GROUP IN AWARENESS CREATION AND ADVOCACY OF CHILDHOOD CANCERS IN GHANA

F. Aveh

University of PROFESSIONAL STUDIES, Accounting, Accra, Ghana

Purpose/Objective: to raise awareness of childhood cancers in Ghana
Materials and Methods: A high profile launching of the Ghana Parents' Association for Childhood Cancers (GHAPACC) in 2009 with publicity about challenges faced by children

affected by cancer and their families. Awareness creation, fundraising walk organised during the International Childhood Cancer day in 2010. Coverage was by national TV. Needs of children affected by cancer and their parents made public through articles in the national daily papers. Members of the parents' group have participated in radio and television talk shows. Members and Oncology Doctors organized awareness talk to over 2,000 school children which will done nationwide. A video clip highlighting the plight of parents and children with cancer will be showing regularly from the 15th of February on almost all the TV stations and also to solicit funds to build a 10-bedroom hostel for parents whose children are on admission. Over 5000 posters distributed by GHAPACC including schools and churches.
Results: Children in one of the schools undertook a sponsored walk and were able to raise over GHC30,000 ($15,000) and bought equipment for the children's oncology day care unit at Korle-Bu hospital.
Conclusions: Level of awareness of childhood cancers in Ghana has improved but more needs to be done. Superstition and stigmatization by society are some of the hindrances to early reporting of cases to health facilities. More education through the media would be an effective way for continued awareness, and improved access and outcomes for childhood cancer.

O-0199

THE ROLE OF ICCF IN PROCUREMENT APHERESIS MACHINE AT THREE GOVERNMENT HOSPITALS

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Purpose/Objective: The activities and presentations of awareness for children with cancer by the Indonesian Childhood Cancer Foundation (ICCF) for twenty years has gained widespread acceptance by the Society and the Government.

It has been proven by the request of proposals ICCF received from three various State General Hospitals to obtain Apheresis Machine which is very much needed for children with cancer.
Materials and Methods: The Apheresis Machine is very useful for the implementation of bone marrow transplant, (stemcells transplant revolutionary program), as a superior program to overcome children with cancer, especially leukemia, which amounted 40% of all children cancers. The use of the machine is to increase the number of healing and reduce the rate of pain and death of a cancer patient especially children with leukemia.

Therefore the beneficial of the machine above for cancer patients, is expected to speed up the diagnosis and therapy of patients with severe thrombocytopenia.
Results: Having those requests ICCF starts giving presentations to several donators and outlining how important this machine is for the treatment and cure of children with cancer. The presentation was able to convince our donator and was welcomed by Prudentials Life Assurance Indonesia who is willing to give the donation to buy this machine for the three hospitals which is located in Jakarta, Surabaya, and Bali.

These machines have all been installed and utilized maximally by each hospitals.

Later the machine is expected to lower the morbidity and mortality of children cancer patients.
Conclusions: Knowing that ICCF was able to obtain Apheresis Machine, other hospitals from other part of Indonesia have called us for the same request.

O-0200

HUE,VIETNAM FAMILY GROUP PROJECT

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Purpose/Objective: The ultimate goal is to enhance the quality of life of children with cancer and their families treated at Hue Central Hospital in Vietnam aiming at developing and empowering the family group to become self-sufficient with capacity building in order to face the challenges of 1) Family and psychosocial support after cancer diagnosis; 2) Treatment abandonment; and 3) Bereavement.
Materials and Methods: The project is ran by a Vietnam family group (CCFGCV) funded by UICC, supported by ICCCP as mentor and ACCL as supporting mentor and auditor of the project financial management. Hue Central Hospital is the collaborating organization in providing support and environment for CCFGCV activities.
Results: CCFGCV has had a valuable opportunity to step forward by participating ICCCP Meeting-Asia 2012 for leadership development and knowledge enhancement, holding family group meetings for providing appropriate education about disease and the best possible care, Collaboration with Hue medical students volunteer group to hold some social activities (i.e. music, performances, games, birthday parties) in the ward has brought warm environment filled with smiles of children and their families. Hospital visits to families of newly diagnosed as well as home visiti to bvereaved family to shar feelings were arranged. A first big challenge, the mega activity (two-days outing with the participants of 50 persons including patients, parents, siblings, medical staffs and medical volunteer students) was very fruitfultul sharing feeling and making precious memories with hope.
Conclusions: The project has supported the capacity building of CCFGCV to empower them to grow and to be a self-sufficient, to be able to deal with the challenges and difficulties. The bond of family group members has brought the active involvement to support each other from the time of diagnosis to the treatment process including making better environment, preventing abandonment of treatment as well as psychosocial support to the bereaved families.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS - FREE PAPERS 2 - ROTARY INITIATIVE

O-0201

ROTARY'S INITIATIVE

E. Grynszpancholc[1], K. Dollman[2]

[1]Fundaci'n Natalí Dafne Flexer, Presidency, Ciudad Aut'noma de Buenos Aire, Argentina; [2]ICCCPO, Board Member, Ciudad Aut'noma de Buenos Aire, Argentina

Purpose/Objective: There is a proposal to approach Rotary International to develop an Alliance with ICCCPO members to promote aawareness of childhood cancer across the globe. The focus will be on increasing awareness for early diagnosis, making childhood cancer available and accesibly and improving pain care management for children wit cancer.
Materials and Methods: This Initiative promotes as many ICCCPO members working with Rotary Clubs, replicating this experince around the world, will help garner at a global level and inspire Rotary to adopt the cause.

Tools and informational materials, follow-up and inspirational cases will be provided during this Presentation.
Results: Rotary expects Polio to be completely erradicated in a few years. We believe this is a good moment to begin a relationship with Rotary as to become top of mind when Polio is erradicated and they look for a new cause to adopt.
Conclusions: Even if Rotary International never adopt the Childhood cancer Cause, we will be able to meassure the results of this Initiative and the benefit gained by ICCCPO members, not only as economic results but the inkind donations and the development of habilities, relations and volunteers in the icccpo members campaigns.

Through ICCCPO membership, Members can gain also new kinf and ways of relationships.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS

O-0202

PARENTS/FAMILIES GIVING BACK TO ASSIST PAEDIATRIC ONCOLOGY RESEARCH AND SUPPORTIVE CARE

M. McGowan

Royal Children's Hospital, Children's Cancer Centre, Melbourne, Australia

Purpose/Objective: Over the past 20 years many inroads have been made in the field of Paediatric Oncology but we still have a long way to go. to reach 100% cure rate we need to support continue research for treatments and supportive care options. Funding for both research and supportive care if extremely limited from government and other sources leaving a large unfilled gap.
Materials and Methods: From the perspective of paediatric oncology the role that consumers and their networks play in contributing to the shared mission of improving outcomes for patients and their families is crucial. Philanthropic groups and volunteers whose lives have been personally affected by cancer play a critical role in providing funds to fill the gaps after government fundign has been recieved.
Results: The drive from families to ''give Back'' has led them to invest thier time, energy and passion to support raising funds for cancer research and supportive care. Consumer engagement at the Royal Chidlren's Hospital (RCH) in Melbounre Australis provides avenues for linking the past, present and future treatments by access world class therapies, cutting edge research and improved outcomes on an ongoing cycle that benefits all who are involved.
Conclusions: The Children's Cancer centre at the RCH has been enriched from being involved in philanthropic groups by being part of the consumers' experience from diagnosis and beyond. The collective contribution by families, staff and volunteers provide a broad understanding of the interplay between research, treatment, recovery, survivorship and volunteering

O-0203

ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE OF ADOLESCENT CANCER PATIENTS USING THE PEDSQLTM 4.0 GENERIC CORE SCALE.

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Purpose/Objective: Improved survival after childhood cancer has shifted the focus to health-related quality of life (HRQL), especially among adolescents. The purpose of this study is to evaluate the HRQL in Korean adolescents with cancer.
Materials and Methods: We assessed HRQL among adolescents and their parents using the PedsQL^{TM} 4.0 Generic Core Scale. This form consisting of 23 items comprises four domains: physical, emotional, social and school functioning. It also consists of adolescent self-report and parent proxy-report.There were 92 adolescents with cancer who had a median of 2.5 years from diagnosis, and 85 parents of them joined in this study. To compare the HRQL, the data were collected from the matched 435 healthy adolescents and 375 their parents.
Results: Compared to healthy controls, the mean PedsQL scores with cancer were significantly lower in the physical, social and school functioning($p < .05$), but they were similar in the emotional functioning($p = .308$). Parent-adolescent concordance was fair in adolescents cancer patients. They reported no difference in three domains except emotional functioning($p < .05$). The parents reported lower emotional scores than the adolescents did. However, the healthy adolescents-parents reported the significantly different scores in emotional, social and school functioning($p < .05$) except physical functioning($p = .05$). Absent times from school for the recent one month, getting treatments nowadays and the shorter period of time after the diagnosis were identified factors as lower scores on their HRQL for adolescent cancer patients.
Conclusions: Overall, adolescent cancer patients reported significantly lower HRQL than their healthy peers. Despite decreased physical, social and school functioning, adolescent cancer patients seem to perceive better emotional adjustment than to be perceived by thier parents. we suggest mediation with communication between the healthy adolescents and their parents who have different HRQL scores. Additional analysis is needed for the long-term follow-up patients after the treatment.

O-0204

GENDER BIAS IN INDIA - THE PERSPECTIVE OF A GIRL SURVIVOR

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Purpose/Objective: Gender Bias (against the female child) in India exists at several fronts as seen in social, educational and healthcare indicators. This extends to childhood cancer with evidence of under-diagnosis, under-registration and of increased treatment abandonment seen in the female child. This has also been our experience at a center in North India where 1 in 3 children at diagnosis were females, and only 1 in 13 of cancer survivors were females. As Childhood Cancer ambassadors, Kidscan Konnect(KCK) - the Cankids teenage and young adult survivor group wanted to understand 1. why there was this bias, 2. what prevented better compliance, 3. what interventions would improve the situation in small towns and rural settings in India. 4. were there any rural - urban differences.
Materials and Methods: Study of all the female cancer cases at the Pediatric cancer Unit(PCU) for the last 2 years Interview all the female survivors and their family members conduct parent support group and KCK forums on the females provide complete financial support to families of females look to create 2 cancer ambassadors to speak up in their support.
Results: Based on the results of the action plan KCK and Cankids would evolve strategies and interventions to improve the position and address the issues, as well as create awareness.
Conclusions: Gender bias must be tackled at the grass root level. Girl Survivors must play an important role to become ambassadors and to provide solutions that will make the difference.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS

O-0205

FAMILY CONTACT GROUP

H. Wattwil, A. Färemo

Södra, Family Contact, Lund, Sweden

Purpose/Objective: In Sweden we have an association called the Children Cancer Parent Association. This association has many sub groups. The focus of the Family Contact group is to put the family first. We try to spread happiness during a difficult situation. We try to make life easier when the children are receiving their cancer treatments. We organize events and trips so that children with cancer can meet other children. We believe that when children receive these positive experiences, that they are encouraged to fight to survive their treatments.
Materials and Methods: One way of spreading happiness is to provide dinner once a week at the hospital where the children receive their treatments. The children, togehter with thier families, sit down to a nice dinner and have the chance to speak to other families and volunteers.They can exchange experiences, support each other and try to find daily routines during treatments.

We organize trips and events with our families, free or at a reduced price, so that the families can afford to do something fun together. This gives the children something to look forward to and something that can be remembered with fond memories.
Results: These events give children and their families comfort in meeting others who have the same experience. Unless you have a child with cancer you can't really understand how it feels. Therefore it is important for these families to meet and share their experiences. It results in the families supporting each other emotionally.
Conclusions: While we can not eliminate cancer we focus on providing comfort and support for those who are affected by cancer. We as an organisation survive together, during and after treatments.

O-0206

10 YEARS WALDPIRATENCAMP IN GERMANY

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Purpose/Objective: The Waldpiratencamp is a camp for kids, teenagers and young adults with and after cancer and their siblings. The camp of the Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation) was established in August 2003 in Heidelberg, Germany. Main goal is to support the young survivors in their return to everyday life. They should relax after the strenuous cancer therapy and gain strength and new courage in a cautious way.
Materials and Methods: The Waldpiratencamp offers 8-day camps for survivors and siblings as well as weekends for different kind of groups, e.g. bereaved parents. The program is always best suited for the needs of the participants. The staff of professional educators and pediatric nurses offers various activities in nature like hiking, rock climbing and canoeing. Collective experiences in outdoor activities should facilitate the exchange of experiences within the survivors / siblings community.
Results: Patients suffer from helplessness and passiveness during their therapy. The camp wants to retrieve the patients from this distressed situation. Every child gets individual support to rediscover his still existing abilities and his power for life. Fears are recognized as 'normal' and self-doubt experienced as surmountable. Group activities consolidate self-esteem and self-confidence. The participants take individual responsibility and consideration for handicapped survivors at the climbing wall and on the high rope course (latter is also suitable for wheelchair users).
Conclusions: There are camps for kids with and after cancer in France, Ireland, Hungary, Italy, Canada and in the United States. The Waldpiratencamp is the only camp of this kind in Germany. In 2008 the Waldpiratencamp was awarded with a price for aftercare for young cancer patients. In 2009 it was elected from the Federal Government of Germany as one of 365 outstanding places in Germany.

O-0207

LOOSING A CHILD IN CANCER

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Purpose/Objective: How do you survive after losing a child? How do others survive? Is there a road out of grief? These are some of many questions that can be raised when the worst case scenario has happened.
Materials and Methods: Losing a child is the worst thing that can happen a human being and a very difficult experience. It raises many questions and emotions and therefore it can feel good to talk to someone else who has experienced something similar ie other parents in the same situation.

What we as an association offers to our members is to provide support for parents that have lost their children in Cancer; a so called 'We who have lost'group. The purpose of the group is to be a charitable support to parents who lost their child to cancer.The leaders of this group is not professionally trained but parents with experience of losing a child in cancer and who are willing and interested in helping other parents in the same situation.

At the meeting with the parents, we work with professional psychologists where we provide 5-6 meetings over a period of 1-1,5 years with a group of maximum 10 parents and no less than 6. The leaders of the group receive professional supervision regularly.
Results: We have more than 5 years experience in working with these groups and our work has been very appreciated by the participants. We have also identified that the brothers/sisters Is another group that has a need of meeting other children in the same situation. We have not started this yet but have plans in doing so.
Conclusions: Our aim is to help other families and organisations in the same situation based on our experience and knowledge

O-0208

TWINNING PROJECT BETWEEN PAU KWONG WUN CHARITABLE FOUNDATION, HONG KONG AND GUANGZHOU GOLD-RIBBON CHILDREN PARENTS CENTER, CHINA.

B. Pau

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Purpose/Objective: Share international insight and exchange experiences between two organizations in running a parent group in Mainland China. Focus is how PKW empower GGCPC to become a self-sufficient group with capacity in Mainland China; to set an example for other local parent group in rest region China.
Materials and Methods: In the process of building GGCPC's capability, PKW assisted GGCPC to get formalized. PKW provided seeding fund for GGCPC to start their activities, and in subsequent years continue to provide financial support for part of the administration fee but on condition that GGCPC to seek for matching private donations.
Results: GGCPC in good relationships with Guangzhou six hospitals in regular meetings with hospitalized cancer children, medical professionals and ward staff with regular visit, talks, fun days and festivals' activities.

PKW encouraged GGCPC Board member to participate ICCCPO Asia Regional Meeting in 2007 and ICCCPO Annual Meeting in 2008 for getting international insight of childhood cancer.

To influence other support/parent groups in rest China, PKW co-organized with GGCPC to stage two China National Parent/Support Group Meeting in Guangzhou (2009) and Chengdu (2011).
Conclusions: GGCPC is the first childhood cancer parent support group formed in China in 2006 and got the registered non-profit status in 2011. This supported the capacity building of GGCPC to empower them to grow and to be a self-sufficient group. The bond between parent group and medical staff was found on mutual trust and support.

In 2012, GGCPC served approximately 325 hospitalized family members, organized 38 parents sharings in hospitals and organized different fund-raising activities, finally GGCPC made a record of raising a total of over RMB 970,000. All these shown with PKW's collaboration, GGCPC undergoing mature development and it's on right track in striving a better quality of life for childhood cancer in Mainland China.

O-0209

EMPOWERMENT OF SURVIVORS THROUGH EDUCATION -A PROJECT OF UGAM - SUPPORT GROUP OF CHILDHOOD CANCER SURVIVORS FROM AFTER COMPLETION OF TREATMENT (ACT)CLINIC

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Purpose/Objective: To create successful program for empowering childhood cancer survivors through educational assistance commensurate with vision statement of Ugam.
Materials and Methods: Ugam,a support group of childhood cancer survivors from ACT clinic at Tata Memorial Hospital (TMH) functioning under survivorship program of Indian Cancer Society(ICS), has facilitated empowerment of cancer survivors through educational assistance. Young survivors who were deprived of education due to socioeconomic constraints,are encouraged & inducted to pursue training to achieve their goals. Ugam has collaborated with reputed vocational institutes and universities to provide educational assistance.
Results: Sujaya Foundation in collaboration with ICS provides basic computer courses to survivors. One of the Ugam member serves as trainer. Certificates are provided by Sujaya Foundation which helps them to explore further carrier in different fields of computer science or by initiating them in jobs to go ahead in their life. Ecole Mondiale International School in Mumbai conducts weekly class where survivors are trained for English language by an able English teacher, motivating them to suppress their social fears. Yashwant Rao Chavan Open University provides degree courses to cancer survivors with maximum 50% concession and a gratuity to those who are from poor financial background.Self Reliant Survivor project of ICS sponsored by Glaxo SmithKline gives them opportunity of vocational training in tailoring. Till date 28 childhood cancer survivors have benefited from these courses. They are now able to clearly voice what they want from their life and are moving ahead successfully to come to mainstream of the society & live normal life after cancer.
Conclusions: This small initiative has helped modest number of childhood cancer survivors to overcome social fears and hindrances regarding career, employment and self image arising from their cancer experience. Ugam proposes to take this program to a larger scale with a mission to nurture childhood cancer survivor's life for a better professional & personnel achievements.

O-0210

THE CHALLENGE AND STRATEGY OF FOLK ORGANIZATION DEVELOPMENT

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Purpose/Objective: There are more than 40,000 children who newly diagnosed with cancer in China every year, but only less than 20% can accept the standard treatment. Their cured rate and life quality was far below the developed countries in Europe and America. Excluding the lack of medical and social security system, most primary reason is: the short of of social concern, and lack of social service by NGOs and welfare institutions.
Materials and Methods: On April 6-7, 2006, 14 cancer children parents were invited to participate in the ICCCPO Asia meeting in Shanghai. On June 30, 2006, Guangzhou Childhood Cancer Parents Group was proclaimed by these parents. After several years, the Group, which is leaded by cancer children parents, has become the first domestic NGO to provide long term multiple services for the cancer children and parents, and the Group formally registered in October 2011 and changed its name to ''Guangzhou Gold-ribbon Special Children parents Center''.('SCPC'for short).
The mission of the SCPC is to minimize the pain and suffering caused by cancer to the children and their families
Results: Till now, Guangzhou Gold-ribbon has provided services to cancer children and parents in eight hospitals in Guangzhou. In additional, there are more than 300 volunteers in Guangzhou Gold-ribbon, and they provided the service to cancer children and parents over 2500 cases per year.
Conclusions: As a NGO, Guangzhou Gold-ribbon was experienced lots of challenges during it's developing, and these experiences will be very worthy for coming new NGOs.

ICCCPO- PARENTS/SURVIVORS: ICCCPO - PARENTS/SURVIVORS

O-0211

PSYCHOSOCIAL CONCERNS EXPRESSED BY CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: Childhood cancer survivors population is increasing dramatically because survival rate of childhood and adolescent cancer have improved remarkably. Long term survivors are at risk of developing spectrum of adverse effects like organ dysfunction, decreased fertility, second neoplasm, death, cognitive impairment, employment difficulties etc. There are contradictory results in existing research about psychological sequel and less work done about understanding real concerns of the survivors in the background of ethnicity, culture, community, socioeconomic status. The aim of the current study is to explore major concerns of the survivors.
Materials and Methods: Qualitative method is used data collection. Survivors and parents workshop conducted to explore their major concerns related to survivorship. Prior to workshop brief interview questionnaire filled up by the participants. Expert panel appointed to address their concerns. Total forty survivors between 17-30 years and parents participated in the group discussion. Thematic analysis is done about the expressed concerns.
Results: Majority of survivors had multiple concerns about future life and self (marriage, fertility, self esteem) and physical health (weight, appetite, hair loss,) some expressed emotional concerns (anger, anxiety, negative body image, fear). Parents expressed concern about recurrence, marriage, fertility and finance. Some expressed need to spread awareness to protect rights of survivors in terms of life insurance, employment, marriage.
Conclusions: Majority of survivors and parents expressed multiple concerns about future life and physical health. Need based intervention planning could help to improve quality of life of the survivors.

O-0212

CAN FACTORS RELATED TO NATIONAL DIFFERENCES INFLUENCE PARENTAL LONG-TERM ADVERSE CONSEQUENCES, SUCH AS PARENTAL SUBJECTIVE MENTAL FATIGUE, IN THE AFTERMATH OF A CHILD'S CANCER?

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Purpose/Objective: The aim of this study is to determine the incidence of parental subjective mental fatigue and possible relationship between individual resilience for subjective mental fatigue in the aftermath of a child's cancer.
Materials and Methods: Participants were 334 parents of 219 Childhood Cancer (CC) patients parents of children treated at two different sites; the specialised CC treatment centre at Astrid Lindgren Children's Hospital in Stockholm (ALCH, and at one Icelandic site: the Children«s Hospital in Reykjavik (CHR), Iceland. Children diagnosed between 1986-2007 at different points in time since child's diagnosis whose child at time for the study was either in treatment, or had completed treatment.

Measuring parents' subjective mental fatigue due to a child's cancer the Maastricht Questionnaire (MQ-21) was used for assessment and the potential protective factor of individual resilience, against parents' subjective mental fatigue, was assessed using the Sense of Coherence (SOC-13). Comparisons of Icelandic and Swedish parents were carried out in the light of factors related to both nations as well as centre types.
Results: Comparisons of 125 Icelandic and 209 Swedish parents indicated similar levels of subjective mental fatigue in both clinical groups. Analysis of single items showed that

Icelandic parents scored significantly higher on 4 of 21 Mental Fatigue-items of the Maastricht Questionnaire. In the entire clinical parent group sense of coherence (SOC) was negatively related to mental fatigue symptoms ($r = -0.631$, $p < 0.01$), indicating SOC:s protective role as boosting resilience against long-term parental subjective mental fatigue.
Conclusions: The findings of this study implicate that there can be organisational factors associated with the smaller treatment center that can increase the risk for long-term parental adverse consequences, such as subjective mental fatigue. Addressing these targets and developing suitable instruments measuring care and parental psychological resources could minimize the effects of the long-term stress often followed childhood cancer.

POSTER SESSION: POSTER SESSION - ACUTE LYMPHOBLASTIC LEUKAEMIA

P-0001

L-ASPARAGINASE STRONGLY AFFECTS TRANSLATION REGULATION AND BIOENERGETICS IN ACUTE LYMPHOBLASTIC LEUKAEMIA CELLS

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Purpose/Objective: L-asparaginase (L-asp) is an important component of childhood ALL therapy. Its cytotoxic effect is based on depletion of extracellular asparagine and glutamine. The exact mechanism of cytostatic effect and resistance development is unclear. The aim of this study was to obtain further insights into the mechanisms underlying the cytotoxic effect of L-asp.
Materials and Methods: We established and studied L-asp-resistant preB ALL leukaemic cell lines derived from the REH (TEL/AML1[+]; very sensitive to L-asp) and NALM6 (TEL/PDGFRB[+]; medium sensitive). Pathway analyses of gene expression profile data from the cell lines and ALL patients samples revealed that protein translation and lipid/glucose metabolic pathways were most significantly changed in resistant cell lines and resistant patients samples. We therefore focused on the effect of L-asp treatment on bioenergetics and translation in leukaemic cells.
Results: Our experiments showed that L-asp inhibited PI3K/Akt/mTOR pathway - the key regulator of translation; mTOR/PI3K inhibition increased significantly sensitivity to L-asp both in sensitive and resistant cells. L-asp also inhibited glycolysis as documented by the decrease of c-Myc (main glycolysis activator), glucose transporter Glut1 and lactate, the terminal metabolite of aerobic glycolysis in cancer cells. Due to inhibition effect of L-asp on glycolysis we were interested in the effect of L-asp on oxidative phosphorylation (OXPHOS) mirrored by the changes in cell respiration. REH and NALM6 cells showed increased capacity of respiratory chain after exposure to L-asp, reflected by the increase of endogenous respiration in uncoupled state. Further analysis revealed that complex II (malonate-sensitive respiration) was enhanced in resistant REH cells.
Conclusions: Our data show that L-asp inhibits PI3K/Akt/mTOR pathway and strongly affects bioenergetic pathways of leukaemic cells. It decreases c-Myc-regulated glycolysis and increases OXPHOS. We conclude from our data that resistance of leukemic cells is likely to be caused by better biochemical adaptability to the nutrient deprived environment.
Grant support: IGA NT12429, 00064203 (FNMotol).

P-0002

INFLUENCE OF TRANSPORT PROTEIN GENE POLYMORPHISMS ON THE EFFECTS AND TOXICITY OF HIGH DOSE METHOTREXATE IN CHILDHOOD PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: To investigate the influence of polymorphisms of SLA19A1(solute carrier family 19, member 1) 80G > A, MDR1(multidrug resistance gene 1) exon26C > T and MDR1 exon21G > T/A on survival and side effects of patients with acute lymphoblastic leukemia
Materials and Methods: DNA was extracted from normal peripheral blood cells in 120 patients with ALL(acute lymphoblastic leukemia) during their remission period. MALDI-TOF MS technique was used to detect the polymorphisms of SLA19A1 80G > A, MDR1 exon26C > T and MDR1 exon21G > T/A. The plasma concentrations of MTX were detected by FPIA. The relationship of genetic polymorphism and survival and toxicity was analyzed using SPSS software Version 20.
Results: Event free survival (EFS) was not related to any polymorphisms of MDR1 and SLA19A1. Patients with mutant types of MDR1 exon26C > T and MDR1 exon21G > T/A show a much higher MTX plasma level on time point 24h and more common hepatic injury.The incidence of infections was increased significantly in patients with MDR1 exon21G > T/A mutants.The polymorphisms of SLA19A1 80G > A, MDR1 exon26C > Tand MDR1 exon21G > T/A had no significant effect on the occurrence of mucosa damage, gastrointestinal reaction, cytopenia, nephritic damage, neurological injury and allergic reaction.
Conclusions: The genetic polymorphisms of MDR1 exon26C > Tand MDR1 exon21G > T/A have a significant influence on hepatic toxicity and plasma concentration of MTX.

P-0003

THE RESEARCH OF THE RELATIONSHIP BETWEEN RFC1A80G GENETIC POLYMORPHISMS AND HIGH-DOSE METHOTREXATE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: To explore the relationship between RFC1A80G genetic polymorphism and high-dose of MTX-related toxicity, elimination delay and the efficacy in childhood acute lymphoblastic leukemia
Materials and Methods: 68 cases of ALL were enrolled in our department from February 2009 to January 2012. All of them were divided into two groups according to the different risk of ALL. HD-MTX was administered as a 24 hours' infusion with 5g/m^2 for high or mediated risk cases, while 3g/m^2 for standard risk cases. RFC1A80G gene polymorphism was detected before HD-MTX treatment. Plasma MTX concentration was detected on time after off HD-MTX 24 to 42 hours. Several routine detections were checked at the same time, including liver function, kidney function and peripheral blood cell count. All data were analyzed by SPSS 16.0.
Results: No association was found between different RFC1 genotypes and plasma MTX concentration at 42 or 66 hours after the beginning of the infusion ($P = 0.573$).
No significant difference was found between RFC1 genotypes in MTX elimination delay and prognosis of childhood ALL ($P = 0.794$).
There was a relationship between RFC1A80G genetic polymorphisms and high-dose methotrexate. The incidence rate of hepatotoxicity in RFC1-AA was 7.2 times higher than RFC1-GG genotypes and the myelosuppression in RFC1-AA was 2.8 times higher than RFC1-GG genotypes, which had significant difference ($P = 0.000, 0.005$).
The related side effects, including digestive tract infections, myelosuppression and mucositis were closely related to the elimination delay at 42 hours after HD-MTX ($P = 0.001, 0.013, 0.003$).
Conclusions: RFC1A80G genetic polymorphisms were associated with hepatotoxicity and myelosuppression after HDMTX chemotherapy and would be used as the risk indicators for MTX-related toxicity. No association was found among plasma MTX concentration, elimination delay and prognosis of childhood ALL.

P-0004

NOVEL GENETIC VARIATIONS IN THE FOLATE RELATED AND ARID5B GENES SHOW ASSOCIATION WITH METHOTREXATE PHARMACOKINETICS AND TOXICITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose/Objective: High-dose methotrexate (HD-MTX) is an important component of the consolidation therapy of childhood acute lymphoblastic leukaemia (ALL). Even with the same treatment protocol the pharmacokinetics of the drug show large interpatient variability. The aim of the present study was to investigate the influence of single nucleotide polymorphisms (SNP) in genes of the folate metabolic pathway, transporter molecules and transcription proteins on the pharmacokinetics and toxicity of methotrexate (MTX) and 7-hydroxy-methotrexate (7-OH-MTX) after HD-MTX treatments in children with ALL.
Materials and Methods: Totally 463 HD-MTX infusions were analyzed. Data of 48 children treated with 5 g/m^2/24h and 70 children treated with 2 g/m^2/24h HD-MTX according to ALL-BFM 95 and ALL IC-BFM 2002 protocols were collected [mean age: 6.4 years (1.1-18 years)]. 63 SNP of 14 genes were genotyped. Hepato-, nephro- and bone marrow toxicities, estimated by routine laboratory parameters were evaluated. Random forest and regression trees were used for variable selection. Linear mixed models were established to prove the significance of the selected variables and to estimate effect sizes. MTX and 7-OH-MTX values were log transformed to ensure correct model diagnostics.
Results: The rs4149056 of SLCO1B1 showed significant association with the serum levels of MTX ($p < 0.001$). SNPs (rs4948502, rs4948496) of ARID5B gene were associated with serum levels of MTX ($P < 0.001$), serum levels and AUC of 7-OH-MTX ($P < 0.001$) and with hypoproteinaemia ($P < 0.001$). Hepato-, nephrotoxicity, granulocytopenia and hypoproteinaemia were associated with novel genetic variations of SLC19A1, SLC22A8, MTR and MTHFD1 genes ($P < 0.05$, respectively).

Conclusions: We confirmed the associations of novel genetic variations in folate related and ARID5B genes with MTX plasma levels and the development of acute toxicity. Further analysis and validation in a larger cohort is necessary to determine the predictive value of these associations.

P-0005

PHARMACOGENETICS OF THIOPURINE METHYLTRANSFERASE IN TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA WITH 6-MERCAPTOPURINE IN TURKISH CHILDREN-DISCORDANT CASES

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Purpose/Objective: Background: 6-Mercaptopurine (6MP), an anti-cancer prodrug, has been succesfully used in treatment of pediatric acute lymphoblastic leukemia. However, efficacy of 6MP is significantly influenced by inactivation of polymorphic enzyme, thiopurine methyltransferase (TPMT). Patients with low activity experience severe or fatal hematological toxicity with standard 6MP doses.
Purpose of Study: Determination of the frequency of TPMT polymorphic variants known to functionally impair TPMT and to evaluate the relationship between genotype and 6MP related adverse reactions in Turkish children.
Materials and Methods: The frequency of four common alleles, *TPMT*2, TPMT*3B, TPMT*3C, TPMT*3A*, were investigated in 206 controls and 156 children with ALL by alele-specific PCR and PCR-RFLP methods. In addition, frequencies of common and rare *TPMT* alleles (TPMT**4-*23*) known for their low activity were determined by MALDI-TOF Mass spectrometry in 156 children with ALL.
Results: Two patients were heterozygous with genotypes of *TMPT**1/*3C and TMPT*1/*3A, and one patient was compound heterozygous carrying both *3A and *3C. Frequencies of *3A and *3C alleles were found 0.5% and 0.6% in controls and patients, respectively. For patients with genotypes of (*1/*3A), (*1/*3C) and (*3C/*3A), maintainance therapy had to be withheld 15%, 28%, and, 42%, respectively, because of febrile neutropenia and infections. In addition, there were two other cases with similar hematological toxicities, that could not be explained by their genotypes since they were wild type. Intrestingly, only one patient was heterozygous with very rare *14 allele, and she succesfully completed therapy with slight side effects.
Conclusions: In terms of common variants, and hematologic toxicities, genotypes (*1/*3A), (*1/*3C) and (*3C/*3A) matched perfectly. In two cases, genotypes of patients did not match with the observed hematologic toxicities (discordont cases). Further research is necessary on those cases.
Acknowledgement: We are grateful to Prof. Matthias Schwab for MALDI-TOF data. This study is partially supported by Turkish Academy of Sciences.

P-0006

THE RESEARCH OF THE ADVERSE EVENTS WITH THIOPURINE S-METHYLTRANSFERASE GENE MUTATION IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: By studying TPMT activity and gene promoter polymorphism, combined with significance of individual chemotherapy in ALL children.
Materials and Methods: HPLC method was carried out to determine TPMT activity(n = 100), which activity at newly diagnosed. At the same time determination of TPMT activity in healthy children(n = 180), these children come from the health care clinic. Using online Primer3 software design primers, PCR products were purified.To sequence TPMT gene of the patients with clinical events(n = 30). According to the method to analysis of correlation between TPMT activity and toxicity.
Results: The average TPMT activity of the ALL group(31.72 ± 10.31) $\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$, while the average TPMT activity of the healthy group(30.70 ± 9.67) $\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$. ALL and healthy group of children, no gender differences in TPMT activity (P = 0.45). The TPMT activity (while newly diagnosed)of ALL patients with clinical events(n = 30) is (24.07 ± 11.43)$\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$. There are significant differences in TPMT activity of severe bone marrow suppression group(20.96 ± 7.24)$\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$ and the group of ALL patients with clinical events($P < 0.05$). The TPMT activity of recurrence children (40.46 ± 8.18)$\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$ is also significantly different ($P < 0.05$).TPMT activity in severe liver toxicity group is no significantly different($P = 0.930$). During the TPMT gene sequencing about ALL patients with clinical events, only 3 children are heterozygosity mutations of TPMT*3C,while othes are homozygous genotype. There are significant differences in TPMT activity of the heterozygosity genotype group(11.99 ± 1.32)$\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$ and the homozygous genotype group (24.95 ± 11.32)$\mu mol \cdot L^{-1}$ 6-MTG $\cdot g^{-1}$ Hb $\cdot h^{-1}$($P < 0.05$). At the vicinity of the promoter region of -100, there are variation of the number of tandem repeats(VNTR) polymorphism, which divided into the six kinds(*V3/*V3*V4/*V4V4/*V6).There is no significant difference in TPMT activity of the six kinds($P = 0.186$).
Conclusions: TPMT activity is related to the gene polymorphism.TPMT activity determination could make prognosis and guide individual treatment.

P-0007

POLYMORPHISMS IN GENES OF THE VINCRISTINE PATHWAY AS NEUROTOXICITY MARKERS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: Acute lymphoblastic leukemia (B-ALL) is the most common pediatric malignancy. Therapeutic advances have increased survival, due in part to standardized treatment protocols. Vincristine is used in different phases of treatment (induction, intensification and reinductions). However, some individuals experience neurotoxicity and there are no markers to predict it. As vincristine has a narrow therapeutic range, pharmacogenetic studies may be useful for predicting toxicity.

Only 4 studies have been performed to date, analyzing a total of 12 SNPs in 3 genes in ALL patients. These studies have produced conflicting results for CYP3A5 gene and no association with vincristine toxicity for ABCB1 and MAPT. The lack of conclusive results may be due to non-homogeneous treatment and/or limited samples and SNPs analyzed.

The aim of the present study was to analyze in depth the role of genetic variations in genes involved in vincristine metabolism and transport as markers of neurotoxicity in a large cohort of children with B-ALL homogeneously treated.
Materials and Methods: DNA was extracted from remission blood samples of 150 pediatric ALL patients, all of them homogeneously treated with LAL/SHOP protocol. We studied 384 SNPs in 16 genes involved in vincristine metabolism and transport with Illumina GoldenGate platform. The association between SNPs and neurotoxicity was analyzed using the Fisher exact test.
Results: Polymorphisms in genes involved in vincristine metabolism and transport could be new neurotoxicity markers in pediatric ALL.
Conclusions: Our results suggest that pharmacogenetic studies may be useful for neurotoxicity prediction and adjustment of vincristine treatment in pediatric ALL patients.

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P-0008

DNMT3A MUTATION IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: *DNMT3A* mutation has been found in approximately 20% of adult AML patients and in 0∼1% childhood AML, and the hotspots of mutations are mainly located in the catalytic methyltransferase domain, thereinto, mutation R882 accounts for 60%. The prognosis of adult patients with *DNMT3A* mutation are dismal, and EFS/OS of the older patients are worse. However, little is known about the incidence and effect on prognosis of *DNMT3A* mutation in childhood ALL till now. Here, we tried to determine the incidence and prognostic significance of *DNMT3A* mutation in childhood ALL.
Materials and Methods: We screened for *DNMT3A* mutation by PCR and direct sequencing in 201 children with ALL (including 182 B-ALL and 19 T-ALL) from 2008 to 2009, treated on BCH-2008 protocol. Correlation of *DNMT3A* mutation and clinical characteristics, fusion gene, minimal residual disease (MRD) at d33 and day 78, and treatment outcome were analyzed.
Results: *DNMT3A* mutation were detected in 2.4% (5/201) of patients. In two of them, only 1

Conclusions: Liver, bone and lymph node metastasis could not be detected with conventinal methods but only could be observed with PET/CT imaging in patients with neuroblastoma and rhabdomyosarcoma.

P-0182

PEDIATRIC SOFT TISSUE TUMORS: DETERMINISTIC FACTORS FOR SAFETY AND ACCURACY OF DIAGNOSTIC YIELD IN IMAGE-GUIDED PERCUTANEOUS CORE-NEEDLE BIOPSIES

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Purpose/Objective: To assess lesion-related and technical factors that affect diagnostic yield and safety in image-guided percutaneous core-needle biopsies (PCNB) of soft tissue tumors in children.
Materials and Methods: Institutional review board approval was obtained for a retrospective study of 150 PCNB performed at our institution from January 2003 to January 2013. Medical records and radiologic data were evaluated for all PCNB performed on soft tissue lesions, excluding vascular malformations. Technical details of the procedure, demographic characteristics of the patients, and radiologic features of the lesions such as the location, size, imaging nature and enhancement were recorded. Procedure-related complications and repeat PCNB or other testing due to poor or non-diagnostic results were noted. Associations between the radiologic characteristics of the lesion, technical factors and diagnostic yield were evaluated using bivariate and multivariate logistic regression.
Results: Mean patient age was 11.4 $\pm$ 7.1 years. Ultrasound guidance was used in 80% of cases. General anesthesia was the most common form of sedation (86% of cases). Mean number of core biopsies was 6.4 $\pm$ 3.2 per case. The overall diagnostic yield was 80%. On bivariate analysis, procedures taking less number of cores (OR 0.75 95% CI 0.57 to 0.99, $p = 0.04$) and involving benign lesions (OR 0.14 94% CI 0.03 to 0.69, $p = 0.02$) were associated with non-diagnostic biopsies. Using a lower gauge needle showed a trend toward improving diagnostic success (OR 1.87 95% CI 0.93 to 3.71, $p = 0.08$). On multivariate analysis, the only factor that predicted low diagnostic yield was whether the lesion was benign (OR 0.14 95% CI 0.02 to 1.00, $p = 0.05$).
Conclusions: Image guided PCNB is a safe and accurate method for the diagnosis of pediatric soft tissue tumors. Particular attention should be paid toward lesions that appear benign on pre-procedure imaging in order to improve diagnostic yield.

POSTER SESSION: POSTER SESSION - RENAL TUMOURS

P-0183

HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION IN CHILDREN WITH RELAPSED OR REFRACTORY WILMS TUMOR

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Purpose/Objective: The overall treatment outcome of Wilms tumor (WT) has been markedly improved, however, treatment outcome remains poor in relapsed or refractory WT. To improve survival rates of patients with relapsed or refractory WT, high dose chemotherapy with autologous stem cell transplantation (HDCT/autoSCT) has recently been used. We analyzed the outcome of HDCT/autoSCT in patients with WT in our institute.
Materials and Methods: Nine patients with WT were treated with HDCT/autoSCT at Seoul National University Children's Hospital from August, 1998 to June, 2011. Seven had relapsed WT, and two were refractory to initial treatment. The median age was 2 years (range, 1-6 years). In the relapsed patients, median time to relapse was 9 months. The conditioning regimen included melphalan (140 mg/m^2/day at d-7 and 70 mg/m^2/day at d-6), etoposide (200 mg/m^2/day at d-8∼d-5) and carboplatin (400 mg/m^2/day at d-8∼d-5).
Results: Engraftment was achieved in eight patients. The median number of days for neutrophil engraftment was 10 days (range, 9-12 days), and the median days for platelet engraftment was 21 days (range, 16-30 days). One patient experienced veno-occlusive disease (VOD), and one patient had suspected VOD and posterior reversible encephalopathy syndrome. One died before engraftment due to acute respiratory distress syndrome developed after HDCT/autoSCT. Secondary acute myeloid leukemia developed in two patients after HDCT/autoSCT, and one of them is alive without disease after receiving unrelated bone marrow transplantation and the other patient died from leukemia progression. Therefore, seven of nine patients are alive without disease with a median follow-up of 6.2 years (range, 1.1-14.1 years) after HDCT/autoSCT. The probabilities of 5-year overall survival and event free survival were 77.8% and 64.8%, respectively.
Conclusions: HDCT/autoSCT can be effective treatment modality to the patients with relapsed or refractory WT. Further studies are needed to analyze risk factors for secondary malignancy after HDCT/autoSCT in WT.

P-0184

TREATMENT OF RECURRENT NEPHROBLASTOMA. SINGLE CENTRE 30YEARS EXPERIENCE

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Purpose/Objective: Since the 80th of last century overall survival of nephroblstoma reaches 80-90%. But recurrence of WT is still serious problem.
Materials and Methods: Median follow-up is 15.5 years (3-31 years). Treatment regimens during 80th of 20$^{th:}$ 'house protocols', later SIOP Nephroblastoma Study regimens. Sixty patients out of 330 (18%) experienced relapse of WT. From 1980 to 2009 we were treated 330 patients with WT: stage I - 198 patients (60%), stage II - 24 (7%), stage III - 39 (12%), stage IV - 43 (13%), stage V - 25 (8%) patients. Distrubution of stages of inicial disease in pts who had relapses: I - 25 pts (41%), II -6 (10%), III - 7(11%), IV - 14 (23%), V - 8 pts (13%). Thirty relapsed into lungs, 10 i tumor bed after nephrectomy, 4 pts had metachronous relapse into contralateral kidney, 2 pts with primary bilateral process relapsed in remaining kidney, 1 pt had a relapse into brain, 2 in liver, and 11 patients had a combined relapses (lungs, lymph nodes, brain or liver).
Results: Apart from 5 patients all relapses were treated with surgery, chemotherapy or radiotherapy. Forty of 60 patients died of further disease progression - OS of the whole group of relapsed pts is 33%. Eight of 16 patients with recurrence in the tumor bed are alive, resp. 11 of 32 patients with recurrence mainly in the lungs. From 8 pts who had isolated relapse or in combination in the liver or brain, only 1 with cerebral recurrence is alive. Pts treated after 1995 had better OS * 52% compared to patients treated before 1995 - 25%.
Conclusions: Outcomes of recurrent nephroblastoma depend not only on availability of modern diagnosticand treatment modalietes at the time of nephroblastoma relapse. But precise diagnostic and therapeutical methods and the time of first diagnosis of renal tumor could prevent or decrease nephroblastoma recurrence.
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P-0185

PROGNOSTIC VALUE OF CT ONLY LUNG NODULES IN LOCALIZED WILMS TUMOUR (LWT): AN EXPLORATORY ANALYSIS OF THE SFCE EXPERIENCE WITH THE SIOP 2001 PROTOCOL DATA.

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Purpose/Objective: to explore the prognostic impact of CT only lung nodules on pulmonary relapse free survival (PRFS) in children treated for LWT.
Materials and Methods: All children enrolled by French centers in the SIOP 2001 protocol, diagnosed before 1st January 2009 with unilateral WT not presenting metastases on pulmonary Xray were considered. All patients were treated with preoperative chemotherapy vincristin dactinomycine without doxorubicin and post operatively according to histology and local stage. PRFS was compared according to the presence or not of CT only lung nodules (CT+ vs CT-) on the radiologic report. Given the very unbalanced sample sizes between CT+ and CT-, 1000 samples (same size as CT+ group) were randomly selected from the CT- population using a bootstrap approach, and compared to the whole CT+ population by a Log-Rank test. The proportion of statistically significant tests was reported.
Results: Out of 289 reviewed records, 36 patients had CT+ (12%) and 253 CT-. No difference was observed between subgroups regarding tumor volume and age at diagnosis (median: 3.2 years, range: 0.4-21.5), and histological risk groups. There were significantly more stage III in CT+ (44%) than in CT- (25%) patients. Pulmonary relapse was experienced by 15 CT- (6%) and 4 CT+ patients (11%). Using the 1000 generated samples, no prognostic

impact of CT only lung nodules on PRFS was found in this series since the proportion of statistically significant tests was 9%.
Conclusions: In spite of no bias in our study (all patients were treated according to the protocol), the low number of CT only (12%) did not allow to show a significant difference. A prospective study with clear description of the imaging on lung CT and a standardized treatment could bring some answers about the prognosis of micro metastasis in WT.
Acknowledgements ALBEC and Enfant/ Sant*.

P-0186

OUTCOME OF PATIENTS WITH PRIMARY PULMONARY METASTASES AT DIAGNOSIS OF NEPHROBLASTOMA IN A DEVELOPING COUNTRY

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Purpose/Objective: To analyze the outcome of nephroblastoma patients with primary lung metastases.
Materials and Methods: Data for patients with nephroblastoma and primary lung metastases were reviewed and analyzed for the following: demographic data, tumour biology, treatment protocol, local treatment and outcome.
Results: There were 23 of 42 patients with stage IV nephroblastoma with primary pulmonary metastasis diagnosed between 1993 and 2008. The male to female ratio was 1.3:1 and the mean age was 69 months (median 59 months; range 22-153 months). Three consecutive SIOP treatment protocols were used in the study period (SIOP 9; SIOP 1993-01 and SIOP 2001). More than half of the children obtained disease free survival ($n = 13$; 56%) while 8 patients had progression of disease (35%). Poor outcome was associated with high-risk histology versus good outcome for low-risk histology. One child died of neutropenic sepsis and one child absconded. Local treatment was variable and there was no standardized approach for either surgery or radiotherapy.
Conclusions: The outcome of children with nephroblastoma and primary pulmonary metastasis depends on the histology of the tumour. A standardized local treatment protocol should be developed in future, especially for non-responding lung metastasis.

P-0187

SIOP AFRICA / PODC COLLABORATIVE WILMS TUMOUR PROJECT

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Purpose/Objective: Significant progress has been made in the treatment of Wilms tumour in high income countries, where survival is now around 85% - 90%. Survival in low income countries is much lower; specific challenges include late presentation, malnutrition, less intense supportive care facilities and failure to complete treatment. Capacity building, earlier presentation, social support, improved supportive care and a treatment guideline adapted to local circumstances are key to improving results. A multi-disciplinary group of African clinicians and 'state of the art' experts published a SIOP PODC consensus treatment guideline which is applicable for children with Wilms tumour in sub-Saharan Africa.
Materials and Methods: Recommendations specific for Wilms tumour care include diagnostic procedures with emphasis on the role of ultrasonography, preoperative chemotherapy with a reduced dosage for malnourished children and post-operative chemotherapy based on surgical staging. This guideline will be implemented as a multi-center prospective clinical trial in 2014 in at least six institutes in the region, expecting about 200 new patients per year. All participating institutes have established Wilms tumour treatment. The aim is that 2 year event free survival will be 50%, with $< 10\%$ failure to complete treatment and $< 10\%$ treatment related mortality.
Results: A comprehensive and detailed treatment and study protocol was developed during a work meeting in Malawi by the participating institutes. Research questions include event free survival, reasons of treatment failure, efficacy and toxicity of preoperative chemotherapy and the comparison of surgical staging, local pathology and central review pathology in stratifying postoperative chemotherapy. Central pathology review and a regional ultrasonography course are planned. The project will facilitate regional networking and collaboration which will positively impact other aspects of childhood cancer care.
Conclusions: Regional collaboration is a key method to promote regional autonomy, build capacity, and improve care in a sustainable way.

P-0188

BILATERAL WILMS' TUMORS TREATED ACCORDING TO THE JAPANESE WILMS TUMOR STUDY GROUP PROTOCOL

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Purpose/Objective: The optimal management of bilateral Wilms' tumor (BWT) is challenging. The Japan Wilms Tumor Study (JWiTS) group was founded in 1997, and a multicenter clinical trial was started. The introduction of multimodal therapy has improved the survival rate; however, the results were not satisfactory in terms of the renal preservation. To establish a new treatment strategy for BWT, we reviewed the results of bilateral cases registered in JWiTS studies.
Materials and Methods: This analysis concerned patients with synchronous BWT registered in the JWiTS between 1996 and 2011. In these trials, the management of BWT included initial tumor resection or biopsy, followed by chemotherapy. The details of their treatment and outcome were analyzed and discussed.
Results: Three hundred fifty-five cases with nephroblastoma were registered in the JWiTS database. Among them, 31 (8.7%) were bilateral cases. They were 16 males and 15 females, and their mean age was 15.2 months (7 months * 5 years). Preoperative chemotherapy was given for a median 12 weeks before tumor resection in eight cases. The details of surgery were available for 16 cases, and the bilateral renal parenchyma could be preserved in 43% of these 16 patients.The pathological diagnosis revealed that eight cases were fetal rhabdomyomatous nephroblastoma (FRN), and there were no anaplastic cases. *WT1* mutation was detected in 80% of the cases. Follow-up data were obtained for 18 cases. Two patients died (one of disease and one of infection) and the remaining 16 have been alive without disease for a median follow-up period of 11 years.
Conclusions: The long-term survival rates for patients with synchronous BWT have been improved, however, more than half of the patients received nephrectomy. These results were not satisfactory, and the protocol should be changed so that preoperative chemotherapy is first performed to shrink the tumors, thereby facilitating subsequent renal salvage surgery after central imaging evaluation.

P-0189

RENAL TUMORS UNDER THE AGE OF 20 IN KOREA FOR 7 YEARS: 2002-2008

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Purpose/Objective: To continue the previous multi-institutional report on pediatric renal tumors in Korea: 1997-2001. Our study was undertaken to obtain valuable demographic data for a better understanding of the biological behavior and optimal management for these tumors in patients under the age of 20 years.
Materials and Methods: The pediatric renal tumor registry form was mailed to 100 hospitals registered in the Korean Urology Association. The seven-year medical records at each hospital were retrospectively reviewed, which included age, presentation, evaluation, treatment and outcome.
Results: We received the pediatric renal tumor registry form from 19 hospitals (response rate 19%). 179 patients (0.1-20.0 years; ave. 4.4 ± 4.9) were enrolled in this registry. Most patients were diagnosed with an abdominal mass before the age of 4 years. The pathological diagnoses were malignant and benign tumors in 92.2 and 7.8%, respectively. A Wilms' tumor was the most common (70.4%) malignant tumor, with a mesoblastic nephroma (3.9%) in the most common benign tumor. 11.2% of patients were accompanied by other diseases, such as hypertension, hemihypertrophy, cryptorchidism and aniridia. The managements were as follows: surgery only (18.4%), chemotherapy and/or radiotherapy after surgery (58.7%), surgery after biopsy and chemotherapy (18.4%) and others (4.5%). The results of treatment included; complete remission (79.9%), incomplete remission (5.6%), no response or aggravation (6.1%) and unknown (8.4%). The overall metastasis rate was 21.2%. The

common metastasis sites were lung (50%) and lymph nodes (34.2%). The outcomes at the last follow up (mean 45.4 ± 31.8 mos.) were alive, dead and unknown due to follow up loss, in 83.2, 6.1 and 10.6%, respectively.
Conclusions: These demographic data and biological behaviors for renal tumors in Korea under the age of 20 years will lead to a better understanding of these rare tumors and to the optimal therapy for these young peoples.

P-0190

FATE OF REMNANT KIDNEY AFTER NEPHRON-SPARING SURGERY FOR UNILATERAL PRIMARY RENAL TUMOR IN CHILDREN

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Purpose/Objective: No data are available on long-term function of remnant kidney in children undergoing nephron-sparing surgery (NSS) for unilateral renal tumor (URT) and normal contralateral kidney. We aimed to assess the efficacy of NSS in terms of preservation of renal mass and function in a unique cohort of children.
Materials and Methods: Prospective pilot study of 11 patients with URT treated with NSS over a 18-year period (Jan 1992 to Dec 2010). Remnant kidney function and volume were assessed at median follow-up of 5 years (range, 2 to 10), utilizing quantitative 99mTc-dimercapto-succinic acid renal scintigraphy (DMSA) and ultrasonography (USS). Repeat assessment was carried out at median follow-up of 12.7 years (range, 2 to 20), utilizing USS and MRI. Percentages of relative remnant kidney volume obtained by the ellipsoid formula or MRI-derived were calculated.
Results: At 5 years' median follow-up, relative DMSA renal function and relative USS renal volume of remnant kidney were 39.2% (range, 13 to 46) and 40.1% (range, 19.1 to 46.8), respectively. A positive correlation between DMSA and USS assessment was found ($r = 0.90$, $p = 0.002$). At 12.7 years' median follow-up, relative MRI renal volume and relative USS renal volume of kidney remnant were 43.9% (range, 20.8 to 49.8) and 40.5% (range, 25.7 to 47.4), respectively. There was a positive correlation between MRI and USS assessment ($r = 0.99$, $p = 0.001$). All patients are event-free, normotensive, and with normal renal function.
Conclusions: Following NSS for URT, relative renal function and volume of remnant kidney remain satisfactory and stable at long-term follow-up. Given the good concordance between USS and DMSA or MRI, USS is an accurate and non-invasive tool for indirect measurement of remnant kidney function

P-0191

NEPHRON SPARING SURGERY FOR UNILATERAL NON-SYNDROMIC WILM'S TUMOR

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Purpose/Objective: Several studies have considered nephron sparing surgery (NSS) following neoadjuvant chemotherapy as a viable surgical alternative for patients with unilateral Wilm's tumor and predisposing syndromes. This approach seems logical as it potentially prevents or postpones the development of chronic kidney disease, which can occur secondary to metachronous development of neoplasms. There are a few publications on the role of NSS for nonsyndromic Wilm's tumor, with the conclusion that NSS is an option for carefully selected stage I neoplasms with low or intermediate risk histology and after good response to chemotherapy. We report our experience with NSS in patients with nonsyndromic Wilm's tumor.
Materials and Methods: During the period Jan 2006 * Dec 2010, 7 children (mean age of 26 months, range 8 months - 7 years) with stage I non-syndromic Wilm's tumor underwent NSS. A needle core biopsy was done in all to confirm the diagnosis and was followed with 6 weeks of chemotherapy. Following NSS all children received post-operative chemotherapy.
Results: No major intra-operative or post-operative complications were noted. After a mean follow-up of 54 months (range 24 * 84) no recurrences were noted and all children had normal creatinine levels.
Conclusions: Nephron sparing surgery is safe option for children with unilateral Wilm's tumor, with good oncological outcomes for the available follow-up.

P-0192

NEPHRON SPARING SURGERY; PARTIAL NEPHRECTOMY VERSUS TUMOR ENCULATION FOR WILMS TUMORS CRITERIA AND OUTCOME: SINGLE CANCER INSTITUTE EXPERIENCE

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Purpose/Objective: Approximately 5 - 10% of children with Wilms tumor present with bilateral disease. The treatment challenge is to achieve a high cure rate while maintaining adequate long-term renal function. In unilateral Wilms' tumor (WT), nephrectomy is the standard surgical approach, whereas partial nephrectomy (PN) is controversially discussed.
Materials and Methods: We prospectively evaluated the feasibility of nephron sparing surgery (NSS) in children with bilateral and unilateral (WT). All patients' receive preoperative chemotherapy for 6 weeks and postoperative chemotherapy. From 2006 to 2011, six patients with bilateral (WT) and 4 patients with unilateral (WT) underwent nephron sparing surgery
Results: Six patients with synchronous, bilateral (WT) were identified, including 3 patients who underwent successful bilateral tumor enculation procedures. Two patients who underwent successful bilateral (PN) and one patient underwent tumor enculation on left kidney and nephrectomy on right one where the tumor destroys whole normal renal tissue. Four patients with stage I polar unilateral (WT) were identified and candidate for (PN). Three underwent successful (PN). One patient develops postoperative heamatoma and positive margin in postoperative pathology underwent radical nephrectomy in second lock operation. Postoperative complications included postoperative hematoma in one patient, wound infection in 2 patients, microscopic residual in one patient. Long-term complications included local tumor recurrence in one patient, incision hernia in one patient, Distant relapse in lung in one patient who saved by lung metastatectomy. non of our patients developed renal failure in follow up period. The overall survival rate was 80% (mean follow-up, 3years); both patients who died had unfavorable histology.
Conclusions: (PN) eliminate the need for, nephrectomy in polar stage I unilateral or bilateral (WT) however enucleative surgery is a reasonable option and oncologycally safe in bilateral multi-centric or central (WT) after receiving preoperative chemotherapy.

P-0193

ORGAN SARING SURGERY IN UNILATERAL NEPHROBLASTOMA

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Purpose/Objective: International treatment protocols in children with Wilms' tumor including preoperative chemotherapy surgery and postoperative chemotherapy with or without radiotherapy depending on histology and stage result in very good survival. In Belarus we achieved 91% long term survival using such protocols. After having good results in survival, we have to think about increasing number of nephron sparing surgery without jeopardizing survival rate. Good imaging technique helps in making surgeon decision.
Materials and Methods: Chemotherapy (ChT) with 2 or 3 agents is highly effective and usually causes remarkable tumor shrinkage and necrosis a large nephroblastoma and as a result localizes tumor mass to the one pole and in some cases facilitates nephron sparing surgery. In SIOP WT 2001 study (stage I-III) 4 weeks preoperative ChT have been recommended. We modified preoperative ChT chemotherapy in case of good response and relatively less affected and functioning kidney. We prolonged ChT giving 6 weeks (50% more) treatment. Since 2005 totally 53 children (stage I-III) with median age 3 year 2 months have been treated using SIOP WT 2001. In 30 pts 4 weeks ChT (VCR + ACT) was given. Twenty three pts were given 6 weeks ChT, evaluating tumor size (US or CT-scan) after 4 and 6 weeks.
Results: Among 35 pts achieving standard 4 weeks ChT, nephrectomy performed in 30 pts and partial resection-5. In 23 pts where prolonged (6 weeks) preoperative ChT was given nephrectomy was done in 10 cases and partial resection-13. During follow up (median 12 months) no evidence of relapse in spared kidney observed. Five-year event free survival was 91 ± 6% in nephrectomed and 89 ± 9% in partially nephrectomed patients (p-0, 64).
Conclusions: Prolongation of preoperative ChT in some cases with unilateral Wilms' tumor may increase number of organ sparing surgery. The optimal choice of treatment in this group of pts still merits further investigation.
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P-0194

THE EFFECTS OF ADJUVANT THERAPY AND RENAL AGING ON ESTIMATED GLOMERULAR FILTRATION RATE IN SURVIVORS OF CHILDREN NEPHRECTOMIZED FOR UNILATERAL KIDNEY TUMOR

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Purpose/Objective: No data are available on nephrotoxicity of chemotherapy and/or radiotherapy in children with an acquired single kidney surviving beyond the age-related physiological decline in renal function. We aimed to evaluate the renal function in a cohort of

adults nephrectomized for unilateral oncological and non-oncological causes during childhood
Materials and Methods: We assessed the long-term follow-up of renal function, blood pressure, and urine proteins among a cohort of 47 patients who underwent nephrectomy for unilateral renal disease between January 1962 and December 1991. The Modification of Diet in Renal Disease equation was used to estimate the glomerular filtration rate (eGFR).
Results: No significant differences were found in mean age (32.4 vs 35.2 years) and in mean eGFR (84.8 vs 85.9 ml/min/1.73m^2) between 15 patients undergoing nephrectomy alone and 32 patients undergoing nephrectomy associated with adjuvant therapy. Stratification of patients for age showed that 10 of 17 (58%) $<$ 30 years old patients were able to restore a satisfactory renal function ($>$ 90ml/min/1.73 m^2). The latter group, in comparison with patients with an age between 31 and 55 years, presented a significant decrease in mean eGFR (from 94.7 to 80.6ml/min/1.73m^2). After the age of 30 years, only 7 patients (23%) presented an eGFR $>$ 90ml/min/1.73m^2. Of the 30 patients with mild-to-moderate renal function, four patients presented hypertension, and two albuminuria.
Conclusions: In adults nephrectomized during childhood for unilateral kidney disease, adjuvant therapy does not seems to have a nephrotoxic effect, whereas aging appears to be a risk factor for renal dysfunctions. The decrease in eGFR seems related with a low nephron endowment more than with hyperfiltration.

P-0195

TREATMENT FOR SOLID TUMORS IN CHILDREN IN NEGLECTED CASES

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Purpose/Objective: Recently scope of photodynamic therapy (PDT) has grown in treatment for advanced solid tumors. Development of optimal PDT regimens using photosensitizer radachlorine at intraoperative irradiation of solid tumors in children.
Materials and Methods: In pediatric surgery department of Chelyabinsk regional children's clinical hospital treatment by PDT was provided to 17 patients. Patients with nephroblastoma prevailed * 41.2%. All patients were provided with treatment by intraoperative method of PDT. Laser equipment 'Lakhta Milon' (Russia) was used. Laser power output was 2.5 W. Emission power density was 0.1 to 0.8 W/sm^2. Amount of administered photosensitizer was calculated as 0.6 * 0.8 mg/kg of patient's body weight. Irradiation duration ranged from 10 minutes to 30 minutes. For irradiation of tumors light guide with microlens at the end was used. Dynamic observation over patients were mainly office based for 3 years.
Results: Estimation of PDT effectiveness was carried out under following criteria: total lack of local relapse (TLL) of tumor * lack of visual (ultrasound investigation of abdominal cavity * US) and palpatory signs of tumor growth; local relapse (LR) * local relapse in 6 months; disease progression (PD) * prolonged tumor growth immediately after operation according to US. During treatment different doses of light energy were used * 150 to 400 J/sm^2, for tumors with deep infiltrative growth * 300 to 500 J/sm^2.

According to cited data, TLL was observed in 14 (82.4%) patients, relapse was observed in 3 (17.6%) patients. 3 relapses were observed only in patients with nephroblastoma, neuroblastoma, germinal tumor. In 3 cases of LR refresher courses of PDT were not carried out due to tumor dissemination. At observation of 14 patients within period from 6 months till 2 years relapses were not observed.
Conclusions: PDT can be used to treat diseases of different origin with satisfactory therapeutic effect.

P-0196

THE CHALLENGES IN MANAGING WILMS TUMOUR IN A DEVELOPING COUNTRY: EXPERIENCE FROM A SINGLE CENTRE IN PAKISTAN

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Purpose/Objective: Wilms tumor (WT) carries an excellent prognosis in developed countries but not in the developing world. This study was carried out to assess the challenges in treating WT in a large cancer hospital in Pakistan.
Materials and Methods: We retrospectively reviewed the medical records of 78 WT patients who were treated at our center between January 2007 and December 2011. Data comprising demographic variables, initial imaging studies, management before oncology referral, stage of disease, treatment details and final outcome were recorded. For outcome analysis, patients were categorized into three groups on the basis of diagnostic procedure; group 1: biopsy only ($n = 29$), group 2: upfront nephrectomy with complete excision ($n = 19$) and group 3: upfront nephrectomy with tumor rupture or residual disease due to incomplete excision ($n = 30$).
Results: Median time to presentation was 8 weeks. Severe malnutrition was noted in 19.2% patients. Histological diagnosis of WT was established by nephrectomy in 63% and a needle/open biopsy was performed in 37% of cases. At presentation, 11% patients had stage I tumors, 22% each had stage II and III tumors while 40% had stage IV disease. Bilateral disease was seen in 5% cases. Best outcome was seen in group 2 with a complete response (CR) rate of 74% compared to 37% in group 1 and 30% in group 3. Twenty four (30%) patients abandoned therapy whereas 20 (26%) died, including 7% who died as a result of treatment related toxicity. In group 3; 27 of 30 patients had stage III or IV disease. More than half of the tumors of this group ($n = 16$) remained unresectable after chemotherapy.
Conclusions: Delayed presentation and sub-optimal surgical treatment before referral were two main factors responsible for poor outcome. Non-adherence to treatment was a big factor which needs special consideration. Better supportive care can prevent treatment related deaths.

P-0197

RESOURCE IMPLICATIONS OF SETTING UP A PROSPECTIVE BIOMARKER STUDY OF CHILDHOOD RENAL TUMOURS IN THE UK

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Purpose/Objective: Childhood renal tumours require international collaboration to make progress in biomarker driven translational research. The use/storage of 'omics' data presents new ethical challenges as we strive to meet personalised medicine aims and parent/patient expectations. Increasing the portfolio of clinical trials is not sustainable due to the resource requirements of pharmacovigilance and regulatory compliance. A new model for prospective clinical studies is required. Collection of high quality, clinically annotated samples is essential. In opening a multi-centre translational study in renal tumours, we have used site visits (SIVs) to ensure local teams understand study aims and responsibilities to ensure success. However, these are resource intensive and their impact needs to be evaluated.
Materials and Methods: Analysis of the study set-up and SIV was undertaken to establish burden of effort in terms of time and money.
Results: It took 11 months (330 days) from point of submission of an ethical permission request to the first centre opening. Within this period preparation of accepted version of study paperwork took 202 days while parental consultation took 30 days. Planning and completion of the SIVs took 76 days. Assuming 80 UK patients per year are recruited, a per patient 'study set up' cost of £166 (USD249) was estimated. Cost of sample and clinical data collection per patient was estimated at £360 (USD 540) (excluding biomarker analysis costs). The survey on the SIV process achieved a 58% response rate. 80% of respondents felt that the SIVs were necessary while 92% thought the SIV increased study understanding. However, 60% felt that SIV did not accelerate the local approval process.
Conclusions: It is important to consider the cost implications when setting up a prospective clinical biomarker study. Such studies are heavily reliant on local effort in particular when rapid turnaround is an aim. SIVs are a necessary part of this process.

P-0198

MANAGEMENT AND PROGNOSIS OF CHILDREN WITH ADRENOCORTICAL TUMORS: 18-YEAR EXPERIENCE WITH 9 CASES FROM ONE CENTER

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Purpose/Objective: To evaluate the clinical characteristic, managetment and prognosis of adrenocortical tumors (ACTs) in children.
Materials and Methods: Records of nine children with ACTs between 1994 and 2012 in our center were reviewed retrospectively. Data recorded of each patient included clinical characteristics, diagnostic methods, treatment, pathologic findings, disease stating and outcome.
Results: All patients were females aging 5months-9yesrs (mean 3.5years). All patients appearanced adrenocortical disorders. Three patients presented with clinical features of virilization as clitorimegaly and precocious pubic hair. Four patients had isolated signs of Cushing's syndrome. One patient presented Cushing's syndrome associated with virilization. One 9-yr girl presented Cushing's syndrome associated with hypertension and hypokalemia. The endocrine pro?le was available in all cases: cortisol levels were raised in six, testosterone in eight. All patients were imaged by ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI). Four masses lacked of homogeneity with foci of necrosis and calcification in imaging, and were confirmed to be malignant by postoperative pathology. All patients were treated by surgical management. Six tumors were surgically complete adrenocortical excision. Two tumors underwent adrenocortical excision but spillaged during surgery. One tumor underwent partial resected. The smallest tumor was 2*1.5*1.5cm and the largest 12.5*10.5*8.5cm. Tumor volume varied from 2.4cm3 to 584cm3 (mean 189cm3). Postoperative pathology confirmed four tomurs were malignant with mass volume more than 164cm3, while other five were benign with mass volume lass than 46cm3. There were five patients with stage I disease, one with stage II and three with stage III. Six patients who undergo complete adrenocortical excision were normal in follow-up to now without palindromia and endocrine disturbance, but other three patients with stage III disease moreover the malignant ones were died.

Conclusions: Capsular rupture during adrenocortical tumors surgery carries a poor prognosis. Tumor size was the most important prognostic factor.

P-0199

CHARACTERISTICS AND OUTCOMES OF PAEDIATRIC RENAL CELL CARCINOMA IN HONG KONG

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Purpose/Objective: We reviewed the characteristics and outcomes of renal cell carcinoma (RCC) in children in Hong Kong.
Materials and Methods: All paediatric cancers diagnosed including RCC in Hong Kong have been prospectively collected by the Hong Kong Paediatric Hematology and Oncology Study Group. This is a review of the clinical data on all children with RCC treated in Hong Kong from 2004 to 2012.
Results: Altogether 5 children with RCC were registered. Median age at diagnosis was 13 years (range, 1-17 years). Four patients were males. They presented with gross hematuria (n = 4), abdominal or flank pain (n = 2), and palpable abdominal mass (n = 2). Two patients had stage I disease, while 1 patient each had stage II, III and IV disease (distant lymph node metastases). Total nephrectomy was performed in all 5 patients. Histology were Xp11.2 translocation RCC (n = 2), clear cell RCC (n = 2), or papillary RCC (n = 1). All 4 patients with stage I-III RCC were disease-free after operation upon follow-up for 0.6-8.9 years. The patient with stage IV translocation RCC received sunitinib after nephrectomy but the metastatic diseases progressed soon and sunitinib was switched to everolimus with stable disease for 4 months. However, he progressed again at 12 months after diagnosis and everolimus was switched to axitinib recently. He is expected to have poor prognosis.
Conclusions: RCC is rare in children and hematuria is the commonest presentation. Xp11.2 translocation RCC appears to be more common in children than adults. Prognosis is good for locoregional disease even with surgical resection alone. Metastatic RCC has extremely poor prognosis. Targeted therapy with vascular endothelial growth factor receptor tyrosine kinase inhibitors or mammalian target of rapamycin inhibitors may prolong survival.

P-0200

EIGHT CASES OF CONGENITAL MESOBLASTIC NEPHROMA:CLINICAL ANALYSIS AND LITERATURE REVIEW

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Purpose/Objective: Congenital mesoblasticnephroma (CMN) is a kind of rare benign tumor which comes from mesoderm. The purpose of this study is to heighten the realization of CMN in children.
Materials and Methods: Eight cases of CMN in our hospital from 2004 to 2012,the age, gender, clinical symptoms, pathological characteristics, Imaging characteristics, therapeutic regimen and prognosis were analyzed retrospectively.
Results: All eight patients received surgical intervention; 4 cases with nephrectomy, 1 case with a half nephrectomy, and 3 cases with tumor enucleation. Pathological classification; classic CMN in 2 children,and cellular CMN in 6.Two cases received preoperative chemotherapy but no response, while 3 cases received postoperative chemotherapy. Two cases of classic CMN were demonstrated as solid mass and 5 cases of cellular CMN were demonstrated as focal areas ofcystic /necrosis / calcificationby ultrasound and CT scan. One case suffered from tumor recurrence eight months postoperatively and received secondary surgical resection. Eight cases except 2 cases lost to follow-up, 6 patients survived uneventfully. The mean follow-up time was14.6 months, the longest was 36 months.
Conclusions: CMN need differential diagnosis with Wilms' tumor, imaging characteristics have part correlation with pathologic characteristics, surgery is the main treatment, preoperative chemotherapy is not sensitive, the effect of postoperative chemotherapy need further study, the prognosis is fairly good.

P-0201

PRIMARY EWING SARCOMA OF THE KIDNEY

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Purpose/Objective: Ewing sarcomas (ES) of the kidney are extremely rare. Clinical symptoms are non-specific, presenting abdominal pain, palpable mass and hematuria. With the identification of the ES-specific EWS-ETS translocation, an advanced differential-diagnosis became feasible. The impact of standard treatment approaches on the outcome of renal Ewing sarcomas remains to be analyzed.
Materials and Methods: Twenty-four cases of primary renal Ewing sarcomas are documented in the database of closed Ewing sarcoma trials of the GPOH since 1980 (n = 2984). All patients were treated according to the EE99 protocol (1998-2009)*. 41% of the patients received definitive surgery, 47% combined modality treatment, 6% definitive radiotherapy, and 6% no local therapy. Fifteen patients (62%) presented with localized disease (R1/R2loc), 4 (17%) with pulmonary metastases only (R2pulm), and 5 patients (21%) with other metastatic sides (R3). Median observation time was 3.71 years.
Results: Median age was 24.9 years (range 11-60). Tumor thrombi in the adjacent renal vessels occurred in 9 patients (56%; n = 16). In 90%, rearrangements of t(11;22) were found. Overall survival (OS) at 3 years was 0.80 (SE = 0.09), and event-free-survival (EFS) was 0.66 (SE = 0.11). Patients with localized disease showed a 3y-OS (EFS) of 0.92 (0.78) compared to a 3y-OS (EFS) of 0.58 (0.45) in patients with metastatic disease ($p = .091$; $p = .164$). 3y-EFS for patients without tumor thrombus was 0.83 (SE = .15) compared to 0.65 (SE = .17) in patients with initial tumor thrombus.
Conclusions: ES should be considered in the differential diagnosis of renal tumors, especially in patients presenting the classical triad of renal cancer: hematuria, pain and palpable mass. Patients with renal ES seem to respond and benefit from standard ES treatment.
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POSTER SESSION: POSTER SESSION - GERM CELL TUMOURS

P-0202

EXTRACRANIAL GERM CELL TUMORS IN CHILDREN: 23-YR EXPERIENCE OF A SINGLE CENTER

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Purpose/Objective: Germ cell tumors comprise 3% of all childhood malignancies. This study aims to evaluate demographic data and treatment results in children with extracranial germ cell tumors (GCTs) in a single institution.
Materials and Methods: GCTs in children were excised without major morbidity or otherwise biopsied. Mature teratomas, stage I testicular and some ovarian GCTs were resected and monitored with AFP and B-HCG ("watch-and-wait" approach). Patients with recurrent stage I disease and all other patients received BEP (bleomycin 15 mg/m^2 on day 1, etoposide 100 mg/m^2/dx5 days, cisplatinum 20 mg/m^2/d x 5 days). Courses were administered every 3 weeks until remission and/or normal AFP/B-HCG was achieved, and then two more courses were given, residual tumor was resected.
Results: Between 1989 and 2012, 94 patients (56 females and 38 males) with extracranial GCT were admitted. The median age was 3 years (2 months-16 years). The median follow-up time from the initial diagnosis was 10.5 years (1 month-22 years); the median number of BEP courses was five (range, three to seven). Sixty-five (%70) were gonadal (40 ovaries, 25 testis), 22 sacrococygeal, 4 mediastinal, 3 nonmidline head and neck. Histologic subtypes were; endodermal sinus tumor % 50 (n = 47), disgerminoma (n = 16), mixed germ cell tumors (n = 19), mature teratoma (n = 6), immature teratoma (n = 6). Twenty-nine patients were treated with surgery alone, and the rest received BEP chemotherapy and delayed surgery. The 10-yr overall survival and progression free survival rates were 87.3% and 84.3%, respectively. Hematologic toxicity was common but manageable, there was no secondary malignancy.
Conclusions: Extracranial germ cell tumors have a good prognosis. BEP chemotherapy applied according to AFP and BHCG levels is effective. Total surgery only in mature and immature teratomas and in testis and in some ovarian endodermal sinus tumors with post-operative normal AFP, BHCG levels seems to be adequate therapy.

P-0203

PEDIATRIC TESTICULAR TUMORS IN KOREA FOR 7 YEARS: 2002-2008

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Purpose/Objective: Our study was undertaken to obtain the valuable demographic data for the better understanding of the biological behavior and optimal management for these tumors.
Materials and Methods: A pediatric testicular tumor registry form was mailed to 100 hospitals registered in the Korean Urology Association. The seven-year medical records at each hospital were retrospectively reviewed, with the exception of which had no histopathologic records.

Results: We received the pediatric testicular tumor registry form from 25 hospitals (response rate 25%). 141 patients (0.1-20.0 years; ave. 5.7 ± 6.7) were enrolled in this registry. Most of the patients were diagnosed with a scrotal mass before the age of 4. Serum AFP and beta-hCG increased to as much as 46.1% (92.9% in yolk sac tumor, 19.6% in teratoma) and 9.2% (11.9% in yolk sac tumor, 5.4% in teratoma) of patients, respectively. Preoperative diagnosis was featured as malignant tumors (61.0%), benign tumors (31.2%), and hydrocele (3.5%). Germ cell tumors were the most common (79.1%) mainly with either the yolk sac tumor (29.4%) or teratoma (39.2%). Primary management was as follows: radical (82.3%), simple (2.8%), and partial orchiectomy (10.6%). Management after surgery included: 77.3% surveillance, 12.1% chemotherapy, 2.8% combination therapy, and 8.1% other methods. The metastasis rate, as a whole, was 13.5% (31.0% in yolk sac tumor, 1.8% in teratoma, 30% in mixed germ cell tumor). The common metastasis sites were lymph nodes (68.4%) and lung (31.6%). The final results of the treatment were as follows: complete remission (77.3%), incomplete remission (3.5%), no response or disease progression (0.7%), and unknown (18.4%). Outcomes at the last follow up (mean of 31.4 ± 26.0 months) were 78.0% alive, 1.4% deceased, and 20.6% unknown status.
Conclusions: The demographic data of pediatric testicular tumors in Korea may lead to a better understanding of these rare tumors and to the development of an optimal therapy for these children.

P-0204

SACROCOCCYGEAL TERATOMA: A 16-YEAR RETROSPECTIVE REVIEW

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Purpose/Objective: Sacrococcygeal teratoma (SCT) is one of the commonest neonatal tumours. The aim of our study was to review the outcomes of SCTs in children in a single institution in Hong Kong.
Materials and Methods: This was a retrospective study of 24 patients with SCT between May 1997 and November 2012.
Results: Among the 24 patients, diagnosis of SCT was made prenatally (n = 5), at birth (n = 14), or later in infancy (n = 5). Of those diagnosed prenatally or at birth, the majority (84.2%, n = 16) were born at term. None experienced antenatal or perinatal complications.

All 24 patients underwent excision of sacrococcygeal teratoma and coccygectomy. Resection was performed by perineal approach alone (n = 16), combined open abdominal & perineal approach (n = 1) or combined laparoscopoic & perineal approach (n = 7), according to the degree of intrapelvic extension. The mean age at operation was 5.6 days for those diagnosed prenatally or at birth and 16 months for those diagnosed beyond the neonatal period. Tumour histology included mature teratoma (70.8%, n = 17), immature teratoma (16.7%, n = 4) and yolk sac tumour (12.5%, n = 3). The three patients with yolk sac tumour all presented at 10 months old or above and required chemotherapy after surgical excision.

Follow-up duration ranged from 3 months to 16 years. Recurrent disease occurred in one patient at 12 months after primary resection of a neonatal mature teratoma, with uncertain resection margin. Three patients suffered from post-surgical neurogenic bladder and six with constipation (3 mild, 3 severe). There was no mortality.
Conclusions: The overall survival of neonatal SCT is high, however there is high risk of malignant transformations in patients who present late. Management of SCT should consist of timely diagnosis, complete surgical excision and long-term follow-up for the associated functional sequelae.

P-0205

DYSGERMINOMA IN A PEDIATRIC MEXICAN HOSPITAL REVIEW OF 15 YEARS

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Purpose/Objective: Dysgerminoma is a germ cell ovarian tumor, uncomon seen in childhood, characteristically in teenagers and young adults. We present our clinical experience in diagnosis and treatment of this entity along fifteen years in a Tertiary pediatric hospital in Mexico.
Materials and Methods: A retrospective study recording age, signs, lag time signs reported, image method used, histology, treatment and survival
Results: We found 42 cases, ages ranged from 2 to 16 with a media of 11.8 years. Evolution of signs and symptoms ranged from one to 96 weeks with a media of 13 weeks. Common signs were volume increase in ninety-three percent, abdominal pain in 76%, weight loss in 38%, malaise in 31%, abnormal uterine bleeding in 26%, constipation in 9%, and ascitis 2%. Bilateral presentation was found in only one patient. Twenty-six tumors were found in the left ovary and 15 in the right ovary. Diagnosis was made by ultrasound in seventy-one percent of cases, tomography scan in 9% and both in 19%. Surgery was performed in other hospitals in sixty-two percent of cases due to acute abdomen and 38% in our institution. Histology showed eight pure dysgerminomas and 34 with mixed histology. According to COG staging we found six patients in stage I, 14 in stage II, 13 in stage III and 9 in stage IV. Nine patients did not receive chemotherapy, the rest received 2 to 6 courses and only one patient received radiotherapy as a rescue modality. Overall survival was eighty-four percent in 125 months. We found no significant differences when analyzing surgery outside our institution, stage or histology.
Conclusions: Dysgerminoma is rare in pediatrics. We present our experience in a pediatric hospital from a developing country with a suitable survival using chemotherapy as the only treatment modality due to the patient's age. Variables like stage and histology was not a prognostic factor for survival.

P-0206

PEDIATRIC GERM CELL TUMORS. CLINICAL AND THERAPEUTIC FEATURES IN A SINGLE MOROCCAN INSTITUTE.

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Purpose/Objective: Germ cell tumours (GCT) comprise 3% of children tumours in literature. They are known to have good prognosis. Our aim is to analyse the clinical and therapeutic features of children with GCT treated in Casablanca university medical center (Morocco)
Materials and Methods: Data of patients aged less than 20 years diagnosed with GCT from January 2003 to December 2012 were retrospectively collected. Were excluded three patients with extra gonadal GCT. The management of these patients was according to the TGM french protocol.
Results: Thirty- eight patients were enrolled. GCT comprises 2% of newly diagnosed pediatric tumours. The median age was 4 years with a peak of frequency between 1 to 3 years. The H/F ratio was 0.3. Twenty- six patients (68%) were classed high risk. The most common primary sites were: sacro-coccygeal (45%), ovarian (29%), testicular (21%) and vaginal (5%). The diagnosis was made histologically in 11 patients (29%). Histolopathology concluded commonly to 17 Yolk sac tumours (45%) and 13 teratomas (35%). Twenty-six of GCT (69%) is secreting tumours. Ten tumours (26%) are metastatic mainly to the lungs. Primary resection was performed in seven patients (20%) and delayed surgery following chemotherapy in seven patients (20%). Eleven patients (28%) kept maintained complete remission after a median follow-up of 40 months. Five patients (13%) relapsed and underwent 2nd line chemotherapy. Three patients died by progressive disease and eighteen patients (48%) were lost to follow-up. The 5-year EFS and OS were 53% and 79.3% respectively.
Conclusions: The prognosis of pediatric GCT is very good. The diagnosis must never be made histologically. Clinical symptoms, biology and radiology are sufficient to make the diagnosis. The high rate of patients lost to follow-up is still high in our conditions which made difficult the management of such tumors.

P-0207

MIXED MALIGNANT GERM CELL TUMOR WITH RHABDOMYOSARCOMA PRESENTING AS GIANT CYSTIC ABDOMINAL TUMOR AT THE SIGMOID COLON IN A 20 MONTHS OLD GIRL

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Purpose/Objective: Since germ cell tumors may contain tissue components of all cell types in the body, development of secondary tumors within a mixed germ cell tumor is occasionally observed; we report on such a rare case.
Materials and Methods: A 20 months old girl, previously healthy, and with uneventful family history, who first presented with marked abdominal distension was examined by ultrasound and MRI showing a monstrous cystic tumour extended from the xiphoid to the symphysis, which contained a solid component of about 10 cm diameter. Staging revealed no metastases; alfa-1-fetoprotein was elevated to 2487 IU/ml, while catecholamins and LDH were normal. No signs of abdominal pain, dysuria, or constipation were present.
Results: A primary resection was performed after controlled puncture and evacuation of the cysts with aspiration of 1300 ml clear fluid. Intraoperatively, the tumor was found to be connected to the sigma loop. The tumor could thus be mobilised, and it was removed by partial sigma resection followed by end-to-end anastomosis of the colon. The alfa-1-fetoprotein value fell to normal within two weeks. The histological analysis revealed a mixed germ cell tumor containing parts of a teratoma and a yolk sac tumor, in addition, large components of a rhabdomyosarkoma were found in the tumor. The cytological analysis of the cyst liquid revealed one isolated nest of rhabdomyosarcoma cells. In with the German germ cell tumor (MAKEI) and soft tissue sarcoma (CWS) study groups, we decided to initiate a chemotherapy including both PEI (Cisplatinum, Etoposide, Ifosfamide) and VAIA (Vincristin, Actinomycin D, Ifosfamide, Adriamycin). Radiation therapy was not performed. The patient is now alive and well 20 months post diagnosis.
Conclusions: We conclude that separate tumor entities present in a mixed germ cell tumor may be require a combined therapeutic approach, as is possible by combining a MAKEI and a CWS therapy.

P-0208

LONG-TERM OUTCOMES OF GERM CELL TUMORS IN CHILDREN: AN EXPERIENCE OF SINGLE INSTITUTION

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Purpose/Objective: To evaluate the outcomes of children with germ cell tumors (GCTs).
Materials and Methods: Seventy-one children with germ cell tumor diagnosed from 1996 to 2012 were analyzed. Resection was performed in children with teratoma without adjuvant chemotherapy. Malignant GCTs were treated with cisplatin-based chemotherapy and resection.
Results: The median age was 4 years (range, neonate * 16.9 years). Histopathologic subtypes were immature teratoma in 25, yolk sac tumor in 24, mixed GCT in 6, germinoma in 5, and others in 11 patients. In 39 patients, primary site was gonad. Among remaining patients, primary sites were mediastinum in 12 patients, retroperitoneum in 11 patients, and other sites in 9 patients, respectively. Sixteen patients have metastatic disease, including lung, peritoneum, liver, bone, or bone marrow. The 5-year event-free survival (EFS) and overall survival was 85.8 $\pm$ 4.9% and 90.1 $\pm$ 3.9%, respectively. The 5-year EFS in patients with GCT in gonad and in retroperitoneum/mediastinum was 90.4 $\pm$ 5.4% and 69.6 $\pm$ 10.9%, respectively ($P = 0.07$). The 5-year EFS in patients without metastatic disease and with metastatic disease was 88.5 $\pm$ 5.0% and 71.5 $\pm$ 12.2, respectively ($P = 0.11$). The level of alpha fetoprotein (AFP) at diagnosis did not affect the EFS significantly (AFP $<$ 10,000 ng/mL vs. $>$ 10,000 mg/mL, 5-year EFS 86.3 $\pm$ 5.2% vs. 77.9 $\pm$ 11.5%, $P = 0.84$). In multivariate analysis, risk factors associated with EFS were primary site in retroperitoneum/mediastinum (HR 4.4, 95% CI 1.0-18.6, $P = 0.04$) and metastatic disease at diagnosis (HR 4.8, 95% CI 1.2-19.6, $P = 0.03$).
Conclusions: Extragonadal GCT, metastasis at diagnosis, and high level of AFP are poor prognostic factors in adults with GCT, showing survival less than 50%. Therefore, more intensive treatments including high-dose chemotherapy are being considered in patients with these factors. However, the prognosis of children with GCT having these factors was favorable with cisplatin-based chemotherapy.

POSTER SESSION: POSTER SESSION - RARE TUMOURS

P-0209

CONSERVATIVE SURGICAL APPROACH IN DIFFERENTIETED THYROID CANCER IN CHILDREN

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Purpose/Objective: The prognosis of Differentieted Thyroid Cancer (DTC) less than 2 cm in diameter without additional risk factors is excellent in pediatric age. Total thyroidectomy is the surgical approach mostly performed as reported in literature but it's associated with a high percentage of complications as recurrent nerve injury and hypoparathyroidism. Currently the extension of thyroid surgery in DTC in children is subject of great attention and debate. On the basis of a retrospective case series, we analyzed differences between the radical surgical approach and the conservative one in low-risk patients (neoplasia limited to one lobe, absence of lymph node involvement and distant metastasis).
Materials and Methods: We reviewed data of 54 patients with a low-risk DTC in a multicentric Italian study, TREP Project (Tumori Rari in Et◦ Pediatrica), with a medium age 14.5 years (range 4-18 years). Among these patients, 34 underwent total thyroidectomy while 20 underwent hemithyroidectomy.
Results: In the group that underwent radical approach post-operative complications included: hypoparathyroidism in 5 cases (14.7%) (8.9% transient; 5.8% permanent) and recurrent nerve injury in 2 cases (5.8%). No complications occurred in the conservative surgery group. At the follow-up we did not observe significant difference in the progression of disease between the two groups.
Conclusions: Pediatric patients with a low risk DTC can be treated by a conservative surgery. Therefore a greater selection of patients is recommended, in order to identify the most appropriate surgical approach.

P-0210

THYROID CANCERS IN YOUNG ADOLESCENTS AT A UNIVERSITY HOSPITAL

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Purpose/Objective: The incidence of a rare tumor, differentiated thyroid cancers in children,have increased dramatically in the years following Chernobyl catastrophe in the territories that are heavily contaminated by radionuclides. Thyroid nodules are at risk of being malignant in 5-20% cases.The most common presenting findings of thyroid cancers are thyroid nodules and cervical lymphadenopathy. Positive family history and neck irradiation are risk factors for development of thyroid carcinoma, although thyroid carcinoma is uncommon in children compared to adults. US is the preferred modality for evaluating the structure of the thyroid gland for nodules.However, thyroid nodules cannot be distinguished as benign or malignant on the basis of the sonographic findings.
Materials and Methods: Between 1990-2013, 20 cases of thyroid carcinoma have been diagnosed. Fourteen were females, 6 were males with a mean age of 15.9 + 3.2 years. One case had neck irradiation due to HD, one had cranial RT for ALL.One had lived in Kiev with positive family history.Histopathologically, 10 cases had differentiated PTC, 7 had papillary thyroid variant, 1 follicular and 1 medullary thyroid carcinoma. In 3 cases thyroid nodules were $<$ 10mm. in size, in 3 there were microcalsification; in 5 there were increased vascularization;
Results: Following surgery, all patients received adjuvant RAI therapy and were put on replacement therapy.In one case there was lymph node infiltration, whereas in one there was distant-lung metastasis. Three patients experienced hypoparathyroidisim, in one there was vocal cord problems. B-RAF mutation studies are carried out in 3 cases in order to add targeted therapy i.e.sorafenib in the metastatic or recurrent cases.The patients are monitored by measuringhuman TG levels and by US for recurrences.
Conclusions: Although the optimal treatment modality in children with thyroid cancers is still controversial, total thyroidectomy + lymph node dissection represent the dominant method of surgical treatment, enabling the success rate of RAI therapy and provide longer disease free survival.

P-0211

SURGICAL MANAGEMENT FOR CHILDHOOD DIFFERENTIATED THYROID CANCER, A 10 YEARS RETROSPECT OF A SINGLE-INSTITUTE.

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Purpose/Objective: Differentiated thyroid cancer(DTC)in childhood is an uncommon childhood malignancy. We reported our experience on surgical management for childhood differentiated thyroid cancer in past 10 years.
Materials and Methods: Twenty-one children cases with DTC from 2003 to 2012 were operated by different operative modes (lobectomy, subtotal thyroidectomy and total thryoidectomy) according to the involved extent of thyroid cancer. Patients with cervical lymph node metastasis were operated by neck dissection. Cases with distant metastases were further treatedby ^{131}I ort hyroid hormone.
Results: The pathologic results are 19 papillary, 1papillary with follicular variant and 1 follicular carcinoma. There are 6 cases of bilateral lesion, one case of microcarcinoma. Followed up for a period of 0.5 to 8 years, there are 1 death case and 3 recurrence cases (in neck) were found in the 21 cases of childhood thyroid cancer, therefore.the rate of local recurrence was 14.2%(3/21). The rate of cervical neck node metastasis was 61.9%(13/21). Extra-thyroidal invasion occurring was 14.3%(3/2 1). The rates of complication with total thyroidectomy was 37.5%(3/8).
Conclusions: Althought it is recommended that total or near-total thyroidectomy and modified neck dissection to remove regional lymph nodes is the optimal treatment for childhood DTC. Our data indicate that for those unilateral cases, the prognosis of lobectomy plus central-compartment neck dissection has no difference with subtotal or total thyroidectomy[3]. The pathologic result of one microcarcinoma case shows the resection of the primary lesion is enough. In extra-thyroidal invasion cases the function integrity of organs and nerves should be preserved as possible as operators can, while the minimal residual cancer can be treated by ^{131} I or thyroid hormone.

P-0212

PRESENTATION AND OUTCOMES OF NASOPHARYNGEAL CANCER IN AN ASIAN PAEDIATRIC POPULATION - A RETROSPECTIVE REVIEW OF PAEDIATRIC PATIENTS TREATED IN SINGAPORE OVER THE PAST 15 YEARS.

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Purpose/Objective: Nasopharyngeal cancer is a common cancer in the Asian population. It is well studied in the adult population and high cure rates have been achieved with the use of

concurrent chemotherapy and radiotherapy. Paediatric nasopharyngeal cancer has been studied in Western populations but remains poorly understood in Asian populations.

To understand the presentation, histological subtypes, incidence, and outcomes of treatment of paediatric nasopharyngeal cancer in Singapore.

Materials and Methods: Patient information was obtained from the Singapore Childhood Cancer Registry. This included all patients treated in public hospitals in Singapore under the age of 21 between 1998 and 2012. Patient records were analysed and stage, histology, treatment modalities and survivorship information was obtained. We also looked at the residual side effects from treatment.

Results: Ten patients were treated in both public hospitals that provide paediatric services in Singapore between 1998 and 2012. Median age of diagnosis was 13 years (9.6 to 16.4 years). Eight patients (80%) were male and 7 (70%) were Malay in ethnicity. Persistent headaches and palpable neck lumps were the commonest presenting complaint. The predominant histological subtype was undifferentiated carcinoma (Type III) 8 (80%). Other subtypes were mucoepidermoid carcinoma (1 patient) and sinonasal carcinoma (1 patient). Patients were between stage II * IVA at diagnosis with many of them presenting with T4 disease. They were mostly EBV positive. 7 (70%) were treated with neoadjuvant cisplatin based chemotherapy regimen followed by radiotherapy to 66-70 Gy to the primary tumour. 5 year overall survival in our group was 76.8%. There were 2 deaths from recurrences. Half of the patients in our study group experienced late effects from the treatment and mostly sequelae from radiotherapy.

Conclusions: Paediatric nasopharyngeal cancer in the Asian population presents a distinct entity compared to the adult disease. Therapeutic approaches should reflect this to obtain the best outcome.

P-0213

SALIVARY GLAND TUMORS IN CHILDREN: A RETROSPECTIVE CLINICAL REVIEW

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Purpose/Objective: To identify clinical, pathological and prognostic features of salivary gland tumors.

Materials and Methods: Clinical, pathological and survival informations were obtained from patients' files and pathology reports. Age, gender, tumor site, stage, histological subtype, facial paralysis, perineural, stromal, vascular invasion, treatment options were analyzed.

Results: A retrospective study of 7 patients with salivary gland tumors (5 parotid, 1 palate and 1 lacrimal gland) who underwent surgery for definitive treatment from 1972 to 2012 was done. The age of the patients at the time of diagnosis ranged from 6.3 to 13 years old, with a mean age of 10.2 years; five were 5 (71.4%) females and two (28.6%) males. Five patients had stage IVA, one patient had stage I, and one patient had stage II disease. All patients had organ-limited disease except one who had lymph node and distant metastases. The minimum and maximum sizes of tumors changed from 1×1 cm to 6×4 cm. The positive surgical margin was found in 5 (71.4%) cases. As a pathological subtype, there were three adenoid cystic carcinoma, two adenocarcinoma, one anaplastic carcinoma and one mucoepidermoid carcinoma. There was pleomorphism in one case. There were five (71.4%) parotid, one (14.3%) lacrimal gland and one (14.3%) palatal involvement. Three patients who had low stage tumors were treated with surgery alone. Four of our cases received adjuvant radiation and chemotherapy. One patient with parotid tumor died with progressive disease. One case with lacrimal gland neoplasm was fine 48 months after discontinuation of treatment. The other palate case was lost to follow-up one month after the begining of the treatment.

Conclusions: Surgery is the primary treatment with adjuvant treatment like radiotherapy and chemotherapy. The individual treatment options are selected and planned for each patient.

P-0214

SUCCESSFUL TREATMENT OF NUT MIDLINE CARCINOMA IN A 9 YEAR OLD – NO TIME FOR THERAPEUTIC NIHILISM

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Purpose/Objective: A subgroup of rare undifferentiated carcinomas is characterized by a t(15;19)(q13;p13), resulting in *BRD4/NUT* Fusion. These carcinomas frequently affect children and young adults. Most common locations are the midline structure of the head and neck and mediastinum. Prognosis is rather dismal with median OS rates of 28 weeks.

Materials and Methods: We report on a 9 year old boy admitted to our hospital with the urgent suspicion of cervically located lymphoma. Ultrasound guided lymph node biopsy led (after worldwide pathology consultations and molecular diagnostics) to the diagnosis of a NUT midline carcinoma originating from the sublingual gland with cervical, supraclavicular and mediastinal metastases.

Results: Encouraged by a literature report of a patient surviving following use of an aggressive soft tissue sarcoma protocol we treated the patient using cycles of vincristine, adriamycine, cisplatinum and ifosfamide plus modified neck dissection and hyperfractionated local radiotherapy. The patient achieved a complete remission and stays well 24 months after termination of therapy. Severe permanent side effects are currently not observed.

Conclusions: Tumors with a t(15;19) bear a rather grim prognosis. Long term remission or even cure may be obtained if rapid aggressive multimodal therapy is applied. We encourage clinicians to report their affected patients to the international NUT midline carcinoma registry at *www.NMCRegistry.org*.

P-0215

REGIONAL CHEMOTHERAPY IN PATIENTS WITH MALIGNANT PERITONEAL MESOTHELIOMA.

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Purpose/Objective: Mesothelioma * is a rare form of cancer that develops from transformed cells originating in the mesothelium. Intraperitoneal chemotherapy * one of the essential components of a multi-modal approach in the treatment of this disease. The safest and most comfortable way of its implementation - using implantable peritoneal port inserted as a stage of cytoreductive surgery.

Materials and Methods: Since 2011 6 children with peritoneal mesothelioma aged 10 to 14 years receiving treatment underwent peritonectomy with one-stage implantation of peritoneal port systems and intraoperative intraperitoneal administration of the Cisplatin drug at a dose of 120 mg/m2 at 90 minutes. Patients received adjuvant chemotherapy according to the Alimpta Scheme 120 mg / m 2 first day, Cisplatin 75 mg/m2 in intraabdominal first day. The interval between courses was 21 days.

The portal body is implanted in the soft tissue of the front abdominal wall in the VIII - X rib area. An approximate 5-cm incision in the skin is made at the selected site. A 'kangaroo' pocket is created approximately two cm away from the incision line and 0.5-cm to 2.0 cm deep into which the portal body is placed. The portal body is fixed in the bottom of the 'pocket'. A catheter is placed into the abdominal cavity and through an opening in the abdominal wall is connected to the portal body. Soft tissue sutured in layers. In the port system Huber needle with a rounded tip is installed, so that it does not cut, but push the silicone chamber membrane.

Results: Patients and medical staff admit ease of the port systems operation. Recurrence of the disease and port systems infection were not noted.

Conclusions: Use of peritoneal ports is easy and safe way of intraperitoneal chemotherapy.

P-0216

RESPONSE TO CRIZOTINIB IN PULMONARY INFLAMMATORY MYOFIBROBLASTIC TUMOR INVADED LEFT ATRIUM

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Purpose/Objective: Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm treated with surgery. When tumor is unresectable, medical therapies with anti-inflammatory drugs or chemotherapeutics are used because of local-aggressive course. Anaplastic lymphoma kinase (ALK) expression is detected in half of cases. ALK inhibitor crizotinib was recently reported with partial response in a patient with IMT.

Materials and Methods: Here we report a second patient with very good clinic response to Crizotinib who have unresectable pulmonary IMT.

Results: Right posterior mediastinal mass was detected in 8-year-old male patient with cough and dyspnea. He diagnosed as ALK positive IMT. Total mass excision with lobectomy was performed. The patient followed-up with small residue for 4 years. He was admitted to hospital with dysphagia and fatigue. Chest CT revealed residual mass progressed and invaded both esophagus and left atrium. Pericardial effusion, pulmonary hypertension, mitral valve dysfunction and stenosis due to mass effect were noted on echocardiography. Medical treatment first with nonsteroidal anti-inflammatory drugs, interferon and high-dose prednisolon, then with VAC chemotherapy and radiotherapy was given for unresectable tumor no response. He became orthopneic and had to be fed by paretlerally. Crizotinib was started due to lack of any clinical or radiological improvement to previous treatments and worsening of his condition. After 4 weeks of crizotinib his clinical condition improved markedly. At 4th months of targeted therapy pericardial effusion, pulmonary hypertension and mitral stenosis resolved. He returned to his normal daily activities and school. He is still on treatment with stable radiologic findings for 9 months. Crizotinib was well tolerated and no major or minor side effects were noted.

Conclusions: Treatment of unresectable IMT can be a challenge. Although majority of patients might have some degree of response to medical treatment side effects can be serious

problem for this benign tumor. Targeted therapy with crizotinib should be an option for selected patients.

P-0217

IMMUNOHISTOCHEMICAL EXPRESSION OF VEGFR1, HER-2 AND PTEN IN PEDIATRIC ADRENOCORTICAL CARCINOMA TUMORS

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Purpose/Objective: Adrenocortical carcinoma (ACC) is a rare neoplasm in children but with huge consequences to patients and the current cytotoxic chemotherapeutic regimens have produced frustrating results. It's necessary to identify possible targets to treatment and increase survival rate. Vascular endothelial growth factor (VEGF) family of ligands and receptors has been correlated with poor prognosis. The mammalian target of rapamycin (mTOR) pathway is also implicated in tumor development and resistance against chemotherapy. Overexpression of HER2 protein in cancer cells confers resistance to apoptosis, promotes cell growth and can activate the PI3K(phosphatidylinositol3-kinase)/ Akt/mTOR pathways in breast cancer cells. The aim of this study was to evaluate the status of VEGFR1, HER2 protein and the key points of the PI3K/Akt/mTOR signaling pathway in pediatric ACC by immunohistochemistry.
Materials and Methods: Clinical presentation, staging, laboratory hormone profile and follow-up were obtained from the patients' medical records.

Formalin-fixed paraffin-embedded tumor tissue samples from 29 patients less than 19 years of age were collected. After histology review, samples were included on the tissue microarray (TMA). The DAKO HercepTest Protocol system was used to analyze HER2 protein. Immunohistochemistry was performed for mTOR (phosphor-Ser2448) * rabbit monoclonal antibody, PTEN * mouse monoclonal antibody and VEGFR1 * rabbit polyclonal antibody.
Results: Most of these patients had stage III or IV disease (69%). All cases were negative to HER2 protein. In contrast, VEGFR1 was strongly positive in all 29 patients. The tumor suppressor PTEN was negative in 14 patients (48,3%) and the active form of mTOR kinase was positive in 10 patients (35%).
Conclusions: VEGFR1 is a major possible target to pediatric ACC, HER2 protein seems not to have any participation in this disease and PI3K/Akt/mTOR signaling pathway is dysregulated. These results provide the framework for clinical trials to test the efficacy VEGFR1 and mTOR inhibitors for the therapy of pediatric ACC.

P-0218

DESCRIPTIVE EPIDEMIOLOGY OF ADRENOCORTICAL CARCINOMA IN THE UNITED STATES: INCIDENCE, OUTCOME, AND RISK OF SECOND MALIGNANT NEOPLASMS

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Purpose/Objective: Adrenocortical carcinoma (ACC) is a very rare and aggressive malignancy. Pediatric ACC has been associated with constitutional cancer-prone conditions such as Li-Fraumeni and Beckwith-Wiedemann syndromes; however, its etiology is not well defined, and population-based studies are lacking. The aim of this study was to evaluate the differences in incidence and outcome of ACC according to age, gender, race, ethnicity, and tumor stage.
Materials and Methods: Cases were identified in the Surveillance Epidemiology and End Results (SEER) from 100-2009 (SEER 18). Age-standardized rates per million (world standard population) (ASR), rate ratios (RR) and 95% confidence intervals (95% CI) were calculated by age, gender, race, and ethnicity. Five-year relative survival by stage and gender was estimated using Ederer II method, and the risk of second malignancies (SMN) was analyzed using SEER 9 (1973-2009).
Results: Of the 820 patients with ACC identified in SEER 18, 48 (5.8%) were children. Age-specific Incidence rates showed 2 peaks: the first one in patients <4 and the second approximately at age 70. Results showed female (ASR male $= 0.71$; ASR female $= 0.95$; RR $= 1.34$; 95%CI: 1.16-1.52) and white race (ASR white $= 0.91$; ASR black $= 0.48$; RR $= 0.52$; 95%CI: 0.38-0.70) predominance. No differences according to ethnicity were observed. Children <4 had higher survival rates (95.3%) than children >4 (24.9%; $p < 0.001$) and adults (35.8%; $p < 0.001$). Survival for patients of all ages with localized tumors (68.0%) was higher when compared with regional (47.2%; $p = 0.006$) and distant (9.7%; $p < 0.001$) disease. Among children, survival rates were higher for Hispanics (77.6%) when compared with non-Hispanics (42.7%; $p = 0.041$). Overall, increased risk of SMN (SIR $= 14.48$; 95%CI: 2.99-42.33) was 8-fold higher in children (particularly for bone tumors) than for adults (SIR $= 1.72$; 95%CI: 1.29-2.24).
Conclusions: ACC incidence has two peaks, and is higher among females and whites. Children have better outcome but a significantly higher incidence of SMN, probably due to its association with Li-Fraumeni syndrome.

P-0219

ADRENAL CORTEX TUMOR (TCA) IN THE WEST OF STATE, BRAZIL PARANA ANALYSIS OF 7 CASES.

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Purpose/Objective: The tumor of the adrenal cortex (TCA) in childhood is rare. But the Paran‡ its incidence is 15 times higher than that observed in other countries. Estimates are about 10-15 new cases of TCA in Paran‡.
Materials and Methods: We describe the clinical, laboratory, treatment and outcome of 7 patients treated at the West of Paran‡, from January 2007 to December 2012.
Results: The mean age at diagnosis was 3.3 years, with a female: male 1.3:1. The most common clinical forms were isolated virilization (71%) and Cushing's syndrome (29%). In 100% of cases, the tumors were functioning, 5 (71%) patients were stage I and two (29%) were stage IV. The average of hormonal measurements at diagnosis was 3786 ug / dL DHEA sulfate, 20.3 ug / dL of cortisol and 959.79 ug / dL of testosterone. Of the 7 children 6 (86%) are alive in clinical and laboratory remission, these five were stage I and one stage IV. Another children, stage IV, died after 2 years of evolution. Two (29%) children stage IV, received treatment of chemotherapy, surgery and mitotano and those with stage I, 3 (42%) were treated with surgery and 2 (29%) with surgery and mitotano. A child with stage I started mitotano for 4 months after first recurrence and remains in clinical and laboratory remission after 4 years the end of the medication.
Conclusions: The staging of TCA childhood, the presence of thrombus injection, the presence or absence of spillage during surgery and complete removal of the tumor and thrombi are important prognostic parameters. The best treatment is still surgery, the association of mitotano with chemotherapy has shown promise. In this disease early diagnosis is fundamental to the increase in child survival.

P-0220

HISTOLOGICAL CHARACTERISTICS OF PHEOCHROMOCYTOMA AND PARAGANGLIOMA FOLLOWED BY LOCAL RECURRENCE AFTER SURGERY IN CHILDREN

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Purpose/Objective: Pheochromocytoma (PH) and paraganglioma (PG) are rare catecholamine-secreting chromaffin cell tumors in children. Although usually benign and only requiring complete resection of the primary tumors, some of them behave as malignancy with a risk of tumor recurrences. We experienced three pediatric cases of PH or PG, one of which developed tumor recurrence after primary surgery. The aim of this study is to analyze the clinical and histological characteristics of those patients.
Materials and Methods: We retrospectively reviewed the three patients with PH or PG, including, clinical characteristics, surgical procedures, histologic findings, PASS (pheochromocytoma of the adrenal gland scaled score) and outcomes.
Results: Patient 1 was a 9-year-old boy with a sporadic PG on the left renal hilum. Patient 2 was a 13-year-old boy with a sporadic left PH. Patient 3 was a 9-year-old boy with a familial bilateral PH. Patient 1 underwent left nephrectomy, and patient 2 and 3 underwent partial adrenalectomy. The tumors were norepinephrine-predominant localized ones measuring $2.8 \times 2.5 \times 2.0$cm, $4.7 \times 4.0 \times 2.8$cm, and $2.9 \times 2.0 \times 1.9$cm (right) and $3.0 \times 2.5 \times 3.0$cm (left) in size, in patients 1, 2, and 3, respectively. Their weights were 32g in case 2, 8.6g (right) and 8.1g(left) in case 3. The principal histologic patterns of each tumor were similar and Ki67 positivity was less than 2%. PASS was 4 in patient 1, and 2 in patients 2 and 3. Although the surgical margin was tumor-negative and PASS was less than 4 in patient 1, the tumor obviously extended into the adjacent adipose tissue. Thirty months after the primary surgery, patient 1 developed local recurrence and underwent surgical intervention. The other two patients had been disease-free postoperatively for 24 months and 12 months respectively.
Conclusions: Our experience suggests that the PH or PG tumor extension into the adjacent adipose tissue may be an important risk factor of local recurrence in children even if the PASS is low.

P-0221

MYELOID SARCOMAS: A SINGLE CENTRE EXPERIENCE FROM INDIA.

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Purpose/Objective: Myeloid Sarcomas(MS) are rare extramedullary manifestations of Acute Myeloid Leukemia(AML). MS are reported in 2.5%-9.1% of AML patients. MS are characterized by distortion of extramedullary tissue due to proliferation of blast cells. A review of the clinical and laboratory profile, with outcomes of MS patients at our centre is presented here.
Materials and Methods: We retrospectively reviewed recorded data of 71 children with AML and/or MS at Sir Gangaram Hospital, from January2006 to December2012.
Results: Nine patients of 71(12.6%) had MS at presentation. Their age ranged from 9 months to 18 years. Six patients were males. Four had orbital MS. The other patients had MS of the maxilla, mandible, porta-hepatis and urinary-bladder whereas an 18y girl with paraplegia had a rare presentation with disseminated MS (involving the spinal-cord, paravertebral muscles, pre-sternal and retro-sternal regions, uterus and the cranio-facial sinuses).

Bone marrow was involved in 8 patients. AML-M2 was the commonest associated subtype. Immunohistochemical staining with Myeloperoxidase was positive on the biopsies. Genetic work-up was done in 7 showing t(8;21) in 3 patients, complex cytogenetics in 2 and normal cytogenetics in 2. Two patients -one with a mandibular MS and another with an orbital MS refused treatment due to financial reasons, and both have expired. Out of 7 treated patients one died with pseudomonal necrositing fasciitis post chemotherapy. Two had refractory disease and both died. Two with orbital MS and t(8,21) are alive and in remission at 6 months and 30 months respectively. The infant with bladder MS and complex cytogenetics has had a very early relapse and is awaiting Stem cell transplant. The child with Maxillay MS and t(8;21) is in clinical remission at 2 months.
Conclusions: MS are rare tumors with varied presentation. Favorable cytogenetics of t(8;21) and orbital MS respond well to therapy and have favorable outcome.

P-0222

EXTRA-RENAL RHABDOID TUMOURS IN CHILDREN: REAPPRAISAL OF HISTOPATHOLOGICAL DIAGNOSTIC FEATURES.

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Purpose/Objective: Extra-renal rhabdoid tumours in children are rare and aggressive tumours of uncertain histogenesis. They share characteristic histomorphology and molecular features similar to renal and posterior fossa rhabdoid tumours. We aim to study histomorphology and immunohistochemistry (IHC) of extra-renal rhabdoid tumours in children in order to re-appraise of the diagnostic parameters. Exclusion of other possible differential diagnoses is essential for choosing appropriate treatment.
Materials and Methods: Histology and IHC of ten cases diagnosed as extra-renal rhabdoid tumour in paediatric age group (less than 15 years of age) were reviewed retrospectively.
Results: The age range of patients was 1to 12 years, male: female ratio was 4:5. No specific site predilection was observed. Concurrent involvement of either kidney or posterior cranial fossa was not seen in any of our patients. Histology of all ten tumours showed remarkable uniformity. Classical 'rhabdoid' morphology was seen in all cases in the form of large nucleus with prominent nucleolus, conspicuous eosinophilic cytoplasm along with paranuclear whorls. Rhabdomyosarcoma was a differential diagnosis in essentially all cases due to morphologic overlap. On IHC, all tumours were negative for INI 1, a diagnostic marker for rhabdoid tumour. Either CK or EMA was positive in all cases. Rhabdomyosarcoma was excluded based on negativity for desmin and Myo D1.
Conclusions: Extra-renal rhabdoid tumours in children differ from those occurring in elderly population where rhabdoid morphology is usually a feature of de-differentiation seen in a variety of tumour types. In children, however, this typical morphology represents a unique tumour type characterised by INI-1 negativity on IHC as demonstrated in our study (representing mutation in hSNF5/INI1 gene). In addition, negativity for muscle markers further helps exclude rhabdomyosarcoma. Thus, appreciation of typical 'rhabdoid' morphology and negative IHC staining for INI-1 are diagnostic parameters in most cases of extra-renal rhabdoid tumours.

P-0223

SOFT TISSUE HEMANGIOENDOTHELIOMA IN CHILDREN

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Purpose/Objective: Soft tissue hemangioendothelioma (STHE) is a rare vascular tumor, which has a prognosis of borderline malignancy. There is a lack of understanding of the disease because of low incidence. So we investigated the treatment of STHE in children.
Materials and Methods: We retrospectively analyzed 7 patients with STHE, which was pathologically confirmed during January 1995 to June 2012. Median follow up period was 92 months.
Results: Four were males and 3 were females. The median age was 4 years. The main symptoms were palpable tumor in 6 patients and facial paralysis in 1 patient. The median tumor size was 4.5cm. Tumor locations were as follows: head, 1 patient; neck, 2; chest wall, 1; sacrococcyx, 1; upper limb, 1; and lower limb, 1. Out of 7, 3 patients underwent microscopic complete resection (R0); 2, macroscopic complete resection (R1); and the remaining 2, macroscopic incomplete resection (R2).

Histopathological examination after the surgery confirmed indeterminate HE, 1; epithelioid HE, 1; and kaposiform HE, 5. FNCLCC grade 2 was confirmed for 2 patients. In the aftermath of the surgery, the main sequelae were gait disturbance and hearing impairment.

Adjuvant IFN therapy was applied to the 3 patients (R1, 2; R2, 1). There were recurrence or regrowth in the 3 patients (R0, 1; R1, 2), and all of them were performed reoperation and IFN therapy. Only one patient (epithelioid HE, FNCLCC grade 2) had the metastasis to the scalp.
Conclusions: For treating STHE in children, R0 should be first considered. However when major seqeulae could be predicted, function preserving surgery could be considered by evaluating the tumor location, size, pathologic subtype and grade.

P-0224

EXPERIENCE OF ISOTREONIN TREATMENT FOR INOPERABLE SOLID-PSEUDOPAPILLARY TUMOR OF THE PANCREAS WHICH PREVIOUSLY DID NOT RESPOND TO ANTICANCER DRUGS AND RADIATION THERAPY

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Purpose/Objective: Solid-pseudopapillary tumor of the pancreas is rare neoplasm and can be occurred among adolescent or young women. Although its treatment of choice is surgery, the patients who are not eligible for resection need other kinds of therapy and there are little reports. Vitamin A and its derivatives such as Isotretionin can regulate the growth and differentiation of epithelial cells and prohibit the tumors' growth in some tumors.
Materials and Methods: The authors would like to show the case of 12-years old female patient with solid-pseudopapillary tumor of the pancreas, which was inoperable and did not respond to chemotherapy and radiation therapy, but, fortunately responded to Isotretionin (Roaccutan®).
Results: She complained intermittent abdominal pain and a lump palpable with tenderness. There was no abnormal finding from blood test. The lump locating in the body and tail of pancreas has heterogeneous signal intensity on MRI. The size was $157 \times 101 \times 133$mm. It was surrounded by fibrous capsule and extended to liver vein, celiac artery, and greater curvature of stomach. It was diagnosed as a solid-pseudopapillary tumor by tissue biopsy. It was not operable, so radiation therapy was implemented after the completion of the 6-cycle of Gemcitabine for 6 months. After that, CT did not show any change of the size of the lump. Additional anticancer agents of Vincristine, Ifosfamide, Etoposide, and Cisplatium were given, but there was no response also. At that time, Isotretionin (Roaccutan®, dose of 100 mg/m^2/day) was administrated daily. After 6 month, abdominal CT showed the tumor was reduced to $110 \times 95 \times 115$mm revealed the trace of necrosis by tissue biopsy. Isotretionin has been administrated over 2 years with good tolerability and the tumor is continuing to decrease that she is waiting the operation schedule.
Conclusions: For inoperable solid-pseudopapillary tumor of the pancreas, authors suggest Isotretionin could be used as treatment.

P-0225

THE TREATMENT OF CHILDREN UNDER ONE YEAR OF LIFE WITH SOLID TUMORS

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Purpose/Objective: To improve the results of the treatment of pediatric patients under one year of life with solid tumors
Materials and Methods: 17 patients (?ale * 9, female - 8) at the age from14 days and 11 month (mean - 7,3 month) with solid tumors, were enrolled between 2011 and 2012 years. 4 patients had neuroblastoma (NB) with IV stage of the disease, 1 patient had NB with IVS stage, 1 patient had stage III of NB, 1 patient had stage IIB of NB, 5 patients had neuroblastoma (NB) with I stage of the disease. 1 patient had extrarenal rhabdoid tumor of the liver (ERRT), 1- alveolar rhabdomyosarcoma (aRMS) stage III, 1- embryonal rhabdomyosarcoma (eRMS) stage III, 1- monolateral nephroblastoma (mNP) stage II, 1- bilateral nephroblastoma (bNP) stage VB. All patients received therapy according protocols after *thoroughly evaluation* (imaging, MIBG, bone marrow morphology, molecular studies, immunohistochemistry). Surgery treatment was performed for 15 patients, 1 patient at the age of 14 days with NB stage IV died before surgery and 1 patient at the age of 11 months with ERRT had progressive disease.

Results: 14 (82,3%) patients (from 17) were alive without disease with a followup of 6 to 12 months. One patient with NB stage IV is alive with the recurrence of the disease.
Conclusions: These results support further investigations. Our data confirm that pediatric patients under one year of life are curable and survival for them is possible.

POSTER SESSION: POSTER SESSION - LIVER TUMOURS

P-0226

MULTI-CENTER ANALYSIS FOR 108 CHINESE CHILDREN WITH HEPATOBLASTOMA. REPORT OF THE CHINESE ANTI-CANCER ASSOCIATION PEDIATRIC ONCOLOGY GROUP

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Purpose/Objective: In 2009 in Wuhan city, the Chinese Anti-Cancer Association Pediatric Oncology Group drafted the protocol of multidisciplinary diagnosis and treatment for children with Hepatoblastoma (HB) (abbreviation HB-WH-2009). The aim of this article is to assess the preliminary efficacy of HB-WH-2009.
Materials and Methods: Retrospective analysis of clinical effect of 108 patients with HB from 11 hospitals in China during 2009-2012.Kaplan-Meier was used to analyze the survival curve.
Results: 78 patients were males and 30 were females, the media age at diagnosis was 13.5 months old. 78.7% children manifested with abdominal mass as their first symptom. 95 patients had preoperative PRETEXT stage, 8 were stage I, 22 were stage II, 32 were stage III and 26 patients were stage IV. 96 children had COG stage after operation, 74 (77.1%) were stage I, 8 (8.3%) were stage II and 14 (14.6%) were stage IV. 79 (73.1%) obtained pathological diagnosis by surgical ablation or biopsy. Eighty-nine patients had clear pathological subtype, 25 (28.2%) were fetal type, 41 (46.0%) were hybrid with fetal and embryonic, 18 (20.0%) were hybrid with epithelial and mesenchymal, 5 were other subtypes. Among 106 patients who underwent chemotherapy, 48 patients (45.3%) received prefer protocol (CDDP + VCR + 5-Fu), 6 (5.7%) patients suffered alternative protocol (CDDP+ adriamycin), 20 (18.9%) patients had both protocols. and the remains had other protocol. All patients were followed up to 30.June. 2012. The median follow-up time was 24 months. The 5-year-overall survival rate was 86.9 $\pm$ 6.5% and 5-year event-free survival rate was 60.2 $\pm$ 10.2%.
Conclusions: Multidisciplinary cooperation should become the standard treatment of the HB. HB-WH-2009 protocol is worthy of further promotion and application in China for its better clinical efficacy and less toxicity. How to predict the responsity to chemotherapy and more effective protocol for metastases patients should be further explored.

P-0227

PEDIATRIC HEPATOBLASTOMA: 20-YEAR EXPERIENCE IN A SINGLE INSTITUTION IN ARGENTINA FOLLOWING THE GUIDELINES OF SIOPEL TRIALS (INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY LIVER TUMOUR GROUP)

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Purpose/Objective: To report the 20-year experience of pediatric patients with hepatoblastoma (HB) treated at a single Institution in Argentina following the guidelines of SIOPEL trials.
Materials and Methods: We retrospectively analyzed 63 consecutive patients (pts) with diagnosis of hepatoblastoma treated at our Institution from May 1992 to May 2012, according to SIOPEL trials. SIOPEL 1: 5 (8%) 2: 13 (21%), 3: 27(43%), 4: 8 (12%) and 6: 10 pts (16%).
Results: Median age: 15.7 months (1-158). M/F: 1.1/1. Localized disease: 84%. Genetic syndromes associated: 2 pts: Beckwith-Wiedemann, 1 pt: Type 1 neurofibromatosis, and 2 pts with very low-birth-weight.

Median serum AFP levels: 253.923 ng/dL ($<$ 3 * 4.659.994), only 1 pt below 100 ng/dl. PRETEXT (pretreatment extent of disease): available in 61/63: PRETEXT I: 1.6, II: 34.4, III: 41 and IV: 23% respectively, vascular involvement: 33%. Complete resection achieved in 93.6% either by partial hepatectomy (88%) or by orthotopic liver transplantation (OLT) (12%). With a median follow up of 68,4 months (0.2 -198), the 5-year Event-Free (EFS) and Overall Survival (OS) was 68% and 75% respectively for the whole group. The 5-year EFS was 76% vs 25% ($p = 0.0004$) and OS 82% vs 36% ($p = 0.0009$) for localized vs metastasic disease respectively. According to PRETEXT I II III and IV, the 5-year OS was 100, 89, 75, and 49%, and 90 vs 58% low vs high risk pts respectively. With a median time of 10.6 months (4.6 to 32), 6 pts (9.5%) relapsed, local: 50%, metastatic: 33% and combined: 17%.
Conclusions: Following SIOPEL strategy (based on the use of pre-operative chemotherapy before definitive surgery) favorable long-term outcome could be obtained in our setting, similar to other series, with a high rate of complete tumor resection (including OLT).

P-0228

COMPREHENSIVE ANALYSIS OF A SINGLE PEDIATRIC LIVER SURGERY CENTER EXPERIENCE WITH LIVER (LRMS) AND BILE DUCTS RHABDOMYOSARCOMA (BDRMS)

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Purpose/Objective: Version:1.0 StartHTML:0000000190 EndHTML:0000002760 StartFragment:0000002444 EndFragment:0000002724 SourceURL:file://localhost/Users/fredericgauthier/Desktop/abstract%20SIOP%20RMS.doc LRMS and BDRMS have a poor prognosis. Our purpose is to report on surgical treatment and outcome of patients referred primarily or after relapse to us for surgery.
Materials and Methods: Version:1.0 StartHTML:0000000190 EndHTML:0000002835 StartFragment:0000002444 EndFragment:0000002799 SourceURL:file://localhost/Users/fredericgauthier/Desktop/abstract%20SIOP%20RMS.doc Retrospective review of surgical procedures, assessment of residual tumor, sites of relapse, and outcome of patients referred from 1990 to 2012. Chemotherapy (CT) and radiotherapy (RT) were performed according to current SIOP protocols
Results: Version:1.0 StartHTML:0000000190 EndHTML:0000003764 StartFragment:0000002446 EndFragment:0000003728 SourceURL:file://localhost/Users/fredericgauthier/Desktop/abstract%20SIOP%20RMS.doc Eleven patients, aged 2.2 to 10.3 (median: 2.8) years at diagnosis, had embryonal LRMS (2) or BDRMS (9).The 2 patients with LRMS underwent respectively a right hepatectomy (RH) extended to diaphragm and a left hepatectomy (LH) with extrahepatic bile duct resection (EHBDR). One died from recurrence despite free margins, the second from surgical complication. From 5 patients primarily referred with BDRMS, one is in first complete remission (CR1) after biopsy complication requiring primary surgery (LH + EHBDR). Two patients are in CR1 after delayed en-bloc EHBDR + LH or RH. The RH patient had malignant cells in liver. Two patients had positive nodes at surgery: one is in CR1 after EHBDR and resection of portal vein, the second had EHBDR and negative biopsies at a second-look operation, but died from local recurrence. From 4 patients referred with relapsed BDRMS, 2 had undergone EHBDR with positive margins, 1 had no local treatment and one was irradiated. Only one patient survived after EHBDR and RT. All of 4 patients dead from disease had local relapses. Follow-up of the 5 survivors is 1 to 14 years.
Conclusions: Version:1.0 StartHTML:0000000190 EndHTML:0000002835 StartFragment:0000002444 EndFragment:0000002799 SourceURL:file://localhost/Users/fredericgauthier/Desktop/abstract%20SIOP%20RMS.doc This experience is consistent with other disappointing results reported in literature for LRMS and BDRMS. Improving assessment of CR and defining what radical surgery should be are mandatory aims, the outcome after relapse being very poor

P-0229

CYSTIC-LIKE LIVER TUMOURS IN CHILDREN: TWO DISEASES WITH SIMILAR APPEARANCE BUT REQUIRED DIFFERENT TREATMENT APPROACH

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Purpose/Objective: Liver tumour only accounts for 0.5-2% of all tumours in children. Cystic-like hepatic tumours such as undifferentiated embryonal sarcoma (UES) and mesenchymal hamartoma (MH) are even rarer. Due to the differences in prognosis and treatment, timely and accurate diagnosis is essential. However, their closely resembling clinical characteristics make the initial diagnosis difficult. We reviewed our experience and tried to identify any unique clinical pattern.
Materials and Methods: This is a retrospective review of patients' charts and database over a 15-yrs period. Clinical and imaging characteristics of indexed patients were analyzed.
Results: 2 cases each of UES & MH were identified and all were confirmed histopathologically. Their age of diagnoses were 10mos, 10yrs, 13yrs & 15yrs and 3 were girl. Both MH patients presented with abdominal distension without other symptoms. In contrary, one UES patient had abdominal distension and pain associated with anorexia and weight loss. There were no remarkable laboratory results except one MH patient had mild elevated liver parenchymal enzymes and alpha-fetoprotein. Both ultrasonography & CT-scan showed multiple cystic +/− solid lesions in all MH & UES patients. The tumours of two MH cases were gross totally excised and the 'cysts' were actually myxoid tissue.
Trisegmentectomy of liver was done due to rapidly mounting abdominal distension and pain in one UES patient. The other UES patient underwent hemi-hepatectomy. Both UES patients received chemotherapy (IRS-IV protocol). All patients achieved long term remission.
Interestingly, both UES patients were found to have multiple hypo-enhancing liver lesions suggestive of metastasis in 6 to 12-months after completing chemotherapy but turned out to be focal nodular hyperplasia by biopsy.
Conclusions: MH & UES had similar imaging appearance and possible pathological overlap; the presenting patterns may be more striking in some UES patients. However, surgical biopsy and excision remained mandatory to confirm the diagnosis and guide the subsequent treatment.

P-0230

THOROUGH LUNG METASTASECTOMY IMPROVES SURVIVAL IN PATIENTS WITH HEPATOBLASTOMA

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Purpose/Objective: Complete surgical resection of the primary lesion in conjunction with chemotherapy is strongly important to cure hepatoblastoma. However, the role of surgery for pulmonary metastatic lesions has not been established. Usually, a single or few metastatic lesions can be resected, but multiple metastases have often been considered as unresectable. From 2007, we started a program to resect every metastatic lesion of the lung even if the lesions remain multiple, bilateral or chemotherapy-resistant after neoadjuvant or adjuvant chemotherapy. We herein present the result of our experience.
Materials and Methods: Retrospective chart reviews of six patients with hepatoblastoma associated with multiple lung metastases were performed. Their age ranged from 1 to 10 years old. All patients had no other distant metastases except the lung. After neoadjuvant chemotherapy and hepatectomy, each metastatic lesion was removed by wedge resection through an open thoracotomy. Intraoperative indocyanine green fluorescence imaging (IR system) was used in 2 patients to detect small non-palpable lesions.
Results: The number of metastatic lesions in each patient ranged from 7 to 40, and the total number of resected lesions was 115. Five patients out of six were alive and serum alpha-fetoprotein level was normalized in 4 patients at the end of follow-up. An 8- years- old girl who underwent resection of 40 metastatic lesions on 8 separate occasion maintained complete remission for 2 years with respiratory function well reserved. A ten years old boy with a tumor thrombus into the right atrium died of uncontrollable multiple organ metastases after lung metastasectomy. An IR system successfully detected some small, non-palpable metastatic lesions.
Conclusions: Our results suggested the effect of thorough resection of lung metastases on survival in patients without other distant metastases. An IR system was very useful for identifying CT-negative or non-palpable small pulmonary lesions.

P-0231

SURGICAL MANAGEMENT AND OUTCOMES OF RELAPSED HEPATOBLASTOMA

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Purpose/Objective: The outcomes and management for relapsed hepatoblastoma are not well defined. We present a single tertiary referral centre's experience of relapsed hepatoblastoma to determine the outcomes and surgical management
Materials and Methods: Patients treated 1995-2013 were prospectively enlisted in a database and charts retrospectively reviewed
Results: A total of 42 patients were treated with hepatoblastoma with a median age of 13 months (IQR 7-34 months). The overall survival was 39/42 (92%). Within this cohort 6/42 (11%) patients relapsed following completion of therapy, and 1/42 patient developed a distant relapse after a long period of stable disease after failure to achieve a normal alpha-fetoprotein. The overall survival of patients with relapsed disease was 5/7 (71%) vs. those who did not have relapse was 1/35(3%) ($P = 0.06$).

Relapse occurred a median of 5 months (IQR 4-9). The sites of relapse were locally (2/7), pulmonary (1/7), locally and pulmonary (1/7), locally and pericardial (1/7) and multiple sites (2/7).

All patients received further chemotherapy, one of which included high dose chemotherapy with stem cell rescue. Early in the series one patient (with local and pericardial recurrence) received local radiotherapy, followed by salvage liver transplant, providing long-term survival. Apart from one patient still on treatment and awaiting surgery, all patients underwent surgical resection of their disease. For local control, apart from the liver transplant this included re-excision of remaining tumour. With regards pulmonary disease this included multiple thoracotomies (3 thoracotomies and 1 sternotomy in one patient over a 3 year period and 3 thoracotomies in another over two years, both are long term survivors). Two patients with disease in multiple sites one has died and the other, mentioned above, is till on treatment
Conclusions: The relapse rate was approximately 10%, however with aggressive surgery to remove local or isolated pulmonary recurrence a reasonable salvage can be expected

P-0232

COMBINATION OF IRINOTECAN AND VINCRISITNE FOR RECURRENT HEPATOBLASTOMA

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Purpose/Objective: The primary objective was to determine the efficacy of the combination of irinotecan(IRN) and vincristine in patients with recurrent hepatoblastoma.
Materials and Methods: We retrospectively studied 5 patients with first recurrent hepatoblastoma, who all had been treated with standard regimen, including doxorubicin, cisplatin, 5-fluorouracil and vincristine, etc. Among them, 4 patients were intrahepatic relapse, one presenting vascular invasion, one with distant metastasis (lung metastasis); 1 patient was intra-abdominal extrahepatic relapse. At diagnosis, the levels of α-fetoprotein all increased $>$200ng/mL. Patients received IRN (20mg/m^2/day, days1-5) and vincristine (1.5mg/m^2, day1), administered intravenously in 3-week cycles up to the point of the feasibility of tumor complete resection, the maximum cycles of 6. No additional chemotherapy for micro-positive patients after operation. Extent-of-disease and toxicity evaluations were performed at the start of next course of chemotherapy.
Results: Common toxicities were grade 4 myelosuppression and grade 2-3 diarrhoea. Because of severe gastrointestinal side effect and worse treatment response, 1 patient stopped receiving chemotherapy after 2 cycles of IRN and vincristine. The other 4 patients all received 4-6 cycles of chemotherapy and achieved partial response(80%) and decreased α-fetoprotein levels, 3(60%) achieved second complete resection of tumor with partial hepatectomy, 1(20%) also achieved complete resection by receiving total hepatectomy and liver transplantation. The patient with initial lung metastasis achieved complete remission of the lung lesion with chemotherapy alone, at the end of the 5th course. During the follow-up, one patients died from EB virus associated hepatic dysfunction. Overall survival at 3 years was 60%.
Conclusions: The combination of irinotecan and vincristine showed favorable effects on recurrent hepatoblastoma, and its compliance was good, most patients could tolerate related side effects.

P-0233

ANEMIA IN HEPATOBLASTOMA: THE ROLE OF HEPCIDIN AND TOLL-LIKE RECEPTOR-4

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Purpose/Objective: Anemia is frequently seen in patients with hepatoblastoma. Anemia in cancer has a complex pathogenesis, but is thought to be associated with iron deficiency or inflammation. Hepcidin, a key regulator of iron metabolism, is regulated by the iron status, hypoxia and inflammation. Moreover, Toll-like receptor (TLR) signaling plays an important role in hypoferremia.
Materials and Methods: Immunohistochemistry (IHC) was used to determine hepcidin and TLR expression level in HB liver tissues (8 with prechemotherapeutic liver biopsy and 8 with postchemotherapeutic hepatectomy tissue). To study the effect of TLR-4 dependency of LPS-enhanced hepcidin production, HB HepG2 cells were pretreated with either anti-TLR-4 or

IgG_{2a} isotype control, then added with IL-1b or IL-6 in the presence of LPS for 24 h, the conditioned media were collected for Hepcidin ELISA detection.
Results: The IHC analysis showed a medium to strong cytoplasmic and nucleus reactivity for hepcidin in 100% of cases of HB before chemotherapy, but positive reactivity in only 25% of cases of HB after chemotherapy. Positive staining for TLR-4 was observed in 100% of HB. LPS and IL-6 has the capacity to stimulate hepcidin production, but IL-1b had little or no effect on hepcidin production. Furthermore, the increase of hepcidin could be inhibited by anti-TLR4 antibody administration.
Conclusions: We demonstrate that hepcidin is expressed by HB tissue, indicating that hepcidin production is increased in HB cells and might play a role in the pathogenesis of HB-associated anemia. In addition, our findings identify that LPS-induced up-regulation of hepcidin and TLR-4 dependency of LPS-enhanced hepcidin production in HepG2 cells. Further studies of factors regulating hepcidin by depriving the cancer cells of iron leading to cell growth arrest and apoptosis, might provide a new strategy for target therapy to HB.

P-0234

FOUR YEARS SURVIVAL DATA AND PROGNOSTIC ROLE OF CANCER STEM CELL MARKERS IN HEPATOBLASTOMA PATIENTS

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Purpose/Objective: The aim of this study *is to* assess the survival outcome in a cohort of HB Egyptian patients and the prognostic value of CSCs markers (*CD133, CD90 and CD44*)
Materials and Methods: disease status for 43 HB patients was evaluated at the main checkpoints of therapy and during follow-up. Treatment included surgical tumor resection and systemic chemotherapy (cisplatin, 5-fluorouracil, doxorubicin, and vincristine). Protein and RNA expressions of *CD44*, *CD 90* and *CD 133* were assessed by immunohistochemistry and quantitative PCR.
Results: the OS for the whole studied patients was 66.5% and 28.3% at 24 and 48 months, respectively. Localized disease stages (I&II) had a better OS than the advanced stages (III&IV) (81.9% versus 30%, $p < 0.001$); total surgical resection was superior to incomplete/ no resection (83.8% versus 25.2%; $p < 0.001$) and tumor response was significantly related to OS ($p < 0.001$). OS significantly correlated to *CD44*, *CD 90* and *CD 133* expression ($p < 0.001$) whereas reduced EFS was associated with CD44 and CD133 expression ($p < 0.001$).
Conclusions: complete surgical resection and systemic chemotherapy both improve outcome in HB with a significantly higher survival rates among patients with less advanced stages of disease. CSCs markers (CD133, 44, and 90) can predict poor prognosis in HB patients, though further studies are required to confirm their prognostic and potential targeted therapy value.

P-0235

POPULATION-BASED TREATMENT RESULTS OF HEPATOBLASTOMA IN CHILDREN OF HONG KONG

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Purpose/Objective: The five hospitals of Hong Kong forming the Hong Kong Paediatric Haematology and Oncology Study Group (HKPHOSG) established a uniform treatment protocol for hepatoblastoma (HB) since 1996 comprising of primary surgical resection for resectable tumour or in most instances, neoadjuvant chemotherapy (cisplatinum, 5-fluorouracil and vincristine or alternative regimen of cisplatinum and doxorubicin) followed by complete surgical resection of tumour. We reviewed the population-based treatment results of HB in Hong Kong.
Materials and Methods: The clinical data of all cases diagnosed between 1-Jun-1996 and 31-Dec-2011 were reviewed up to the date of 31-Dec-2012. Each case was assigned as standard risk (SR) or high risk (HR) according to the following criteria, HR: presence of either AFP $< = 100$ ng/ml or unresectable tumour or tumour rupture or distant metastases or portal vein thrombosis; SR: resectable tumour without the HR features.
Results: During the study period, a total of 51 cases of HB including 35 SR and 16 HR cases were diagnosed. Twenty-eight (55%) were males. The median ages of the whole group, SR and HR were 1.2 years (range, 0.1 to 14.6 years), 1.0 year (0.1 to 14.6 years) and 1.2 years (0.3 to 11.3 years), respectively. The median follow up duration was 3.7 years (range, 0.0 to 15.8 years). The 5-year event-free survival (EFS) and overall survival (S) of the whole group were 74.5% and 79.9%, respectively. The 5-year EFS and S of the SR cases were 93.4% and 100% whilst those of the HR cases were 36.5% and 41.7%, respectively ($p < 0.0001$ for SR v HR).
Conclusions: The treatment results of the SR HB are significantly better than those of the HR cases. Future goals may aim at reducing the chemotherapy for the SR cases and improving the survival of the HR cases.

P-0236

UNDIFFERENTIATED SARCOMA OF THE LIVER IN CHILDHOOD: AN UPDATE

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Purpose/Objective: Undifferentiated sarcoma of the liver (UESL) is the third most common hepatic tumor in children. In 2002 we reported a long-term disease-free survival rate of 70% on 17 children with UESL treated with the same multimodal approach. Therefore, a dedicated protocol for children with UESL was designed. We describe the results obtained in 9 children so far treated.
Materials and Methods: From 1996 to 2012 children were treated with the same multimodal approach: initial surgery/biopsy at diagnosis, chemotherapy (CT) according to the VAIA (vincristine, actinomycin, ifosfamide and adriamycin) regimen, disease evaluation after the initial 3 cycles, second-look surgery. A total of 9 CT cycles were administered
Results: Male/female = 6/3. Median age: 8.3 years (range, 3.7-14.3). Clinical presentation: abdominal mass (n = 4), acute abdominal pain (n = 4), abdominal distention (n = 4) with associated fever in 3, shoulder sore associated with serotine fever (n = 1), infection with fever (n = 2). Tumor involvement: right lobe (n = 7), left lobe (n = 1), both (n = 1). Tumor size: 5-10 cm (n = 2), > 10 cm (n = 7). Lung metastases were evident in 1 child.
Liver tumor resection was attempted at diagnosis in 5 children: 3 complete (1 metastatic patient), 1 with microscopic and 1 with macroscopic residue. Biopsy was performed in 4.
Response to CT was evaluable in 5 patients: partial response (n = 2), minor response (n = 1), tumor stable (n = 2). Second-look surgery resulted complete in 6 children.
Radiotherapy was administered in 2 cases.
Outcome (follow-up of 3-13 yrs): all patients are alive in 1st CR of their UESL but 2 children developed a second malignancy (Ewing sarcoma, hemangioendothelioma).
Conclusions: Our update confirms the good prognosis of children with UESL when an effective multidisciplinary protocol is utilized. UESL patients seems at high risk of second malignancy.

P-0237

COMPARISON OF CDDP/THP-ADR VERSUS CDDP/ADR AS THE FIRST LINE CHEMOTHERAPY FOR HEPATOBLASTOMA

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Purpose/Objective: Although cisplatin (CDDP) and Adriamycin (ADR) is the most common combination as the first line chemotherapy for hepatoblastoma, a combination of CDDP and tetrahydropyranyl-ADR (THP-ADR) has also been used in Japan. THP-ADR is considered as less cardiotoxic and more myelosuppressive than ADR. However, there was no report discussing the differences between the two chemotherapies for hepatoblastoma. Here we reviewed retrospectively the efficacy and adverse events in two groups.
Materials and Methods: Patients who had been diagnosed as hepatoblastoma and treated with CDDP/THP-ADR or CDDP/ADR between December 1999 and July 2012 in Saitama Children's Medical Center were retrospectively analyzed. Eight patients were treated with CDDP/THP-ADR, whereas 12 patients were treated with CDDP/ADR.
Results: CDDP/THP-ADR group required more red blood cell ($p = 0.01$) and platelet ($p < 0.001$) transfusions in a course compared to CDDP/ADR. The interval of each course was significantly shorter in CDDP/ADR, with a median of 22 days versus 27.5 days, respectively ($p < 0.001$). Febrile neutropenia was observed more frequency in CDDP/THP-ADR than in CDDP/ADR (43.5% vs 16.0%, $p = 0.02$). Decline of AFP levels in each course between two groups were almost identical ($P = 0.372$). The acute cardiotixicities have not been observed in both groups.
Conclusions: Although we need more cases to evaluate, CDDP/THP-ADR is inferior in terms of early toxicity and intensity of treatment compared with CDDP/ADR.

P-0238

SONOGRAPHIC ASPECTS OF EARLY DIAGNOSIS OF HEPATOBLASTOMA

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Purpose/Objective: Analysis cases of primary ultrasound investigation (USI) of hepatoblastoma in infants for early stage of disease.
Materials and Methods: We analysed the data of 7 patients of both sexes under the age of one year (median - 3 months) with morphologically verified diagnosis of hepatoblastoma. Stage of disease was "II" for all. All children were from the group of the 18 patients with hepatoblastoma under 1 year ages. From 1990 to 2008 they were examined and treated in the two oncological clinics. In 100% of the cases USI was first of the method of primary visualization of the tumor in general clinical network.
Results: In the absolute majority of the patients there was no suspicious medical history concerning tumor of the liver during the prenatal USI Minimum tumor size in greatest dimension by USI was 7,4cm, maximum * 11,5 cm and average volume - 282 (211-514) ml (Median; 25-75 percentile). Time the moment of birth to diagnosis of the tumor ranged from the first days to eleven months of life (130 (41,5-183,5) days). The number of tumor doubling from of alleged minimum volume of visualizing 1 ml till to actually installed volume was 8,1 (7,7-9,0). Given the minimal period of doubling of hepatoblastoma (on its own data - about 10 days) its growth beginning with 1 ml till to actually installed volume may be during 77-90 days as minimum.
Conclusions: USI is the method of choice for primary diagnosis of hepatoblastoma in infants. Hepatoblastoma usually diagnosed for volume of the tumor significantly higher than the minimum volume of possible visualization. By planning screening programs for diagnosis hepatoblastoma in infants the intervals between USI should not exceed 2,5-3 months.

POSTER SESSION: POSTER SESSION - NEUROBLASTOMA

P-0239

TREATMENT OUTCOME OF CHILDREN WITH NEUROBLASTOMA UNDER EIGHTEEN MONTHS OF AGE TREATED ACCORDING TO THE TURKISH PEDIATRIC ONCOLOGY GROUP NEUROBLASTOMA 2009 (TPOG-NBL-2009) PROTOCOL

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Purpose/Objective: In order to determine the clinical characteristics, treatment regimens, and outcome of the patients with neuroblastoma under eighteen months of age who were treated with the Turkish Pediatric Oncology Group Neuroblastoma 2009 Protocol (TPOG-NBL-2009).
Materials and Methods: One hundred and eighty-nine (n = 189) patients were eligible. The treatment regimens were changed according to their risk group including only surgery, surgery plus several courses of combination chemotherapy (vincristine, cyclophosphamide, ifosfamide, etoposide, cisplatin, doxorubicin, dacarbazine) or high-dose chemotherapy with autologous stem cell transplantation. Maintenance therapy with 13 cis-retinoik ascit was given for intermediate and high risk group.
Results: Median age was 7 months and male/female ratio was 1.4. Median LDH, ferritin and NSE levels was 576.5 U/L (N = 0-450), 111 ng/ml (N = 24-336) and 61 ng/ml (N = 0-20), respectively. Three patients had opsomyoclonus and two patients had Kerner-Morrison syndrome. Urinary VMA level was high in 65% of patients. Patients distribution by stage and risk gorup was as follows: 21% stage I, 15% stage II, 20% stage III, 33% stage IV, 11% stage IVS; 39% low risk, 34% intermediate risk, 27% high risk group. At 3 years event-free survival (EFS) rate was 72% ± 10%, 3 years overall survival (OS) rate was 79% ± 7%. Children with stage IV disease had significantly lower OS rates (41% ± 2%). Overall survival rate was also poorer in high risk patients.
Conclusions: The treatment outcome of children with neuroblastoma in infant treated according to the Turkish Pediatric Oncology Group Neuroblastoma 2009 Protocol (TPOG-NBL-2009) is satisfactory. Stage and risk group were found significantly related to survival rates.

P-0240

THE PRELIMINARY TREATMENT RESULTS OF THE PATIENTS WITH HIGH RISK NEUROBLASTOMA WHO WERE TREATED WITH THE TURKISH PEDIATRIC ONCOLOGY GROUP-NEUROBLASTOMA 2009 PROTOCOL (TPOG-NBL-2009)

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Purpose/Objective: To evaluate the clinical characteristics, treatment regimens, and outcome of the patients with high risk neuroblastoma who were treated with the Turkish Pediatric Oncology Group Neuroblastoma 2009 Protocol (TPOG-NBL-2009)
Materials and Methods: 140 patients with high risk neuroblastoma who were treated with Turkish Pediatric Oncology Group protocol were analyzed. In this protocol intensive chemotherapy including 6 courses of alternated
dacarbazine + cyclophosphamide + adriamycin + vincristine and
cyclophosphamide + cisplatin + etoposide have been used. Surgery has been applied to all patients if possible after 6 course induction chemotherapy. If the patient had residual tumor, radiotherapy and two courses of intensive chemotherapy have been given. Afterwards all patients were treated with 6 cycles maintenance treatment. 95 patients were available for survival analysis.
Results: Age range was 1 month-17 years with a median of 2.6 years. Male/female ratio was 1.5. 106 patients had stage IV disease, 32 stage III, and, two patients had stage II and high amplified N-MYC oncogene. Median LDH level was 1029 U/L (N = 0-450), median ferritin level was 229 ng/ml (N = 24-336). 31 patients out of 74 cases who were analyzed for N-MYC amplification.had N-MYC amplification. Two year overall survival rate was 60%, two-year event-free survival rate was 36%. 37 patients out of 95 (39%) were disease-free, 24 patients with disease were under treatment, and 32 cases died with progressive disease, two cases died with treatment related complications.
Conclusions: The preliminary results of our high-risk protocol were encouraging with this intensive chemotherapy regimen. Long-term results will be given in following years.

P-0241

TREATMENT OF RECURRENT HIGH RISK NEUROBLASTOMA IN CHILDREN WHO ACHIEVED COMPLETE REMISSION AFTER FIRST LINE THERAPY.

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Purpose/Objective: Treatment of high-risk neuroblastomas relapse (HR NBL) has an extremely uncertain outcome, often in these situations just palliative chemotherapy is chosen
Materials and Methods: From 2003 to 2011 32 children with newly diagnosed neuroblastoma were treated with the HR-NBL-1/SIOPEN regimen, 11/32 (34.3%) had a relapse after achieving complete remission or very good (CR/VGPR). The median time from diagnosis of relapse was 15.48 months (9; 26). Localization of relapses: skeleton - 11, bone marrow - 4, lymphnodes - 5, liver -1.
Results: In the treatment of relapses we used different 'salvage' regimens. Combination TVD (vincristine, topotecan, doxorubicin) (1-6 cycles) - 10, therapeutic MIBG - 6, 3 times with concomitant chemotherapy (topotecan) -, 2nd megatherapy with autologous stem cell rescue - 1, oral temozolomide - 3, local radiotherapy - 4, and RIST combination (rapamycin, dasatinib, irinotecan, temozolomide) in 2 pts. The group is very heterogeneous and does not allow comparison of individual treatments.

Results: 2/11 reached the second CR, one child lives for 5 years from relapse (relapse localized in one bone), the second pt had another relapse and is alive with disease, 2/11 achieved PR, but this was followed by further recurrence of disease, so 1 pt died, the second one is alive with disease, 7/11 demonstrated different degrees of response to therapy but very soon further progression occurred. The median time from relapse to death was 9.8 months (20.9, 2.5).
Conclusions: The prognosis of relapses of HR NBL is extremely uncertain and the hope of long-term survival are only those with localized relapse.

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P-0242

HYPERCALCEMIA DURING 13-CIS RETINOIC ACID TREATMENT IN HIGH RISK NEUROBLASTOMA PATIENTS

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Purpose/Objective: Treatment with cis-retinoic acid (RA) is considered standard consolidation treatment for high risk neuroblastoma. Hypercalcemia has been reported as side effect of RA treatment. We analysed frequency, symptoms and the course of hypercalcemia after RA treatment.
Materials and Methods: Data of patients registered in the German Neuroblastoma trials, treated on high risk protocols including either megatherapy or maintenance therapy and having received RA consolidation were retrospectively analysed. Hypercalcemia was defined as elevation of the serum calcium level above 2.9 mml/L (= CTCAE $\geq$ grade 2).
Results: Out of 413 patients treated with RA between 2002 and 2010, 48 patients presented with hypercalcemia (11.6%). Hypercalcemia occurred in 47 patients having received megatherapy prior to RA treatment, but only in one patient treated with maintenance therapy. Additional data on symptoms and treatment of hypercalcemia were available in 36 patients (48 RA cycles with hypercalcemia). The maximum serum calcium level was 3.45 $\pm$ 0,48 mmol/L. Hypercalcemia developed at a median interval of 10 days of RA treatment and mostly during the first cycle (29 patients, 81%). Twenty-seven patients (75%) presented with hypercalcemia only in one cycle, six in two and three patients in more than two cycles. In 30 cycles (63%), symptoms of hypercalcemia were reported (bone pain: 27%, stomach pain: 17%, QT-prolongation: one patient). Because of hypercalcemia, 11 RA-cycles were stopped, three were continued with reduced dosing, and treatment was applied in 16 cycles (intravenous hydration 8 cycles, diuretics 7 cycles, bisphosphonate 1 cycle). The RA consolidation was continued with further cycles without reduction in 25 patients (69%), with reduced dosing in 10 patients (28%), and stopped completely in one patient.
Conclusions: In this cohort, hypercalcemia was observed more often than previously reported. Patients showed hypercalcemia mostly at the beginning of RA consolidation and after megatherapy and presented often with symptoms.

P-0243

IMPACT OF DIFFERENT TREATMENT MODALITIES ON METASTATIC NEUROBLASTOMA OUTCOME

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Purpose/Objective: Metastatic neuroblastoma in children > 1-year-old has poor outcome. Different strategies have been proposed to improve the survival. We reviewed our experience in this aspect.
Materials and Methods: This is a retrospective review of a local patient cohort from Jan-1988 to Dec- 2011. Patients (> 1yr) with INSS Stage 4 neuroblastoma were treated with OPEC/OJEC, N4SE/N6 & N7 protocols at different time period. Local RT, autologous hematopoietic transplant (auto-HSCT), anti-ganglioside antibody (anti-GD2, 3F8) and cis-retinoic acid (RA) were adopted according to the protocols.
Results: From Jan-1988 to Dec-2011, there were 71 stage4 patients > 1yr recruited. Single variant analysis showed that N7 protocol, use of anti-GD2, auto-HSCT, and local RT were all associated with better event free survival (EFS) but not use of RA. 5-yrs EFS for N7 (n = 31) vs N6/N4SE (n = 30) & OPEC/OJEC (n = 9) were 43.5% vs 11% vs 0% respectively, p = 0.0019. Some of the relapsed patients on non-N7 protocol used anti-GD2 during relapse, 5-yrs EFS for use of anti-GD2 (n = 37) was 34.6% vs 9.8% without anti-GD2 (n = 34), p = 0.035. Auto-HSCT was adopted in both N6/N4SE and N7 but not OPEC/OJEC protocols. Patients underwent auto-HSCT (n = 45) performed better than those without (n = 26), 5-yrs EFS was 30.9% vs 4.2%, p
Conclusions: Our long term follow-up data showed that the EFS of older children with metastatic neuroblastoma improved with time. Since there were multiple confounding variables involved, it might be difficult to ascertain which strategy contributed to the improvement. Our data suggested that use of anti-GD2 containing regimen with auto-HSCT may help to improve the long term survival.

P-0244

INADEQUATE RESPONSE TO INDUCTION CHEMOTHERAPY IN CHILDREN WITH HIGH-RISK NEUROBLASTOMA: AN INSTITUTIONAL ANALYSIS

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Purpose/Objective: One current therapeutic strategy for high-risk neuroblastoma (HR-NB) is induction chemotherapy followed by myeloablative therapy (MAT) only for those patients who have an adequate metastatic response (complete response, very good partial response, or partial response [PR] with no detectable disease on morphology in the bone marrow [BM]). Patients who have not achieved this level of response receive second line treatment and if a further response is achieved then proceed to MAT. The role of additional therapy in non-responders remains unclear.
Materials and Methods: Medical records of all HR-NB patients treated at the Royal Marsden Hospital (RM) between January 2000 and September 2010 with an inadequate metastatic response to proceed to MAT were retrospectively reviewed with the aim of describing their outcome and characteristics.
Results: Thirty four (33%) of 104 HR-NB patients had an inadequate response to induction and 26 were evaluable (PR with BM involvement [12], No Response (NR) [9], Mixed Response (MR) [3] or Progressive Disease (PD) [2]). Patients received 1 to 6 (median 2) lines of additional treatment (topotecan, vincristine & doxorubicin; temozolomide & irinotecan; cyclophosphamide, vincristine & doxorubicin and MIBG-therapy). 7/12 (58%) patients with PR and 5/14 (36%) with NR, MR or PD showed an improved response with second line therapy and received MAT. The median progression free survival (PFS) for patients whose response improved following second line therapy was 75.8 months compared to 56.3 months for those that did not.
Conclusions: Overall 46% of patients showed an improved response following second line therapy. However, the benefit of additional chemotherapy compared to proceeding directly to MAT to improve long term survival still remains unclear and needs to be addressed in a prospective randomised trial.

P-0245

TANDEM HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL RESCUE IN HIGH RISK NEUROBLASTOMA PATIENTS: A SINGLE CENTER EXPERIENCE

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Purpose/Objective: It has been well-established that high dose myeloablative chemotherapy with autologous stem cell rescue has improved the long term prognosis of advanced neuroblastoma. The intent of this research was to investigate the clinical effectiveness of tandem high dose chemotherapy (HDCT) and autologous stem cell rescue therapy.
Materials and Methods: During the period between October 1997 and December 2010, we analyzed 59 children with high-risk neuroblastoma who received single or tandem HDCT and autologous stem cell transplantation. Medical records of all patients were reviewed retrospectively.
Results: The median age of 59 patients was 2.8 years old (range, 0.3-10.8 yr). The conditioning regimen of single HDCT consisted of MEC (melphalan, etoposide, carboplatin) or CTM (carboplatin, topotecan, melphalan), and tandem HDCT consisted of TTC (topotecan, thiotepa, carboplatin) followed by MEC. Modified MEC, which uses reduced doses of carboplatin, was applied after June of 2007 for notable acute renal failure demonstrated in patients. Tandem HDCT was designated to patients after March of 2002, resulting in 24 patients designated to single HDCT and 35 patients to tandem HDCT. The overall 5-year overall survival rates and event-free survival rates after first HDCT were 76.2% and 34.4% in the single group, and 88.6% and 63.2% in the tandem group (P = 0.295, P = 0.49). In patients with tandem HDCT, which used modified MEC, the overall 5-year overall survival rates and event-free survival rates were 92.9% and 66.6%, which reflected survival benefits from lower tretament-related mortality (TRM).
Conclusions: Tandem HDCT could improve survival in high-risk neuroblastoma patients. Conditioning regimen related to renal toxicity may play a factor in increasing TRM, and further investigation of an optimal conditioning regimen is warranted.

P-0246

HIGH DOSE 131I-MIBG TREATMENT IN STAGE 4 NEUROBLASTOMA PATIENTS IN A TERTIARY CENTRE IN HONG KONG

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Purpose/Objective: To review the outcome of high dose radioactive ^{131}I-MIBG treatment in stage 4 neuroblastoma
Materials and Methods: We performed a retrospective chart review looking for outcomes including overall survival (OS) and progression free survival (PFS), post-treatment MIBG

scan results and treatment related hypothyroidism and liver toxicities for all ^{131}I-MIBG treatments done in a tertiary hospital in Hong Kong

Results: From Aug-2003 to Jan-2013, 22 patients with stage 4 neuroblastoma with MIBG-avid lesions at diagnosis received ^{131}I-MIBG therapy. The median age was 2.9 years (range 0.5 to 15.4 years). Twenty-one ^{131}I-MIBG-therapies were administered as part of conditioning regimen for haematopoietic stem cell transplantation and two for palliative treatment. Median dose of ^{131}I-MIBG administered for curative treatment was 12mCi/kg (Range 5.8 to 12.9mCi/kg). Lugol's solution was given for thyroid protection.

Post-treatment MIBG scan were performed in 16 patients at a median interval of 3.9 months (range 1.8 to 4.8 months) from treatment. It was negative for uptake in 7 patients, positive but decrease uptake in 2 patients, static in 5 patients and positive with increased MIBG-avid lesions in 2 patients. 2 years PFS between patients with positive and negative post-treatment MIBG scan uptake were not significantly different (38.9 $\pm$ 17.3% vs 50 $\pm$ 20.4%; p = 0.46).

At a median follow up of 1.2 years (range 0 to 9 years), 12 out of 21 patients receiving therapeutic ^{131}I-MIBG treatment relapsed and 8 of them died. The estimated 2-years OS and PFS was 66.1 $\pm$ 12.5% and 39.7 $\pm$ 11.2%, respectively.

Among 15 patients who had evaluable thyroid function result, 9 (60%) developed primary hypothyroidism with elevation of TSH at 0.3 to 2.9 years post-treatment and 4 required thyroxine replacement. No patient experienced liver derangement.

Conclusions: ^{131}I-MIBG therapy is a safe treatment modality for high risk neuroblastoma though hypothyroidism is common. Early post-treatment MIBG scan does not correlate with survival outcome.

P-0247

LYMPHOPENIA AFTER 131IODINE-METAIODOBENZYLGUANIDINE THERAPY: POTENTIAL USE AS AN IMMUNOTHERAPY ADJUNCT

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Purpose/Objective: The use of adoptive cellular immunotherapy is an attractive option for the treatment of neuroblastoma, as recent data has shown that administration of T cells modified with a chimeric antigen receptor targeting GD2 was safe and effective. Although encouraging, antitumor effects could be improved with sustained persistence of transferred T cells. Host lymphodepletion, typically accomplished using cytotoxic chemotherapy with or without whole body irradiation, has been shown to enhance *in vivo* T cell expansion and persistence of engineered cells. ^{131}Iodine-metaiodobenzylguanidine (^{131}I-MIBG) as a lymphodepleting agent in neuroblastoma patients would be an optimal adjunct to cellular therapy, as single agent ^{131}I-MIBG has been shown to be active in heavily pre-treated neuroblastoma.

Materials and Methods: To evaluate the potential of ^{131}I-MIBG as a lymphodepleting regimen, we retrospectively evaluated the changes in lymphocyte counts before and after 29 individual single agent ^{131}I-MIBG treatments administered to 22 patients at Cincinnati Children's Hospital Medical Center. Absolute lymphocyte counts were obtained at least once during the week before treatment, and on average twice weekly for 8 weeks after completion of the ^{131}I-MIBG infusion. Values were averaged relative to the treatment date, and analyzed for significant lymphopenia.

Results: Patient's ages ranged from 20 months to 14 years (median age of 5 years) and included 12 females and 10 males. The ^{131}I-MIBG dose received was 18 mCi/kg in 28 treatments and 14 mCi/kg in 1 due to maximum cumulative dose. There were no unanticipated toxicities. The average pre-^{131}I-MIBG lymphocyte count was 1.2 K/mcL, and 0.28, 0.36, 0.5, 0.59, 0.83, 0.78, 0.65, and 0.89 K/mcL during weeks 1 to 8 after ^{131}I-MIBG therapy, respectively. All post-treatment lymphocyte counts differed significantly relative to pre-treatment values ($p < 0.01$).

Conclusions: These results support the investigation of ^{131}I-MIBG therapy as an alternative lymphodepleting regimen prior to novel cellular therapies for patients with neuroblastoma.

P-0248

BUILDING A THERAPEUTIC 131IODINE-METAIODOBENZYLGUANIDINE PROGRAM: A MULTIDISCIPLINARY APPROACH

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Purpose/Objective: Meta-iodobenzylguanidine (MIBG), a norepinephrine analog, is concentrated selectively in sympathetic nervous tissue. MIBG labeled with iodine-131 (^{131}I) has demonstrated activity against neuroblastoma, both in relapsed and newly diagnosed patients. As a single-agent in a Phase 1 dose-escalation study, ^{131}I-MIBG showed a response rate of 37% in children with relapsed neuroblastoma and dose-limiting hematologic toxicity was circumvented with autologous stem cell rescue. A Phase II study showed a 36% response rate and 34% stable disease after MIBG therapy. Additional work has focused on using ^{131}I-MIBG for patients with newly diagnosed disease, and a new Children's Oncology Group (COG) pilot utilizes ^{131}I-MIBG for all patients with MIBG-avid disease in Induction.

Materials and Methods: We have built a successful therapeutic MIBG program through the collaborative efforts of a multidisciplinary team including Nursing, Radiation Safety, Nuclear Medicine technicians and physicians, Medical Social Workers, Nurse Educators, Child Life personnel, and Pediatric Oncologists.

Results: At Cincinnati Children's Hospital, and have treated approximately 100 patients over the past 5 years, with close to 30 patients treated in the past year with ^{131}I-MIBG. Our multidisciplinary team meets weekly to review upcoming patients and potential protocols. As a part of standard evaluation of potential patients, our team systematically analyzes medical inclusion and exclusion criteria as well as social barriers to successful treatment such as travel obstacles and feasibility of family member support and care delivery. We also discuss Standard Operating Procedures as a group and have created procedures for everything from continuous infusion versed anxiolysis to waste pipe decontamination. Additionally, our team has analyzed dose exposure to Nuclear Medicine technicians, and has implemented and studied system changes that have resulted in significantly less dose received by staff.

Conclusions: Taken together, our physical structure and multidisciplinary approach to ^{131}I-MIBG delivery, protocol development, and patient and staff safety has resulted in an effective and successful program.

P-0249

DUMBBELL NEUROBLASTOMA AND EARLY-/ LATE ADVERSE EVENTS

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Purpose/Objective: Dumbbell neuroblastoma (NBL) is a specific type of NBL originating from the neural crest, with the tumor growing through the intervertebral foramina into the spinal canal. To evaluate the prevalence of early and late adverse events in dumbbell NBL patients in 2 separate studies.

Materials and Methods: 1: Retrospective single centre cohort study (AMC) of all eligible childhood dumbbell NBL patients who survived $\geq$ 5 years after diagnosis.

2: Prospective multi-centre, multi-disciplinary follow-up outpatient dumbbell NBL clinic, (AMC/ SKZ) based on the findings our cohort study, concentrating on early and late effects in dumbbell NBL patients.

Results: 1: Cohort study: From 1980 to 2007, 19 patients (75% female) received primary cancer treatment for dumbbell NBL in the AMC of which 100% survived $\geq$ 5 years after diagnosis. Median age at diagnosis: 1, 2 years (0, 5- 10, 8 years). Median Follow-up time 15, 5 years (7, 2- 29.5 years).

At presentation the neurological symptoms ranged from asymptomatic (n = 8, 42%), moderate (n = 9, 47%) to severe (n = 2, 11%). All received a combination of treatment modalities (neuro-(surgery), radiotherapy, ^{131}I-MIBG therapy and/or chemotherapy. Late sequelae found are neurological (moderate n = 8, 42%) and orthopaedic (n = 14, 74%). Restrictions in everyday activities were also analysed.

2: We have thus far included 9 patients; median age 1, 1 years at diagnosis (0- 2, 9 years), 100% survival. Median follow-up time 3, 0 years (0, 4- 6, 2 years). Neurological symptoms at diagnosis ranged from asymptomatic (n = 3, 33%) to mild (n = 6, 66%). At our follow-up clinic, we found orthopaedic late effects (n = 5, 56% and n = 4, 44% no symptoms) and quality of life sequelae (n = 5, 55%). We aim to report on 20 patients.

Conclusions: Early and late effect sequelae can be found in dumbbell NBL patients. Identifying these sequelae earlier on, can possibly prevent or diminish late sequelae.

P-0250

ANALYSIS OF NEUROBLASTOMA WITH BRAIN METASTASIS

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Purpose/Objective: To summarize the risk factors and clinical profiles of neuroblastoma with brain metastasis

Materials and Methods: A retrospective analysis of clinical materials was conducted towards neuroblastoma with stage

III and IV in single center between 2005 and 2012. Descriptive and suvival analysis was conducted for data.

Results: Eight cases of neuroblastoma with brain metastasis were documented out of 72 cases. Occurance rate is estimated to be 11%. Age at initial diagnosis was between 2 and 4 years of age. The median age is 3 years. All of them were with stage IV. The ratio of male:female is 7:1. Seven males had bone marrow involvement and one girl had bone

involvement. N-myc was positive for two patiens out of four patients. Lactate dehydrogenase(LDH) was between 207U/L and 3906U/L(median 605U/L).Brain metastasis for the two patients with N-myc(+) occured after 1 and 2 month since initiation of maintenance therapy. For the other six patients brain metastasis occurred 2 weeks and 9 month after discontinuation of maintenace therapy. Overall survival of neuroblastoma with brain metastasis for 2 years is 25%(2/8). It is worthy of note that the two survival patients undergo cytokine induced killer infusion.
Conclusions: We conclude from the limited data that age, gender, bone marrow and bone involvement, LDH are associated with brain metastasis for neuroblastoma.

P-0251

SURGERY ALONE OR OBSERVATION AS PRIMARY THERAPY FOR PATIENTS WITH LOW-RISK NEUROBLASTOMA: EXPERIENCE OF A CASE SERIES IN CHINA

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Purpose/Objective: To evaluate the safety and effect of surgery alone or observation for patients with low-risk neuroblastoma.
Materials and Methods: Total 22 patients with low-risk neuroblastoma were treated in the Children's Hospital of Fudan University between Jan 2009 and Dec 2011. The medical records of these patients were reviewed.
Results: The primary lesion was located in adrenal gland in ten patients, retroperitoneum in six, posterior mediastinum in 5 and neck in 1. The tumor size was median 5.18 cm (range, 1.98*11.41cm). The stage of the patients were as follows: stage 1 in 14, stage 2 in 5, and stage 4s in 3. All patients were in the low-risk group according to the COG risk stratification criteria. No patients showed MYCN amplification. 21 patients were treated by surgical resection alone and 1 stage 4s patient receive observation only. The median follow-up period was 27.95 months (range, 15*45 months). Tumor relapse was seen in only 2 patients. One patient with tumor recurrence in primary location underwent reoperation and received chemotherapy and now had no evidence of disease till follow up, the other one had bone metastases because of the absence of follow-up and received chemotherapy currently.
Conclusions: As long as the patis were able to closely follow-up, surgery alone or observation is a safe and effective treatment strategies for low-risk neuroblastoma.

P-0252

SURGICAL OUTCOMES OF EXTRA-ABDOMINAL NEUROBLASTOMA: A SINGLE CENTRE EXPERIENCE

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Purpose/Objective: The prognosis for children with extra-abdominal neuroblastoma is more favorable than for those with abdominal disease. However, the morbidity associated with the resection of these sites is high, and this may influence the quality of life of survivors. The aims of this study were to report our experience in the management of extra-abdominal neuroblastoma and to evaluate the incidence and severity of complications.
Materials and Methods: Between November 2004 and January 2013, 40 consecutive patients (25 males and 15 females) with extra-abdominal neuroblastoma (mediastinum: 24, cervical: 10 and pelvis: 6) were included in this analysis.
Results: The median age at diagnosis was 35 months (range 4 - 120). Thirty four (85%) tumors were localized (stage 1 in 6 patients, stage 2 in 3 and stage 3 in 25) and 6 (17.5%) tumors were disseminated. Fourteen patients had radiological evidence of intraspinal extension (thoracic 12, pelvic 2) of disease; five of these patients required decompressive surgery. The number of low, intermediate and high-risk patients were nine (22.5%), 27 (67.5%), and four (10%), respectively. Seven patients underwent upfront tumor resection, the remaining received chemotherapy prior to surgery. Gross total resection was achieved in 27 patients, more than 95% in 10 and biopsy alone in 3 patients. There was one mortality and five postoperative complications (leg weakness (1) transient impairment of deglutition (3) and intestinal obstruction (1)) excluding Horner's syndrome. Seven patients had disease relapse and one patient developed secondary leukemia. After a median follow-up of 32 months, 31 patients are alive and five are alive with disease. All except one patient with incomplete excision survived. The probability of 5-yr OS and EFS rate was 85% and 71%, respectively.
Conclusions: Our data confirms the excellent survival for extra-abdominal neuroblastoma. Complete excision is feasible in majority with acceptable morbidity and incomplete excision does not result in poor outcome.

P-0253

THE ROLE OF SURGERY IN THE TREATMENT OF STAGE 4 NEUROBLASTOMA PATIENTS 18 MONTHS OR OLDER AT DIAGNOSIS

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Purpose/Objective: Although intensive multimodal treatment has improved the prognosis of metastatic neuroblastoma patients, the impact of primary tumor resection on outcome is a matter of medical debate.
Materials and Methods: Stage 4 neuroblastoma patients $\geq$18 months at diagnosis of the German prospective clinical trial NB97 were included. Operation notes and imaging reports were reviewed by two independent experienced physicians. Finally, the extent of tumor resections was correlated with the presence of Image Defined Risk factors (IDRF), local control rate, and outcome.
Results: A total of 278 patients were included in this study. Image defined risk factors present at diagnosis were found to be predictive for the extent of tumor resection at first ($p < 0.001$) and best ($p < 0.001$) operation. No patient died from surgery. Prior to chemotherapy, complete resection, incomplete resection, and biopsy/no surgery was performed in 6.1, 5.0, and 88.5% of patients, respectively. The extent of first operation had no impact on event-free survival (EFS, $p = 0.207$), local progression-free survival (LPFS, $p = 0.195$), and overall survival (OS, $p = 0.351$). After induction chemotherapy, 54.7% of patients underwent complete resection of the primary tumor, 30.6% incomplete resection, and 13.3% had only biopsy or no surgery of the primary tumor. The extent of best operation also had no impact on EFS ($p = 0.877$), LPFS ($p = 0.299$), and OS ($p = 0.778$). Moreover, multivariate analyses showed that surgery did not affect event-free, local progression-free, and overall survival.
Conclusions: In high-intensive-treated stage 4 neuroblastoma patients $\geq$18 months at diagnosis, surgery of the primary tumor site has no impact on local control rate and outcome. The resection of the primary tumor should be attempted but extensive surgery for complete resection is not necessary.

P-0254

DOES A RESIDUAL TUMOR MASS IN CASES OF INTERMEDIATE-RISK NEUROBLASTOMA INFLUENCE THE PROGNOSIS?

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Purpose/Objective: The prognosis of patients with intermediate-risk neuroblastoma is good, with more than an 80% survival. However, it is unclear whether a residual tumor mass following surgical resection influences the prognosis.
Materials and Methods: We retrospectively reviewed 20 patients with intermediate-risk tumors treated at our institution during the 20-year period between 1993 and 2012. We examined their clinical course and prognosis at the end of treatment.
Results: The ages of the patients ranged from zero days to seven years old, and the mean observation period was 13.5 years. The 5-year overall survival rate was 94.4%. Thirteen patients had stage 3 disease, seven cases had stage 4 disease. Nine cases showed intra-spinal extension. Seventeen of the 20 cases received chemotherapy (range: 6 to 20 courses, average: 10 courses). Twelve patients had a residual tumor mass at the completion of therapy, and eight showed intra-spinal extension. Five of these 12 cases showed MIBG uptake at the end of treatment, but the uptake disappeared during the follow-up period. Except for one patient who died as a complication of treatment, the rest all are alive, and nine were alive with a residual mass. We performed a biopsy or subtotal resection for the residual mass in four of the nine cases, but the residual tissue had differentiated into ganglioneuroma or changed to necrotic tissue. For the three cases with neurological symptoms at the end of treatment, slight neurological symptoms still remained during the follow-up. Five cases with an intra-spinal mass eventually presented with new symptoms, such as scoliosis or hydronephrosis.
Conclusions: The presence of a residual mass at the end of treatment did not influence the patients' prognosis. Therefore, an invasive radical surgical resection should be avoided for intermediate-risk cases. The cases with a residual intra-spinal mass require a long-term follow-up to assess the neurological prognosis.

P-0255

WEB-BASED CASE DISCUSSION TO IMPROVE OUTCOMES FOR CHILDREN WITH NEUROBLASTOMA IN RESOURCE-LIMITED COUNTRIES

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Purpose/Objective: Despite steady improvement in outcomes of children with neuroblastoma (NB) in high-income nations, significant challenges remain for children in resource-limited countries (RLC). The aims of our project were: (1) Establish a weekly web-based neuroblastoma tumor board (WTB) for clinicians in RLC to discuss challenging patients with neuroblastoma in real-time; (2) Guide decision-making based on available resources and appropriate risk stratification; (3) Identify health system issues that could improve care for all pediatric cancer patients.
Materials and Methods: A weekly, WTB was conducted via www.cure4kids.org allowing participants to present patients for an interactive discussion using powerpoint format. Patient demographics, diagnostics, pathology, initial treatment considerations, alteration in management based on discussions, resource limitations, and follow-up were recorded.
Results: Since 2010, participation has increased from 7 members in 5 countries to 206 multi-disciplinary members in 47 countries, with a median of 25 participants per meeting. To date, 75 cases have been presented, of which 56 are analyzed here. Of 56 patients, 43 presented at Stage 3 or 4. In 25 cases *MYCN* data was not available for INRG risk-stratification. Four of 31 patients with available data had *MYCN* amplification. Upfront therapies varied significantly based on local approaches, and therapy availability. Additional challenges identified were: diagnostic evaluation, particularly, lack of MIBG scan, infrastructure limitations for disease monitoring, and supportive care. Online educational sessions were held for pathology, surgical management, marrow transplant, and infectious complications. A dedicated neuroblastoma registry form has been established via www.POND4kids.org to facilitate outcome evaluation.
Conclusions: To date, we demonstrate that a multidisciplinary WTB has resulted in refining treatment plans for numerous patients with neuroblastoma. Continued challenges remain for appropriate risk-stratification and therapy, given resource limitation. Adapted treatment guidelines based on resource availability will promote consistency and gradual improvements in care. Data collection using www.POND4Kids.org will facilitate outcome analysis based on treatment delivered.

P-0256

10 YEARS EXPERIENCE IN NEUROBLASTOMA TRANSPLANT IN A SINGLE INSTITUTION

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Purpose/Objective: To review the experience in patients diagnosed with stage IV neuroblastoma who received autologous HSCT over a period of 10 years.
Materials and Methods: Performed a retrospective study of medical records of patients diagnosed with stage IV neuroblastoma who were referred to our unit, where was performed autologous HSCT. In the period established between October 2002 to october 2012.
Results: 187 HSCT were performed in the unit in the period between October 2002 and October 2012. Of which 54% were allogeneic HSCT and 46% autologous. Within autologous HSCT 36% were neuroblastoma.

The 6% of patients had no effective mobilization and therefore required a second mobilization and bone marrow harvesting. There were 52 apheresis procedures (1.6 procedures / patient), in which there were no major complications. The most frequent complications observed were nausea and vomiting, cold sweats in isolated cases secondary to hypocalcemia, which yielded after completion of the procedure and the correction of calcium. At the time of HSCT 84.4% of patients were in complete remission (CR) and 15.6% in partial remission (PR). During follow-up (1-13 m) 38% of patients relapsed. Patients with CR before transplantation showed 37% relapse while patients were in PR showed 40%.
Conclusions: The mobilization is effective in patients with stage IV neuroblastoma in childhood.

During the apheresis procedure patients showed no severe complications.

The autologous HSCT is safe and effective for stage IV neuroblastoma.

No significant difference between patients according to status disease at the time of HSCT in this study, given the short follow-up presented in this study does not demonstrate statistically significant differences.

P-0257

NEUROBLASTOMA TREATED WITH TANDEM PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN CHILDREN. ONE CENTER EXPERIENCE

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Purpose/Objective: The results of treatment in children remain unsatisfactory. The survival rates after high-risk neuroblastoma treatment is 25- 40%.
To improve such unsatisfactory result we considered tandem high-dose chemotherapy followed by hematopoietic stem-cell transplantation.
Materials and Methods: Three patients with high-risk neuroblastoma underwent two courses of high-dose chemotherapy followed by autologous PBSC transplantation as consolidation regimes. All patients were females aged 2, 5, 6 years. The first patient received tandem transplantation for high-risk neuroblastoma (stage III, n-myc amplification-positive), the others * for early local recurrence of neuroblastoma following 4 courses of second-line therapy. The first high-dose regimen was given with busulfan and melphalan. The second one with topotecan and cyclophosphan was received at 2.0-3.0 month intervals.
Results: All patients successfully copleted first high-dose chemotherapy. The time to an ANC more then 500/μL after PBSC was 11-15 days, a platelet recovery after PBSC was 16-28 days. Neurotoxicity as repeated short-term tonic-clonic seizures was reported in one patient after the second high-dose chemotherapy. The chemotherapy was discontinued achived 2/3 dose of cyclophosphamide and complete dose of topotecan. The patient had neurosis like appearances during previous treatment. Two other patients underwent chemotherapy without major complications. All patients experienced grade 4 neutropenia and thrombocytopenia, oral mucositis with varying degrees of severity. The time to an ANC more then 500/μL after PBSC was 9-14; a platelet recovery was 12*22 days. Currently, all 3 patients with no signs of recurrence continue treatment. The follow-up period is 2-5 months.
Conclusions: Tandem high-dose chemotherapy followed by peripheral blood stem cell transplantation is feasible method in pediatric high-risk neuroblastoma treatment. The toxicity of chemotherapy regimens is dose-proportional. Further studies are required to determine the effectiveness of the method.

P-0258

CLINICAL FEATURE OF NEONATAL NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma(NBL) is one of the most common malignant tumors of neonates, but there were few studies and little things were known about neonatal NBL. The purpose of this study is to investigate the clinical features, treatment and prognosis of neonatal NBL by reviewing our experiences.
Materials and Methods: 19 cases of neonatal NBL were detected antenatally or presented within 28days after birth from 527 patients diagnosed with NBL from January 1998 to February 2013. Retrospective medical record reviews were performed on these patients.
Results: Eight patients (42.1%) were diagnosed prenatally. All patients were full-terms and weighed over 2500g except one patient who were born in the 35 + 1 weeks. In patients who diagnosed postnatally, 2 patients first presented with palpable neck mass, 1 patient with palpable abdominal mass and 1 patient with palpable multiple mass at scalp, neck and abdomen. 1 patient had vomiting for first presenting symptoms. Other 6 patients were diagnosed with NBL incidentally during examination for other diseases. 7 patients were stage 1, 2 were stage 2, 3 were stage 3, 4 were stage 4 and 3 patients were stage 4s. 8 patients were in low risk group, according to risk group by Children's Oncology Group, 6 patients were intermediate risk group and 3 patients were high risk group. 4 patients were conducted preoperative chemotherapy and 7 were conducted postoperative chemotherapy, 17 patients were performed mass excision. All patients were survived except one patient whose parents refused the therapy and other patient who were loss to follow-up. Sixteen of 19 (84.2%) are alive without evidence of recurrences.
Conclusions: The neonatal NBL showed a favorable outcome. Patients, who were in high stage or high risk group, also showed good results with proper treatments, unlike non-neonatal NBL patients.

P-0259

NEUROBLASTOMA IN CHILDREN UNDER 1 YEAR: CLINICAL CHARACTERISTICS AND TREATMENT RESULTS. DATA FROM SINGLE CENTER

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Purpose/Objective: To investigate the long-term survival in neuroblastoma patients aged less than 1 year a retrospective study has been conducted in Pediatric Oncology and Hematology Center, Regional Children's Hospital, Ekaterinburg, Russia.
Materials and Methods: Among 179 children with primary neuroblastoma admitted to our clinic since January 1991 till November 2012 were 65(36%) patients under 12 months (median of age 4 months). All the patients were treated according to OPEC/OJEC, NB90, NB97 and NB2004 protocols: 1(1,5%), 6(9,2%), 13(20%) and 45(69,3%) correspondingly. Gene rearrangements were investigated by PCR and MLPA in 54 out of 65 cases.
Results: Patients' distribution by stage was as follow: stage I*22(33,8%); stage II*6(9,2%); stage III*15(23,1%); stage IV*5(7,7%); stage IVS*17(26,2%). MYCN amplification has been detected in 4(7,4%) patients. Complete remission and very good partial remission have been achieved in 62(95,4%) patients. Unfavorable events (relapses, progressive disease and therapy related deaths) were observed in 10(15,4%) cases. At present time 57(87,7%) patients are alive; 55(84,6%) are alive without progression; 1(1,5%) patient was lost to follow

up. 15-years event free survival (EFS) is 81% ± 5% and overall survival (OS) is 85% ± 4% in comparison with older group: 40% ± 4% and 58% ± 10% ($p < 0,001$) respectively. Out of 17 children with stage IVS*4(23,5%) died from therapy related complications and 1(5,8%) from progressive disease; 12(70,5%) patients are alive without progression; EFS in this group is 68 ± 11%. MYCN-amplification and expression of PHOX2B gene in bone marrow had a significant negative influence on outcome: EFS in MYCN(+) and PHOX2B(+) were: 0% and 52% ± 15% vs. 73% ± 6% and 95% ± 4% correspondingly ($p < 0,05$).
Conclusions: The results of the present study confirms that EFS and OS are significanly better in group of children under 12 months. Stage IV, MYCN-amplification and expression of PHOX2B had the significant negative influence on outcome.

P-0260

NEUROBLASTOMA IN INFANTS < 12 MONTHS: SINGLE CENTER EXPERIENCE IN RUSSIA

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Purpose/Objective: The aim of the study was to assess clinical presentation, stage distribution and cytogenetic abnormalities in the cohort of patients < 1 year of age with neuroblastoma treated in federal cancer center in Russian Federation.
Materials and Methods: 26 patients < 1 year of age with neuroblastoma treated in Federal Research Center of Pediatric Hematology, Oncology and Immunology during the period 01.2012 - 01.2013 were included in the analysis. We examined their age at diagnosis, presence of image-defined risk-factors, stage according to the International Neuroblastoma Risk Group Staging System (INRGSS) and the International Neuroblastoma Staging System (INSS) where appropriate. Cytogenetic analysis done by FISH included *MYCN*, 1p and 11q status.
Results: M:F ratio was 1:1. Median age at diagnosis was 6 months (range 0.5-11.9). 7 cases were diagnosed at the age 4-6 and 7-9 months, 6 cases at the age 0-3, 10-12 months. Topography of primary tumor included adrenal gland (14 cases, 53.8%), retroperitoneum (6 cases, 23.0%), posterior mediastinum (5 cases, 19.2%), pelvis (1 case, 4.0%). Stage distribution according to INRGSS: L1 - 9 (34.6%), L2 - 5 (19.2%), M - 5 (19.2%), MS - 7 (27.0%). Stage distribution according to INSS (25 patients): stage 1 - 8 (32.0%), stage 2 - 3 (12.0%), stage 3 - 2 (8.0%), stage 4 - 5 (20.0%), stage 4S - 7 (28.0%). FISH analysis revealed amplification of *MYCN* gene in 2/24 cases (8.3%), 1 p deletion in 1/20 (5.0%), 11q deletion in 1/19 (5.2%). Unfavorable genetic changes were not observed in patients < 4 months. 21 (80.7%) patients were stratified to observation group, 3 (11.6%) - to intermediate risk group, 2 (7.7%) - to high risk group. 14 (67.0%) out of 21 patients in observation group did not receive chemotherapy.
Conclusions: Our data confirmed the favorable profile of neuroblastoma in infants < 12 months including stage distribution and low frequency of unfavorable cytogenetic abnormalities.

P-0261

PERINATAL NEUROBLASTOMA - A REPORT FROM KK WOMEN'S AND CHILDREN'S HOSPITAL, SINGAPORE

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Purpose/Objective: This is a retrospective review to report our experience with perinatal neuroblastoma in the largest paediatric hospital in Singapore.
Materials and Methods: We obtained retrospective data from the Singapore Childhood Cancer Registry (SCCR) as well as hospital chart records. We included all patients with neuroblastoma or adrenal masses diagnosed antenatally or within the first 6 months of life, between 1998 and 2012.
Results: In the 15-year period (1998 * 2012), there were nineteen patients with neuroblastoma diagnosed before 6 months of age. Six of them had abdominal masses first detected antenatally. Eight presented in the first 3 months; while the remaining five presented between 3 to 6 months of age. The site of the primary tumour was mostly the adrenal (9 patients, 47%) or abdominal retroperitoneal (7 patients, 37%). Other sites involved included pelvic, thoracic and neck (1 each). The disease was of low-stage (INSS Stage 1 or 2) in 11 (58%) patients, Stage 3 in 3 (16%) patients, Stage 4S in 3 (16%) patients and Stage 4 in 2 (10%) patients. For the 11 patients with localized non-infiltrative disease, 6 were treated with surgical resection while 5 were managed expectantly. Chemotherapy was given to 4 patients with Stage 3 or metastatic disease. We had one mortality * an infant with Stage 4S neuroblastoma who was given chemotherapy for worsening respiratory distress, and subsequently died from sepsis. The median follow-up duration was 2.6 years (range 0.1 * 13). Two patients returned to their home country and were lost to follow up.
Conclusions: This series shows excellent outcome of our perinatal neuroblastoma. Expectant management has been a feasible alternatve for some patients, but may be challenging for regionally-referred patients for whom close observations may not be possible.

P-0262

CLINICAL ANALYSIS OF MULTIDISCIPLINARY TREATMENT FOR 91 CHILDREN WITH NEUROBLASTOMA

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Purpose/Objective: To summarize clinical features of neuroblastoma (NB) in children, and analyze the relationship between International Neuroblastoma Staging System(INSS), tumor biological factors and the efficacy of recent treatment.
Materials and Methods: According to NB protocol in our hospital (BCH-NB-2007 protocol), the patients were divided into three groups of low-risk (LR), medium risk (MR) and high-risk (HR). All children followed up to May 31, 2012.
Results: Total 91 NB with children, 59 males,32 females, median age 37 (4.5∼192 months), 69 of INSS- IV and 2 of IVs,7 of LR, 17 of MR and 67 of HR cases, 35 of primary postmediastinal tumor, 56 of retroperitoneal and pelvic tumor. Bone marrow metastasis in 53 cases (58.2%),56 of bone metastases (61.5%),21 of distant lymph node metastasis (23.0%), 13 of liver metastases (14.3%). Of 72 patients with fully known biologic features, 45 cases of NB or NB chemotherapy change, 26 cases of ganglioneuroblastoma(GNB), only one for ganglioneuroma(GN). 58 cases of NB had the N-myc gene copies by FISH, the average of N-myc gene copies of 58 cases was 5.96 ± 7.81, 4 had N-myc amplification. Total 70 cases for treatment, among 7 cases of LR, 2 of INSS-4S, followed up median 52months, progression-free, 4 were in complete remission(CR). 11 of MR followed up median 31 months, 5 were the CR. 52 of HR,follow up for median 33 months, 22 occurred event, 5 were relapsed after stopped treatment for median 20 months, 15 were tumor progression. The expected 3-year overall survival rate was 64.3%, HR was 55.8%.
Conclusions: NB was progressive disease. The most common metastasis was the bone and bone marrow. Children with metastasis (HR-NB) had poor prognosis. The most important role was multidisciplinary treatment in order to improve children with HR-NB survival rates and life qualities. And we should follow up NB children regularly after stopping treatment for 3-5years, in order to detect any suspicious residual disease.

P-0263

COULD HIGH-RISK NEUROBLASTOMA BECOME CHRONIC DISEASE?: A RETROSPECTIVE ANALYSIS IN A SINGLE INSTITUTION FOR 27 YEARS

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Purpose/Objective: The disease-free survival rates (DFSR) of high-risk neuroblastoma (HRNB) are approximately 40% in Japan. Recently the overall survival rates (OSR) have become higher. In this study, we have evaluated the efficacy of multimodal treatment for HRNB in a single institution.
Materials and Methods: From 1985 to 2012, in Nihon University Itabashi Hospital, we have treated 70 newly diagnosed HRNB patients. We separated 27 years into 4 periods according to treatments. Induction chemotherapy (IC) was consisted of cisplatin, pirarubicin, vincristine or etoposide and cyclophosphamide during all periods. 1st period: 1985-1992; 31 cases, myeloablative high-dose chemotherapy (MHC) was consisted of VAMP/VMP and TBI. Surgical therapy (ST) was sandwiched between IC. 2nd period: 1993-1998; 10 cases. MHC; MEC and TBI. ST; sandwiched between IC. 3rd period: 1999-2004; 15 cases. MHC; MEC and TBI. ST; delayed after MHC. 4th period: 2005-2012; 14cases. MHC; MEC. ST; delayed after MHC. In 4th period, in case of relapse or refractory; tandem MHC; BU/MEL with autologous stem cell rescue and FLAG/CY with allogenic cord blood rescue and sandwiched ST between tandem MHC. Or; continuing long-term maintenance chemotherapy consisted of irinotecan, topotecan, temozoramide, ifosfamide, carboplatin and isotretinoin.
Results: The DFSR of each periods were 32.2 ± 8.3%, 30.0 ± 14.4%, 53.3 ± 12.8%, 40.8 ± 13.5%, respectively. But the OSR were 45.1 ± 8.9%, 40.0 ± 15.4%, 60.0 ± 12.6%, 85.1 ± 9.7%, respectively ($P < 0.05$ between 1st and 4th periods). And in 4th period, 7 of 14 patients are still alive after relapse or under the treatment during 3years 2 months to 6 years 11 months.
Conclusions: The OSR was significantly better in 4th period and some HRNB patients could become 'chronic'. Although further accumulation of experience should be needed,

long-term maintenance chemotherapy or tandem MHC would be useful for keeping 'chronicity'.

P-0264

A 16-YEAR RETROSPECTIVE REVIEW OF NEUROBLASTOMA IN A SINGLE TERTIARY CENTER

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Purpose/Objective: To study the surgical management of intra-abdominal neuroblastoma in paediatric group.
Materials and Methods: In this retrospective study, the surgical outcomes in the management of neuroblastoma in a tertiary center in Hong Kong were studied. A total of 34 cases of neuroblastoma (23 males: 11 females) from 1996 to 2012 were included.
Results: The median age at diagnosis was 20 months (range from 1momth to 15years). Most of the primary tumours were originated intra-abdominally (17 adrenal, 9 retroperitoneum and 1 omentum). Among those 27 intra-abdominal neuroblastoma cases (2 stage I, 4 stage III and 19 stage IV disease), 25 had undergone laparotomy by paediatric surgical team. All except 4 children, whose preoperative diagnosis was not neuroblastoma, received neoadjuvant chemotherapy according to risk stratification protocol designed by Children Cancer Center of our hospital (2 low risk, 4 intermediate risk and 15 high risk).

Nineteen out of the 25 laparotomies resulted in complete macroscopic removal. The median operative time was 310 min. The median blood loss was 150 ml (range from 50ml to 3800 ml) with 14 children experienced major bleeding with intra-operative transfusion was given. No other intra-operative complications were encountered. Post-operatively, 23/25 received chemotherapy and further radiotherapy and stem cell transplant was given for advanced disease. The only postoperative complication was a child with splenic and bowel infarction. At a median follow-up of 43 months, 10 children experienced tumour recurrence (1 local, 1 local and distant and 8 distant) including 3 cases with incomplete excision and later on with distant recurrence. Seven of these 10 recurrent cases died. Ten children experienced disease-free survival while 8 children survived with residual disease.
Conclusions: This study concluded our experience in the surgical aspect in the management of neuroblastoma. Nevertheless, multidisciplinary management approach toward neuroblastoma is essential in order to achieve a good long-term outcome.

P-0265

HIGHLY ELEVATED LIVER ENZYMES RELATED TO THE USE OF GABAPENTIN IN A CHILD TREATED FOR HIGH-RISK NEUROBLASTOMA

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Purpose/Objective: According to High-Risk Neuroblastoma (HR-NBL-1/SIOPEN) protocol, eligible patients are randomized for immunotherapy to ch14.18/CHO with or without aldesleukin (IL-2). The chimeric monoclonal antibody ch14.18/CHO recognizes the ganglioside GD2 on neuroblastoma cells, but its use is accompanied by visceral and neuropathic pain. (Pre)medication with gabapentin and morphine treatment during each course is recommended.
Materials and Methods: Case Review
Results: Case-description. A young male patient was randomized to ch14.18/CHO only. Three days prior to each cycle of immunotherapy, according to protocol guidelines, oral gabapentin was started and continued until the end of ch14.18/CHO course. During the first 3 courses, aspartate-transaminase (AST) increased up to 285 U/L (reference 11-40 U/L) and alanine-transferase (ALT) up to 312 U/L (reference 7-40 U/L). After 3 days of gabapentin premedication, before start of the fourth ch14.18/CHO course, a severe increase in AST (502 U/L) and ALT (500 U/L) was observed. There were no other concomitant drugs known to cause elevated hepatic levels. Gabapentin was suspected as causal agent. Its administration was stopped promptly and laboratory values improved gradually. Serological investigations excluded infection with EBV, adenovirus, cytomegalovirus and hepatitis (A, B,C). Abdominal ultrasound revealed normal liver pattern.

A Naranjo score was calculated to determine a causality-relation. A highly probable relation score between use of gabapentin and high increase in hepatic enzymes was obtained.
Conclusions: The time-relationship between ingestion of gabapentin and increase of hepatic enzymes strongly supports causality. The Belgian Federal Agency for Medicines and Health Products was informed. They assigned a 'possible' causality score (code 3), according to World Health Organisation criteria.

Physicians treating children for high-risk neuroblastoma with ch14.18/CHO should be cautious and alert on this adverse reaction. Gabapentin is used off-label for age and indication, as is current practice for drugs given at childhood age. This again strengths the need for pharmacological research on drugs in children.

P-0266

EARLY TARGETS OF MIR-34A IN NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma (NBL) is a childhood cancer that originates from precursor cells of the sympathetic nervous system. It occurs primarily in children under the age of 5 years. Among miRNAs with relevance in NBL development, miR-34a can influence its pathogenesis as a tumor suppressor. Several genes are already known direct targets of miR-34a and encode proteins involved in cell proliferation, invasion and apoptosis, with possible effects on many more genes as predicted by bioinformatics based on miR34a seed sequence.
Materials and Methods: We here investigated early targets of miR34a in NBL by quantitative bottom-up proteomics in two different NBL cell lines: SHEP TET-ON miR34a cells and SH-5YSY TET-ON miR34a cells.
Results: The effects of miR-34a expression on the cellular proteomes were evaluated at early time points (6, 12, 24 h) in these tetracycline-inducible miR34a cell systems. Among the 2082 proteins detected and quantified, 172 were found regulated, with 113 down-regulated and 68 up-regulated (at 6 and 12 h of analyses). When considering proteins with a predicted seed-matching site, only 33 showed the seed sequence in the 3' UTR of their corresponding mRNA, as predicted by the PITA.

We then combined the proteomics data with Kaplan Meier analyses using publicly available overall survival analyses. Here, we identified 7 proteins whose genes correlated to poor clinical outcome when overexpressed in NBL. Their regulation upon miR43a expression was confirmed using a 3'UTR luciferase system. These genes are involved in several stages of NBL development which include differentiation (*LYAR*, *CTCF*), apoptosis and proliferation (*TGM2*,*Ki67*), molecular transport (*TIMM13*, *ABCF2*) and metabolism (*ALG13*).
Conclusions: Using String analyses and protein interaction databases, we were able to identify several new pathways controlled by miR34a, including TGF-β, Wnt, and Src.

These analyses highlight the importance of miR34a in NBL and identify new early targets for possible therapeutic intervention.

P-0267

LINCRNA EXPRESSION PROFILING OF SIDE POPULATION CELLS IN THE HUMAN NEUROBLASTOMA SK-N-SH CELL LINE

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Purpose/Objective: Large intergenic non-coding RNAs (lincRNAs)) are emerging as important regulators of cellular pluripotency and differentiation and are widely expressed in various tumors. However, expression profiling of lincRNAs has not been reported in cancer stem cells (CSCs).
Materials and Methods: Side population (SP) cells and non-side population (NSP) cells were isolated from SK-N-SH cell line by the method of hoestch staining of which SP cells were identified as CSCs. And an Agilent 60k sureprint G3 expression microarray was used to investigate their lincRNAs expression profile. The analysis of gene function was done using GO (P-Value < 0.01) and Pathway (P-Value < 0.05) software.
Results: The microarray revealed that 123 lincRNAs were significantly up-regulated and 120 lincRNAs were significantly down-regulated in SP compared to non-SP cells. Using co-expression network analysis, we found linc-LRCH2-1 may have a key role in regular genes expression between SP and NSP. The core regulatory factors in SP was lincRNA A_19_P00330953(SP downregulate) (degree $= 35$, Supplementary Table 3), in NSP were lincRNA LOC100129034(SP downregulate), ZNF876p(SP upregulate), FLJ42393(SP downregulate), LOC441666(SP upreguate), LOC728978(SP donwreguate) (degree $= 42$). Above two co-expression networks revealed that the core regulatory factors was lincRNA XLOC_008213.
Conclusions: lincRNA may play important roles in tumorigenesis of neuroblastoma cancer stem cell. The study of lincRNAs contributes to elucidate the molecular mechanism of neuroblastoma cancer stem cell. And the linc-LRCH2-1 may be a potential target of anti-cancer therapy.

P-0268

MOLECULAR CHARACTERIAZATION OF ALK ABERRATION AND ITS RELATIONSHIP WITH N-MYC AMPLIFICATION AND ACTIVATION OF AKT/MTOR SIGNALING IN NEUROBLASTOM

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Purpose/Objective: Neuroblastoma (NB) is the most common extracranial pediatric solid tumor and the most frequently diagnosed neoplasm during infancy. Anaplastic lymphoma kinase (ALK) has recently been found to be involved in the pathogenesis of this disease. In the present study 84 cases of NB samples were collected for addressing the molecular mechanism of ALK activation and investigating its relationship with *N-Myc* amplification and activation of AKT/mTOR signaling pathway.
Materials and Methods: DNA was amplified by PCR and sequenced to investigate the point mutations of the *ALK* gene. FISH was used to detect the amplifications of *ALK* and *N-Myc* genes. Immunohistochemical staining was performed to detect the expression of ALK, phosphor-ALK, phosphor-AKT, phosphor-mTOR, phosphor-4E-BP1, and phosphor-p70S6K. Follow-up data were collected and survival analysis was performed to correlate these markers and the clinical pathological findings.
Results: The aberration of *ALK* presented as point mutation and gene gain, lead to overexpression and/ or phosphorylation of ALK protein. The overexpression and phosphorylation of ALK protein could activate the downstream AKT/mTOR pathway. Activation of ALK was not observed in some cases carrying *ALK* gene gain, suggesting that gene gain is not sufficient enough to activate ALK. There was no correlationship between *ALK* aberation *N-Myc* amplification, but 15 cases owned both the amplification/gain of *N-Myc* and *ALK* gene had a much poor prognosis. Survival analysis showed that expressions of ALK, phosphor-ALK, phosphor-AKT, phosphor-p70S6K, *N-Myc* gene abnormalities had prognostic significance, of which phosphor-ALK, phosphor-AKT, and *N-Myc* gene amplification were of independent prognostic values.
Conclusions: ALK gene mutation and gain is the main cause of ALK overexperession or phosphorylation in NB. There is no correlationship between *ALK* aberration and *N-Myc* amplification, but they together confer the patients to bad prognosis. Both overexpression and phosphorylation of ALK could activate its downstream AKT/mTOR pathway. Expression of ALK and phosphor-ALK were new prognostic factors of NB.

P-0269

THE EXPRESSION AND CLINICAL SIGNIFICANCE OF ALK IN NEUROBLASTOMA

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Purpose/Objective: Abnormality of ALK gene was associated with the pathogenesis of neuroblastoma. This study was to investigate the expression and the clinical significance of the ALK in NB in China.
Materials and Methods: We collected the clinical informations and the tumor samples of the patients untreated and diagnosed in the Sun Yat-Sen university cancer center from may 2001 to October 2011 and an anaplastic large cell lymphoma sample to investigate the expression and the clinical significance of ALK in NB by immunohistochemistry.
Results: 77 patients were enrolled. 52 in 77 patients were males with median age of 4 years and median following-up time of 20.3 months. The positive expression rate for ALK in neuroblastoma patients was 36.3%(28/77)and the high expression rate was 26.0% (20/77). The 5-year OS of patients with ALK high expression and the low expression were $27.9 \pm 14.8\%$ and $56.5 \pm 10.8\%$,respectively, $P = 0.134$. The expression of ALK was correlated with the age of NB patients, with higher expression rate in patients more than 1.5-year old was 30.6% but 6.7% in patients less than 1.5-year old. The 3-year overall survival(OS) for the patients diagnosed stage III with ALK High expression and the low expression were 0 and $79.5 \pm 13.1\%$,respectively, $P = 0.023$; but the expression level of ALK did not significantly affect the survival of the stage I, II, IV and IVS patients.
Conclusions: The positive expression rate of ALK in neuroblastoma in China was high, especially in the patients with age more than 1.5-year old. ALK high expression may be a poor prognostic factor for the stage III NB. The pathogenesis of the correlation between ALK protein and ALK gene aberrations in neuroblastomas were needed further research.

P-0270

EXPRESSION OF N-MYC DOWNSTREAM-REGULATED GENE 2 IN NEUROBLASTOMA

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Purpose/Objective: N-myc downstream-regulated gene 2 (NDRG2) is a member of the NDRG gene family and has been implicated in cell proliferation, differentiation, and neural development. Importantly, it is also a candidate tumor suppressor in several cancers. We recently identified NDRG2 from proteomic analysis of high-risk neuroblastoma (NB). To date, there are no reports that link NDRG2 to NB. The purpose of this study was to investigate the expression of NDRG2 protein in NB tumors to gain insights into its role in NB tumor biology.
Materials and Methods: Immunohistochemical analysis was used to determine the expression and distribution of NDRG2 protein in primary NB tumors with varying degrees of maturation and differentiation.
Results: In poorly differentiated NB tumors, we found there was no staining of NDRG2 protein in neuroblasts. In differentiating NB, there was strong cytoplasmic staining of NDRG2 protein in differentiating neuroblasts and weak staining in the neuropil. Similarly, mature ganglion cells in ganglioneuroma showed strong cytoplasmic staining of NDRG2 accompanied by moderate staining in the schwannian stroma.
Conclusions: We described for the first time the expression of NDRG2 protein in primary NB tumors. Our data show that NDRG2 expression is closely correlated with neuroblastic differentiation and the development of schwannian stroma, indicating that NDRG2 plays a role in NB tumor biology and potentially could be a differentiation marker as well as a therapeutic target for NB.

P-0271

COPY NUMBER VARIATION IN NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma is a tumour of the sympathetic nervous system,with a clinical phenotype resulting from complex patterns of genetic abnormalities. The purpose of this study was to identify DNA copy number variations associated with neuroblastoma, looking forward to identifying a molecular profile of this condition.
Materials and Methods: Copy number variations in paired, blood and tumour DNA samples from 7 patients were analysed by microarray assays in an Affymetrix platform with Cytogenetics Whole-Genome 2.7 M Array® and Affymetrix® Chromosome Analysis Suite software. Gains and losses were estimated with 95% confidence intervals; chromosome allocation, size of alteration and genomic position were estimated. Variations were subsequently validated by real-time-quantitative Polymerase Chain Reaction (PCR).
Results: Forty four copy number variations were identified. Thirty four genes were included in altered regions while 11 altered regions did not apparently contain known genes. Five changes were present both in tumour and blood DNA in four patients suggesting presence of germline and/or somatic changes maintained throughout tumorigenesis. Furthermore, some similar or identical changes were observed in different patients. The X chromosome showed the largest number of alterations.
Conclusions: Our study showed that copy number variations affected several genes involved in neural cell migration, testes development and normal cell division, providing a preliminary molecular profile for neuroblastoma.

P-0272

CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH NEUROBLASTOMA PRESENTING GENOMIC AMPLIFICATION OF LOCI OTHER THAN MYCN

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Purpose/Objective: The aim of this study is to describe the frequency, clinical characteristics and outcome of neuroblastomas (NB) harbouring amplicons at loci distinct from *MYCN*.
Materials and Methods: Between 2003 and 2011, tumor samples from 1100 patients with NB from French centers were addressed to the laboratory for genetic analysis by array-CGH. The 1100 array-CGH profiles were re-examined specifically for amplification. We included patients for whom amplifications distinct from the *MYCN* locus were seen. Patients treated at Institut Curie from 2000 to 2011, and whose tumours harbored a *MYCN* amplicon without

other amplifications were included as a control group. Clinical data were retrospectively collected.
Results: A total of 56 patients were included in this study and were categorised into 3 groups according to the type of amplification observed in their tumour.

8 NBs (Group 1) presented regional amplifications distinct from *MYCN*, without *MYCN* amplification. These amplifications occurred at 7 distinct loci, of which the amplicon at 12q13-14 was the only recurrent one (4/8 cases). The overall genomic profile were atypical of NB in 5/8 cases. In this patient group, all INSS stages, different primary locations and various histology were observed.

26 patients (Group 2) harboured *MYCN* amplification associated with amplicons at loci distant from *MYCN*. As a control group, 22 patients treated in our institution (Group 3) were identified with amplification of *MYCN* only. Patients of Group 2 and 3 shared similar clinical features.

Outcome was globally poor for the 3 groups but survival analysis suggested a better overall survival for group 1 compared to group 2 and 3 (3 year OS: 83% vs 40%, $p < 0.05$)
Conclusions: NBs harbouring regional genomic amplifications without *MYCN* amplification are rare (0.01%) and seem to show atypical features in clinical presentation and genomic profile. This study should be confirmed on a larger series of cases.

P-0273

PROTEOMIC ANALYSIS OF HIGH-RISK NEUROBLASTOMA

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Purpose/Objective: The survival rate for patients with high-risk neuroblastoma (NB) has improved little over the years. To improve outcomes for these patients, a better understanding of NB tumor biology is essential for developing rational and targeted therapies. In contrast to increasing knowledge of genetic alterations in NB tumors, relatively little is known about its proteome. The purpose of this study was to characterize the proteome of high-risk NB to identify key proteins and disease pathways.
Materials and Methods: Protein extracts of untreated NB tumors obtained from surgical biopsy of high-risk patients were pooled and analyzed by two-dimensional gel electrophoresis (2-DE). Protein spots were excised and digested with trypsin before liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. Selected proteins were verified by immunoblot and immunohistochemical analyses.
Results: A 2-DE reference map of high-risk NB proteome containing 1024 protein spots was established. A total of 602 spots were manually excised for LC-MS/MS analysis, of which 361 were successfully identified as having 1 or more proteins present. In total, 399 unique proteins were identified with a minimum of 2 peptides matched. Gene ontology analysis of the identified proteins provided insights into their biological properties and functions. Among the proteins identified were a number of previously reported biomarkers for NB, including chromogranin A, nucleophosmin, ferritin, *etc*. Importantly, there were also a number of proteins that have not been described in NB before, such as stomatin, N-myc downstream-regulated gene 2, paraneoplastic antigen and others.
Conclusions: We have established the first known 2-DE protein map of high-risk NB and compiled a list of proteins that could serve as a foundation for future biomarker studies in NB. Our data highlights the value of profiling primary NB tumors, which yielded several new candidate proteins for further investigations that should provide new insights into NB tumor biology.

P-0274

ONCOLOGIC PHENOTYPE OF PERIPHERAL NEUROBLASTIC TUMOURS ASSOCIATED WITH PHOX2B MUTATIONS

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Purpose/Objective: *PHOX2B* gene encodes for a homeobox transcription factor involved in autonomic neuron development, and regulates the transcription of key enzymes of the catecholamine synthesis, including the Tyrosine hydroxylase (TH). Germline mutations in *PHOX2B* predispose to peripheral neuroblastic tumors (PNT), frequently in association with other neurocristopathies such as Hirschsprung disease (HSCR) or congenital central hypoventilation syndrome (CCHS). These syndromic presentations are commonly thought to have a good prognosis. Although some *in vitro* data suggest *PHOX2B* mutations impair neuronal differentiation, their physiopathological role in PNT remains speculative.
Materials and Methods: We have analysed eight patients from six different families presenting with peripheral neuroblastic tumors associated with non-polyalanine expansion mutations in *PHOX2B*. We describe clinical features, somatic arrayCGH profiles, and histological pattern including INPC (International Neuroblastoma Pathology Classification) and immunohistochemistry with PHOX2B and TH antibodies.
Results: Four patients had hypoventilation syndrome and/or HSCR, four had no neurocristopathy. We found three ganglioneuromas and two ganglioneuroblastomas, hence illustrating that *PHOX2B* mutations are found in predominantly differentiated tumors. All tumours showed a retained nuclear expression of *PHOX2B* protein, while TH was variably expressed. Among the syndromic forms, we report two patients with stage 4 disease and one patient with stage 3 disease. Segmental chromosomal rearrangements, associated with aggressive disease, were found in four tumours by arrayCGH profiling. One patient died of the tumour, one died of hypoventilation and six patients were alive, with a median follow-up of 14 months.
Conclusions: Our series finally suggests that *PHOX2B* mutations preclude neither tumour differentiation nor TH expression, but may be associated with aggressive genomic patterns.

P-0275

CAN VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION COMPARE TO NMYC AMPLIFICATION AS A PROGNOSTIC FACTOR IN NEUROBLASTOMA PATIENTS?

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Purpose/Objective: NMYC amplification (NMA) is considered the most important prognostic factor in neuroblastoma patients. However, approximately 70% of neuroblastoma patients do not show NMA and need other risk factors for stratification. Our objective was to establish correlation between NMA and vascular endothelial growth factor (VEGF) expression as predictors of survival in neuroblastoma patients.
Materials and Methods: We analysed 54 neuroblastoma samples from patients aged from 2 months to 12 years, treated in the period from 1998 to 2008. We analysed the data according to age, sex, disease stage, histopathological subtype, NMA and VEGF expression. Duration of follow-up was 60 months. NMA analysis was performed using fluorescent in situ hybridisation (FISH). VEGF expression was determined using semi-quantitative scoring of immunohistochemically stained specimens.
Results: We analysed NMA in 53 patients. We found 12 patients who were positive for NMA (22.6%) to have significantly reduced survival rates ($p = 0.0002$). We investigated VEGF expression in 54 patients, where we observed 42 patients with high VEGF expression (77.8%). Patients with high VEGF expression showed significantly lower survival rates than patients with low VEGF expression ($p = 0.0053$). All patients with low VEGF expression survived.
Within the NMA negative group there was a variance in prognosis between patients with high and low VEGF expression ($p = 0.0290$). All NMA negative patients with low VEGF expression survived, compared with 11 NMA negative patients with high VEGF expression (75.6%) who died.
Conclusions: Our results indicate that VEGF expression together with NMA analysis might give additional information for the purposes of risk stratification in neuroblastoma patients. Other than known high-risk NMA positive patients, we might have discovered a group of high-risk NMA negative patients who exhibit high VEGF expression and possibly require a more intensive treatment approach. These results may indicate the need for a larger scale study.

P-0276

KIR GENOTYPES IN NEUROBLASTOMA PATIENTS

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Purpose/Objective: Neuroblastoma is the most commonly seen cancer in infants and most common extracranial tumor of childhood. Natural killer cells have cytotoxic effects on neuroblastoma. Gene polymorphisms governing NK cell function, therefore,may have influence pathophysiology and prognosis.It has been shown KIR-HLA immunogenetics represents a prognostic marker for patients undergoing autologous HSCT for high risk neuroblastoma. Patients lacking HLA-C1 ligand for KIR2DL2/KIR2DL3 experienced highest survival after auotlogous transplants. In this study we investigated the KIR genotypes and their effect on prognosis in our neuroblastoma patients

Materials and Methods: Study group consisted of thirty six patients (15 males, 21 females) with a median age of 36 mos (range 3 mo-113 mos). Twelve of the patients had stage 1,2,3 or 4S disease and 24 patients had stage 4 disease.Control group included 100 healthy children. KIR genotyping was performed on DNA samples by sequence spesific oligonucleotide probe (SSOP) methodology. Statistical analysis was done using Fisher's exact test.
Results: The activating KIR gene (KIR2DS3) and the inhbitory KIR genes (KIR3DL1 and KIR2DL3) have found to be overexpressed in neuroblastoma patients compared to the control ($p = 0.019$,$p = 0.042$ and $p = 0.02$). However,another activating gene, KIR2DS4, is expressed significantly lower than the control ($p = 0.036$).
Conclusions: Overexpression of KIR2DS3,KIR3DL1 and KIR2DL3 and underexpression of KIR2DS4 genotypes can trigger neuroblastoma formation.

P-0277

MIR-129-3P NEGATIVELY REGULATES ALK IN NEUROBLASTOMA AND IS ASSOCIATED WITH ADVERSE PROGNOSIS

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Purpose/Objective: Anaplastic lymphoma kinase (ALK) has been identified as a major oncogene associated with familial and sporadic Neuroblastoma (NB). MicroRNAs (miRs) are small non-coding RNAs involved in post-transcriptional regulation and function as oncogenes or tumor suppressors. We explored mechanisms leading to activation of ALK in 61 NB patients.
Materials and Methods: We evaluated copy number changes and mutational status of ALK gene, expression levels of ALK mRNA and protein, and of miR-129-3p. All the results were correlated to clinical parameters and outcome. Following transfection of miR-129-3p mimic or inhibitor into a MYCN amplified cell line, we evaluated the levels of ALK protein and proliferation rates.
Results: Gain of the ALK gene, high ALK mRNA levels, high protein levels and low miR-129-3p significantly correlated with poor outcome($p = 0.03$; 0.004; 0.002 and 0.03, respectively). We identified significant inverse correlation between miR-129-3p levels and cytoplasmic ALK protein levels defined by specific staining. This suggests that miR-129-3p may regulate ALK. By synthetically upregulating miR-129-3p in NB cell line we observed a significant decrease in ALK protein levels and proliferation rate of the cells.
Conclusions: We suggest an additional mechanism for the regulation of ALK in NB. miR-129-3p negatively regulates ALK, and can serve as a new biomarker by identifying patients with poor outcome that could benefit from therapy using ALK inhibitors. Over-expressing miR-129-3p could be an additional potential therapeutic approach in NB.

P-0278

VANDETANIB INHIBITS NEUROBLASTOMA MIGRATION AND INVASION VIA THE SDF-1/CXCR4 AXIS AND MATRIX METALLOPROTEINASE 14 IN HUMAN NEUROBLASTOMA CELLS

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Purpose/Objective: Vandetanib (also known as ZD6474) is a tyrosine kinase inhibitor with activity against RET. The goal of this study was to investigate whether vandetanib inhibits proliferation and metastasis of neuroblastoma cells in vitro and to explore the potential mechanisms of this action.
Materials and Methods: The effects of vandetanib on SK-N-SH and SH-SY5Y cells proliferation, apoptosis, and cell cycle in vitro were assessed by MTT and flow cytometry analysis. Phosphorylated protein levels of RET and EGFR were detected by Western blot. Cell migration and invasion was determined by the transwell assay. The effects of vandetanib on the mRNA and total protein expression levels of RET, C-X-C chemokine receptor type 4 (CXCR4), and matrix metalloproteinase 14 (MMP14) in neuroblastoma cells were evaluated by qPCR and Western blot.
Results: In the current study, we demonstrated that vandetanib inhibits the proliferation of SK-N-SH and SH-SY5Y cells and that this inhibition is mediated by the induction of G1 phase cell cycle arrest and apoptosis. In addition, vandetanib treatment was effective in inhibiting RET phosphorylation. In the presence of vandetanib, the migration and invasion of two neuroblastoma cell lines were markedly decreased compared with the control group ($p < 0.01$). In addition, our data showed that the levels of CXCR4 and MMP14 mRNA expression in neuroblastoma cell lines treated with vandetanib were significantly lower than those in the cells that were treated with vehicle ($p < 0.01$), and similar results were obtained for protein levels as determined by a Western blot analysis. Finally, an immunofluorescence analysis showed that the treatment of two neuroblastoma cell lines with vandetanib resulted in the downregulation of CXCR4 surface expression.
Conclusions: Vandetanib may inhibit the proliferation, migration and invasion of neuroblastoma cells in vitro.

P-0279

COMPOSITE NEUROBLASTOMA WITH HISTOLOGICALLY AND BIOLOGICALLY DISTINCT COMPONENTS: A REPORT FROM JAPAN NEUROBLASTOMA STUDY GROUP (JNBSG)

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Purpose/Objective: The International Neuroblastoma Pathology Classification (INPC) lists a group of composite tumor composed of histologically and biologically different clones, under the category of Ganglioneuroblastoma, nodular (GNBn) (composite, Schwannian stroma-rich/stroma -dominant and stroma-poor). Recently, a case of composite neuroblastoma (NB) with 2 different clones was reported. Those 2 clones were histologically and biologically distinct, but both were classified into the Neuroblastoma category (Schwannian stroma-poor) according to the INPC.
Materials and Methods: Four cases of composite NB were identified among 360 peripheral Neuroblastic tumors in the file of Japan Neuroblastoma Study Group (JNBSG). All patients were male and diagnosed between 15 and 60 months of age. All had adrenal primary tumors with bone and/or bone marrow metastases.
Results: In three cases, 2 different tumor components (biologically favorable and unfavorable) were clearly distinguishable and separately identifiable under the microscope without transition from one component to the other. One case showed different histology between primary tumor and metastatic lymph node. All four tumors included at least one unfavorable histology (UH) clone showing a histology of poorly differentiated NB with high MKI. By FISH assay using FFPE, MYCN status was successfully assessed for each component in three patients. In one patient, both of 2 components were UH, but MKI was different in 2 components; low MKI and high MKI. One component with low MKI showed no MYCN amplification, while other with high MKI showed MYCN amplification.
Conclusions: We report four cases of composite neuroblastoma. In these cases, each morphologically distinct component could be classified into FH or UH by INPC and further effort should be addressed to clarify clinical and biological importance.

P-0280

TYROSINE HYDROXYLASE EXPRESSION AS A MARKER OF MINIMAL RESIDUAL DISEASE AND ITS IMPACT ON OUTCOME OF PATIENTS WITH HIGH – RISK NEUROBLASTOMA FOLLOWING AUTOLOGOUS BONE MARROW TRANSPLANTATION

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Purpose/Objective: We investigated whether detection of minimal residual disease (MRD) in peripheral blood stem cells (PBSC) by using tyrosine hydroxylase (TH) expression could predict outcome of patients with advanced neuroblastoma.
Materials and Methods: Quantitative real time PCR was performed for the detection of tumor contamination using TH-mRNA and correlated to clinical parameters and outcome in 20 out of 40 patients with high-risk neuroblastoma.
Results: We studied a total of 20 samples from patients with high risk neuroblastoma for TH and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) expression. All cases were negative for TH expression and positive for GAPDH ensuring good quality and quantity of the tested cDNA. The 24-month overall survival (OS) for the whole group of patients (40) was 64.7%, while the 12-month disease-free survival (DFS) was 55.5%. We did not find any significant correlation between different prognostic factors (age, stage, *MYCN* amplification, resectability, status before HSCT, radiation therapy) and TH mRNA expression except for the viability of PBSC (p-value of 0.008). Marginal significance was found in OS among patients with negative TH (57.2%) as compared to patients in whom MRD by TH was not done (70%)

with P = 0.104. However, there was no statistical significance in DFS among both groups (P = 0.384).
Conclusions: The cumulative OS for patients who had negative TH expression was lower than that for patients in whom MRD by TH was not done (statistically of near significance).Also, the DFS for patients who had negative TH expression was lower than that for patients in whom MRD by TH was not done (statistically not significant). Our results obtained in a small cohort of homogeneously treated high-risk patients suggest that all 20 cases were negative for TH expression. This indicates a need to increase sample size in a long-term clinical outcome study to clarify the importance of TH mRNA contamination in PBSC.

P-0281

PHARMACOKINETICS OF ISOTRETINOIN IN INDIAN PATIENTS WITH HIGH RISK NEUROBLASTOMA AND ITS IMPACT ON SURVIVAL

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Purpose/Objective: To evaluate pharmacokinetics (PK) of isotretinoin in Indian pediatric patients with high risk neuroblastoma and factors affecting it. To evaluate impact of plasma concentration on survival outcome.
Materials and Methods: Children were enrolled after completion of induction/ consolidation therapy for high risk neuroblastoma. They received isotretinoin 160mg/m^2/day in two divided doses.Those who were unable to swallow capsules, the contents were extracted & mixed with yogurt prior to administration. PK samples were collected on days 1 and 14 of cycle 1(C1D1,C1D14) and cycle 4(C4D1,C4D14) at 0,1,2,4 and 6 hours after the morning dose .Plasma isotretinoin levels were determined by High Performance Liquid Chromatography (HPLC). Area under the concentration-time curve from 0-6 hours (AUC_{0-6}) was estimated using linear trapezoidal rule. All patients were genotyped for **2*, **3* and **4* variants of *CYP2C8* by PCR-RFLP. An 'Event' was defined as disease progression or death.
Results: Twenty eight children (M = 20, F = 8) were enrolled since April 2010. The median age was 4 (1-13) years. High inter-patient variability in pharmacokinetics was observed (AUC_{0-6} C1D1, CV = 130.15%). AUC_{0-6} on day 1 was higher compared to day 14 in both cycles (P = NS). Children who swallowed the capsules (N = 19) achieved higher AUC_{0-6} compared to those who could not (N = 9) (17.09 ± 5.07 vs. 10.88 ± 4.66 μM*hr/L, P = 0.45). None of the studied genetic variants of *CYP2C8* were encountered, and therefore the effect of *CYP2C8* polymorphisms on PK could not be ascertained. The median EFS was 18 months. Patients who were event free at one year had higher AUC_{0-6} on C1D1 compared to those who progressed or died (19.0 ± 8.52 vs. 11.59 ± 5.18, p = 0.47). The median EFS was slightly greater in patients who achieved maximum plasma concentration > 2 μM/L on C1D1 (17.89 ± 2.1 vs. 15.35 ± 3.78 months, log rank P = 0.15).
Conclusions: Method of administration affects PK of isotretinoin. Maximum concentration achieved and total exposure up to six hours can impact survival outcomes.

P-0282

THE ROLE OF SERUM CHROMOGRANIN A TO MONITOR NEUROBLASTOMA DISEASE

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Purpose/Objective: Neuroblastoma is a neuroendocrinal neoplasia, the most prevalent among solid extra-cranical pediatric tumors. Chromogranin A (CgA) is a tumoral marker for neuroendocrinal neoplasia. The aim of this study is to evaluate CgA as a diagnostic tool in Neuroblastoma.
Materials and Methods: We analyzed variations of CgA at diagnosis, during treatment, follow-up and relapse in 28 patients (17M, 11F) with Neuroblastoma, aged 1 to 324 months (mean 38 months), comparing to other tumoral markers: Neuron-specific Enolase, Thymidine Kinase and Ferritin. Eight patients were stage I, 2 were stage II, 5 stage III, 9 stage IV and 4 stage IVS; two of 28 tumours were MYCN amplified. We excluded patients with renal failure. Serum CgA levels were determined by radioimmunoassay. Patients were included from April 1994 to March 2012.
Results: Serum CgA was increased (> 100 ng/ml) in all our patients (specificity 100%) at diagnosis. Mean serum CgA, correlated with disease stage, shows a greater increase in metastatic disease (stage IV and IVS). Higher serum TK, NSE and Ferritin levels are also associated with metastatic disease, whereas are lower in stage IVs. We observed a gradual reduction of CgA in correlation with tumor burden reduction in stage IVS. This cannot be extended to other tumoral markers. Serum tumoral markers levels were increased in progression or relapse of disease. During the follow-up, one patient showed clinical symptoms of relapse, but level of CgA remained normal (< 100 ng/ml), bone marrow biopsy showed myeloid leukemia.
Conclusions: We suggest that CgA might be a routine test, useful tool to diagnose Neuroblastoma in children patients during treatment and follow-up. It is a non-invasive test that can indicate early relapse if associated with imaging techniques

P-0283

"THE SENSE AND SENSIBILITY OF PHILADELPHIA SCORE" IN STAGE 4S NEUROBLASTOMA PATIENTS.

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Purpose/Objective: Neuroblastoma (NBL) is the most common malignant tumor in infants. Stage 4S NBL is a unique kind of metastatic NBL; it has a more favourable outcome than other metastatic tumors and frequently shows spontaneous regression. A subgroup of patients, however, can progress rapidly. Disease course can be monitored using a semi-quantitative scoring system known as the Philadelphia score (PS).
Materials and Methods: Retrospective, multi-centre, cohort study (AMC and SKZ). We reviewed all medical charts from patients diagnosed with stage 4S NBL (1980-2012) noting patient characteristics, treatment, response, outcome and PS.
Results: A subgroup of stage 4S NBL presents with an aggressive disease, 8 out of 34 (24%) patients had progressive disease (PD) (of which 5 were younger than 2 months at diagnosis). Twenty six patients are alive (77%), 5 patients died of disease (15%) and the outcome of 3 patients is unknown (lost to follow up). Four out of 5 patients that have died were younger than 2 months at diagnosis. Abdominal distension and hepatomegaly are common presenting symptoms. The category ' hepatic' in PS is nearly always normal. Treatment consisted of chemotherapy, radiotherapy, ^{131}I-MIBG therapy and/or surgery. PS is infrequently noted in medical charts, but is a useful scorings method. Treated patients had a higher PS score than non-treated patients, if documented; a PS ≥ 2 was often used to start treatment. Because, category hepatic was less useful, we suggest changing the PS by removing hepatic and replacing with increase of abdominal distension.
Conclusions: Twenty-four percent of patients with stage 4S NBL showed PD, either by tumor growth or by progression to stage 4 NBL. PS helps to identify patients that need urgent treatment. We suggest using the PS more actively by physicians and we propose to change the PS by adding in increase of abdominal distension instead of 'hepatic'.

P-0284

EVALUATION OF AUTOLOGOUS PERIPHERAL BLOOD STEM CELL MOBILIZATION AND COLLECTION EFFECT IN THE COMBINATION THERAPY TREATMENT OF NEUROBLASTOMA IN CHILDREN

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Purpose/Objective: This study aimed to evaluate the influence factors of mobilization and collection of blood stem cells in autologous peripheral blood stem cell transplantation in children with neuroblastoma.
Materials and Methods: Thirty one patients with NB received autologous peripheral blood stem cell transplantation. The mobilization and collection protocle such as timing,peripheral WBC count were retrospectively reviewed.
Results: Thirty one NB patients were divided into two groups,CD 34+ cells were higher in CVP chemotherapy protocle than CAV protocle,*P* value < 0.05,while MNC shows no difference in both group,*P* value < 0.05. According peripheral WBC count,31 patients were divided into three groups,the higher WBC count,more MNC and CD34+ cells we got for the autologous peripheral blood stem cell transplantation.
Conclusions: The WBC count on the day of collection could influence the result of blood stem cells collection. chemotherapy protocle in mobilization also have an effect on the result,hematopoietic function recovered faster in patients with relatively weak chemotherapy protocle,so the time consuming could be shorter in mobilization and collection of blood stem cells in autologous peripheral blood stem cell,then the cycle of chemotherapy could be shortened.

P-0285

DIFFUSION WEIGHTED WHOLE BODY IMAGING WITH BACKGROUND BODY SIGNAL SUPPRESSION (DWIBS) IN STAGING FOR NEUROBLASTOMA

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Purpose/Objective: To evaluate diagnostic potential of diffusion-weighted whole body imaging with background body signal suppression (DWIBS) in detection and staging of

neuroblastomas. DWIBS is a new technique in magnetic resonance imaging that holds promise in assessment of solid tumors in children
Materials and Methods: Six children (4 males and 2 females in the age group of 12 to 32 months) diagnosed with primary abdominal neuroblastomas underwent diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) and T2 fat suppressed imaging as part of the staging process. The technique is based on the principle of restricted diffusion in tumors due to their increased cellular density compared to normal tissue. Exponential apparent diffusion coefficients (eADC) which are quantitative parameters derived from diffusion images maybe considered as biomarkers of cellularity of solid tumors. The method employs DWI acquisition using short tau inversion recovery (STIR) combined with single shot echoplanar imaging (EPI) sequences under free breathing conditions. Multiple b-values of 0,600 and 1000 s/mm^2 were used. Inversion of gray scale DWIBS images results in PET PET-like images. T2-fat suppressed or STIR images provide anatomic detail and thus improve confidence levels.
Results: The primary tumor and metastases showed high signal intensity (restricted diffusion) on DWIBS images in all patients. DWIBS showed lymph node involvement in all six cases and bone marrow involvement in three patients. Both primary tumor and metastases showed eADC values ranging between 0.25 to 0.3 $\times$ 10^{-3} mm^2/s.
Conclusions: DWIBS is a new MR sequence which holds much potential in initial staging work up and post treatment evaluation of primary neuroblastomas in children. Metastatic lymph nodes and bone marrow, important criteria in staging of neuroblastomas, are better visualized using this technique. DWIBS has distinct advantages of no exposure to ionizing radiation and relatively shorter imaging time.

P-0286

SYNERGISTIC ANTITUMOR INTERACTIONS BETWEEN PANOBINOSTAT AND CONVENTIONAL CHEMOTHERAPY DRUGS IN HIGH-RISK NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma remains a therapeutic challenge in pediatric oncology despite decades of intensive research and therapeutic trials. Patients with high-risk metastatic neuroblastoma have long-term survival rates of less than 40%. Therefore, new agents are urgently needed to overcome chemotherapy resistance so as to improve the treatment outcome of children with this deadly disease. Histone deacetylase inhibitors (HDACIs) are a promising new class of anticancer drugs. In this study, we sought to investigate the antitumor activity of panobinostat (LBH589, a novel second generation HDACI) in combination with conventional chemotherapy drugs in high-risk neuroblastoma cell lines.
Materials and Methods: Extent and direction of antitumor interactions between panobinostat and cisplatin, doxorubicin, or etoposide were determined by MTT assays and standard isobologram analyses. Cell cycle progression and apoptosis induced by the drug treatments were determined by propidium iodide (PI) staining and flow cytometry analysis. Effects of drug treatments on protein levels were determined by Western blotting.
Results: Treatments of 4 high-risk neuroblastoma cell lines with variable clinically achievable concentrations of panobinostat resulted in dose-dependent potent induction of apoptosis. When administered simultaneously, panobinostat synergistically enhanced the cytotoxicities of cisplatin, doxorubicin, or etoposide in all the neuroblastoma cell lines determined by MTT assays and standard isobologram analyses. Co-treatments of the neuroblastoma cell lines with panobinostat and cisplatin, doxorubicin, or etoposide resulted in synergistic induction of apoptosis. Interestingly, panobinostat suppressed the expression of checkpoint kinase 1 (CHK1) and abrogated the G2/M cell cycle checkpoint activation induced by the chemotherapy drugs. Current studies are underway determining the role of CHK1 in the synergistic induction of apoptosis by the drug combinations and *in vivo* antitumor efficacy of these drug combinations in SCID mice bearing neuroblastoma xenografts.
Conclusions: Our study may provide compelling rationale for the combination of chemotherapy drugs and HDACIs in high-risk neuroblastoma clinical trials.

P-0287

STAGE4 NEUROBLASTOMA ARISING IN AN OVARIAN TERATOMA

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Purpose/Objective: We report a case of neuroblastoma presented as a malignant transformation from a mature cystic teratoma of ovary.
Materials and Methods: Case report.
Results: A 15-year-old girl was referred to our hospital because of left ovarian tumor. The tumor was successfully excised but para-aortic lymph nodes were unresectable. Pathological examination revealed that the tumor consisted of 10% of teratoma elements with 90% of ganglioneuroblastoma elements. MYCN was not amplified. NSE was elevated to 129ng/ml, but catecholamine metabolites were not elevated. Bone marrow aspiration showed a patchy infiltration of NSE-positive neuroblastoma cells. Imaging studies revealed enlargement of mediastinal and para-aortic lymph nodes, but bone metastasis was not detected. The tumors did not take up meta-iodobenzylguanidine. We diagnosed her with neuroblastoma arising in an ovarian teratoma with multiple metastases. Multiagent chemotherapy for neuroblastoma (cyclophosphamide, vincristine, adriamycin and cisplatin) was initiated immediately. Mediastinal and para-aortic lymph nodes remarkably reduced in size but did not disappear. After the five courses of chemotherapy (5 months after diagnosis), we administered high-dose chemotherapy consisting of busulphan and melphalan followed by autologous peripheral blood stem cell transplantation. Post-transplant course was uncomplicated and neutrophil engraftment was achieved on day 12. She underwent lymphadenectomy of residual para-aortic lymph nodes on day 48 and 19.8 Gy of local irradiation to mediastinum and retroperitoneum on day 68 to day 83. She started receiving 13-cis-retinoic acid 9 months after diagnosis, and is alive without any evidence of disease 17 months after diagnosis.
Conclusions: Only 3 cases of neuroblastoma arising in a teratoma was previously reported. Multimodality therapy for neuroblastoma seemed effective for our patient. To study biology of this rare type of tumor may elucidate the pathogenesis of neuroblastoma, that is an enigmatic tumor.

POSTER SESSION: POSTER SESSION - SURGERY (IPSO)

P-0288

IMPLANTABLE VENOUS PORT SYSTEMS IN PEDIATRICS.

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Purpose/Objective: Central venous catheterization is a complex procedure essential in the treatment of many diseases. Our aim was to reduce the number of central venous catheterization, general anesthesia, complications, to get a safe technique providing vascular access.
Materials and Methods: From 2010 to 2013, 278 child cancer patients aged 4 months to 17 years were implanted subcutaneous venous port systems. All implants were performed in the operating theatre with the use of C-arm under endotracheal anesthesia with intravenous sedation of Propofol or Sevorane. To reduce the risk of complications an internal jugular vein was punctured after a preliminary ultrasound marking and after giving the patient Trendelenburg position. In some complicated cases, the puncture was performed under direct ultrasound navigation.
Results: No hemopneumothorax or lung injury occurred. Inserting a port catheter into the superior vena cava was performed under X-ray control to prevent migration of the distal end of the catheter into the neck veins, which was noted in 38 cases (13.6%), 11 (3.9%) - in the subclavian vein in 2 (0.71%) - in the internal jugular from the opposite side. In the first attempt we managed to puncture a vein in 275 cases (98.9%), and 3 (1.07%) - in the second. First attempt to advance a guidewire into the superior vena cava failed in 259 patients (93.1%), 10 (3.5%) - in the second, and 5 (1.79%) - the third and 4 (1.43%) - failed, requiring the subclavian vein puncture. In 2 cases (0.71%) the port systems got infected owing to the errors in operation, 6 (2.15%) - their clotting.
Conclusions: Implementation of implantable venous systems helps to reduce the number of general anesthetics and medical staff workload, to improve the quality of life of patients, to minimize the risk of complications. Ultrasound and intraoperative fluoroscopy increases safety and reduces the duration of the operation.

P-0289

SURGERY OPTIONS AND RESULTS OF TREATMENT OF CHILDREN WITH SOLID PSEUDOPAPILLARY TUMORS OF THE PANCREAS

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Purpose/Objective: Development rational surgery for solid pseudopapillary tumor (SPT) of the pancreas and implementation of endosurgery.
Materials and Methods: 13 children with SPT were operated since 2004 to November 2012. We analyzed clinical data, operation options and results of treatment.
Results: All patients were females age from 9 to 15 years (median 13y.o.). Localization tumors in pancreas: in the tail * 5, in the body * 5 and in the head - 3. The size: 1.5-8.7sm (median 4.2sm). 5 children underwent laparoscopic distal pancreatectomy with splenic preservation, 1 - laparoscopic central resection; 2 - gastropancreatoduodenal resection, 2 * central resection of pancreas; 1 - distal subtotal resection with resection of the superior mesenteric vein, 1 - uncinate process of pancreas resection with resection of duodenal wall. Time of operations: 95 * 290 min (median 198min.). Bleeding: 50-200ml. (median 115ml.) Complications occurred in 5 patients: in 3 cases * pancreatitis with pancreatic fistula, 1 - bleeding from the pancreatic branch of the splenic artery after Whipple operation and 1 - pneumonia. There were 2 reoperation for complications.The observation period of the

patients was from 1 month to 8 years. All patients are alive without evidence of disease recurrence.
Conclusions: The main method of treatment is surgery, however there is a moderate risk of complications because of tumor localization. Great attention should be paid to the prevention of postoperative pancreatitis. A promising method is endosurgery providing early rehabilitation and cosmetic effects.

P-0290

EXPLOITATION OF VARIOUS CENTRAL VENOUS CATHETERS IN CHILDREN FOR THE PURPOSE OF CHEMOTHERAPY: 5-YEAR EXPERIENCE OF ONE INSTITUTION.

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Purpose/Objective: The central venous catheterization is a dangerous but common procedure, without which chemotherapy course is impossible. Complications with the installation and operation are likely to disrupt treatment protocols, increase period of hospitalization and treatment costs.
Materials and Methods: From 2008 to 2013 we observed 1529 cancer patients aged of 3 months to 17 years. 278 patients were implanted venous port systems, 1114 - traditional subclavian catheters, 137 - Broviak's catheters.
Results: In patients with implanted subcutaneous venous ports periportal tissue infection was observed in 3 cases (1.07%). Catheter-associated bloodstream infections were not observed. Port catheter thrombosis was observed in 5 cases (1.79%). In patients with subclavian artery catheter insertion site infection was noted in 673 cases (60.4%). The development of catheter-related bloodstream infections was noted in 97 cases (8.7%). Catheter thrombosis was observed in 764 cases (68.5%), thrombosis of the subclavian vein - in 7 (0.62%) and developed after 3 months of operation. In patients with Broviak's catheters catheter-associated bloodstream infections were detected in 2 cases (1.45%), thrombosis - in 23 (16.7%). When thrombosis, a solution containing urokinase was used. In the treatment of subclavian catheter thrombosis in 252 cases (22.6%) needed to be replaced. As a solution to close the catheter systems heparin or a solution containing taurolidine was used. In the latest case occurrence of catheter-related bloodstream infections was not reported. In cases of infection complications the S. epidermidis and S. aureus were identified as causative agents, for the treatment we infused taurolidine with exposure of 6 hours and systemic antibiotic Vancomycin.
Conclusions: The incidence of complications is significantly higher in patients with subclavian catheters, the treatment often requires the catheter replacement. Insertion of implantable venous port system reduces the number of central venous catheterization and has minimal risk of complications. Broviak's catheters are accompanied by a significant number of thrombotic complications.

P-0291

THE COMPLICATION OF GASTRO-ENTERIC FISTULISATION IN NEUTROPENIC ENTEROCOLITIS SECONDARY TO APLASTIC ANAEMIA.

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Purpose/Objective: We report the case of a 27 month-old male with an unusual complication of aplastic anaemia and neutropenic enterocolitis. He suffered persistent neutropaenic sepsis and clinical deterioration forced the strategy of matched sibling haematopoietic stem cell transplantation. With engraftment and clinical recovery post-transplant, enteral feeding was re-established. Despite continued improvement the child began to vomit faeculent stomach content. Barium swallow showed gastro-colic and gastro-enteric fistulisation with contrast passing directly from stomach into descending colon and directly into jejunum. Laparotomy confirmed complex fistulae between the gastric body, the splenic flexure of the colon and the jejunum.
Materials and Methods: This is a case report intended for poster presentation and reflects the clinical experience and outcome of an individual treated at our institution by both medical and surgical means.
Results: Following intensive medical and surgical therapy this child achieved full engraftment and recovery.
Conclusions: The primary management of neutropenic enterocolitis should be supportive, with most cases being managed effectively with bowel rest, intravenous fluids, broad-spectrum antibiotics and antifungal therapy. Early recognition of this condition is of paramount importance to allow the best possible outcome whilst avoiding unnecessary laparotomy in these patients with little physiological reserve.

The clinical course in our patient was unusual. Free perforation into the abdominal cavity is far more commonly recognized than internal fistulation. Fortunately, perforation into the abdominal cavity did not occur during the period of profound pancytopenia. The mortality with surgery in this circumstance is likely to have been very high.

P-0292

PREVALENCE OF C-KIT MUTATION IN NEUROBLASTOMA

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Purpose/Objective: To study the prevalence of *c-kit* gene mutation in neuroblastoma.
Materials and Methods: In this prospective study, 41 neuroblastoma specimens were evaluated, of which 10 were pre-chemotherapy and 31 post-chemotherapy. All specimens were histologically confirmed to be neuroblastomas. DNA was isolated from frozen tissues. *c-kit* mutations were analysed by PCR amplification followed by sequencing, for the four hotspots exon 9, 11, 13 and 17. Ethical clearance for the work was obtained from the Institutional ethical review board.
Results: Out of 41 patients whose tissue specimens were evaluated,30 (73%) were males and 11 (27%) females.Age ranged from 1-132 months (mean 39.36; SD 32.59). Fourteen (34%) were below 18 months of age.Thirty-two (78%) tumors were abdominal, 9 (22%) were thoracic orthoraco-abdominal.No *c-kit* mutations of exon 9, 11, 13 or 17 were detected in any of the specimens.
Conclusions: *c-kit* mutations have been shown to play a pivotal role in some tumors like GIST and have both prognostic and therapeutic significances. Despite frequent *c-kit* protein expression in neuroblastoms, *c-kit* gene mutations are rare. Two earlier reported studies, failed to show any *c-kit* mutation, for exon 11. Another reported work analysed *c-kit* mutations on DNA extracted from archival tissue, by denaturing HPLC, for exon 9, 11, 13 and 17, also did not show any mutation. In the current work *c-kit* mutations were analysed on DNA extracted from frozen tissues, by sequencing for four hotspots exons 9, 11, 13 and 17 but still no mutations could be demonstrated either in pre-chemotherapy samples nor in post-chemotherapy samples.

c-kit gene mutations are uncommon and may not play a pathogenic role in the development of neuroblastoma. However, frequent occurrence of *c-kit* expression in neuroblastoma still needs to be explained.

P-0293

PEDIATRIC THYROID CANCERS: PRESENTATION AND OUTCOMES

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Purpose/Objective: To review the presentation, treatment and outcome of children with thyroid cancer.
Materials and Methods: Retrospective review from the records of children with thyroid cancer enrolled from 2005 through 2012.
Results: 8 children, 5 females and 3 males,in the age range 60 to 144 months (mean 105 $\pm$ 33 months) were enrolled.Seven presented with a neck nodule.Oneasymptomatic patient, sib of a MEN 2A child was referredfor prophylactic thyroidectomy. All were euthyroid. Five had papillary carcinoma (PCa) and 3medullary carcinomathyroid (MCT).All three MCT were members of a single family with raised calcitonin levelsand all carried the C634Y mutation in the RET proto-oncogene.Distant metastasis, to spine was present in 1 patient(PCa) who refused surgery, was referred for palliative care and was subsequently lost to follow-up. Six (3MCT + 3PCa) underwent total thyroidectomy with reimplantation of one parathyroid.One (PCa), a second malignancy following treatment for recurrent wilms tumor,had a subcentimeter nodule and underwent hemithyroidectomy. Post-operatively 4 developed hypocalcemic tetany that responded to calcium supplementation.None underwent radio-iodine ablation. Post-operative thyroxin replacement was prescribed to all 6 who underwent total thyroidectomy, 4 of whom also required calcium supplements and alpha D3 for hypoparathyroidism.Patients were followed using clinical exam, serial USG, CT, radioactive iodine scans and calcitonin levels (MEN-2A patients). Seven (87.5%) were alive at last follow up without recurrence.
Conclusions: Pediatric thyroid cancers usually present as a nodule, are commonly papillary carcinoma and have good long-term outcome following surgical treatment.

P-0294

CORYNEBACTERIUM INFECTIONS IN CENTRAL VENOUS CATHETER IN PEDIATRIC ONCOLOGY

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Purpose/Objective: Venous catheters are considered a quality pattern in the treatment of oncological patients. Bacterial infections are complications frequently observed during treatment procedures, including pediatric patients. Microorganisms of the genus *Corynebacterium* are still considered as underappreciated community and nosocomial pathogens in oncological patients. Of the few literature records in the corynebacterial infections the vancomycin is still the preconized treatment. Therefore, cases of infections by *Corynebacterium* associated to central venous catheters in pediatric oncology patients from a Brazilian Cancer Hospital were presented in this study.
Materials and Methods: In this retrospective and descriptive study, twelve pediatric patients and carriers of (silicone or polyurethane) central venous catheters - CVC (three with solid tumors and eight with hematological tumors) out of 38 oncology patients with *Corynebacterium* infection were identified during a period of two years. The catheter type, presence of neutropenia, comorbidity of the oncology treatment and the conduct to the infection were also described.
Results: *C. amycolatum* (10) strains were mostly detected from blood samples and/or catheter tips, followed by *C. jeikeium* (01), *C. fermentans* (01) and *Leifsonia aquatica* (*C. aquaticum*) (01). Three patients had neutropenia when corynebacterial infections were identified; CVC was preserved only in one opportunity.
Conclusions: Multiresistant corynebacterial pathogens, such as *C. amycolatum*, may infect pediatric oncological patients carrying silicone central venous catheters. Additional studies of actions and medications that influence in the bacterial adherence to the material can contribute to more effective drugs and new guidelines.

P-0295

HORMONALY ACTIVE GONADAL TUMORS: SURGERY IS CURATIVE

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Purpose/Objective: The study aimed at reporting and studying cases with biologically active gonadal tumors in the last ten years in a single institute.
Materials and Methods: All infants and children with hormonally active gonadal tumors admitted in the Pediatric Surgery department,University of Alexandria,Egypt, over a period of ten years were studied concerning: the demographic data,ways of presentations, modalities of diagnosis and the surgical treatment.The outcome and prognosis was also recorded.
Results: Among all cases of gonadal tumors reported over a period of ten years,seven cases of hormonally active tumors had been recorded.They were 3 males and 4 females with the age range was from 6 moths to 7 years. All cases presented with pseudo-prococious puberty.Ultrasonography was the only modality confirming the diagnosis. All children were treated with unilateral gonadectomy without any sequelae in the long term follow up.
Conclusions: *Biologically active gonadal tumors are very uncommon in infants and children.
*High index of suspicion is needed for early diagnosis.
*They are mostly benign and unilateral gonadectomy is curative

P-0296

USE OF A PORT-A-CATH POLYSITE TYPE IN PEDIATRIC ONCOLOGY PATIENTS

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Purpose/Objective: The new chemotherapy drugs improved survival of pediatric cancer patients, and now must improve the administration of drugs, reducing the number of venipunctures and other complications of drug administration. The Port-A-Cath is a closed system comprising a chamber that is implanted subcutaneously attached to a catheter placed in a central vein, its membrane which is accessed with a Huber needle through the skin and may tolerate up to 1000 punctures, literature reports that the use of this system provides safety and patient comfort to the patient. The objective is to evaluate the use of a port-a-cath, Polysite type in pediatric oncology patients
Materials and Methods: The clinical files of 66 patients with cancer were revised to who were placed a port-a-cath, Poyisite type, during the period of July 2006 to April 2012, aged between 6 months and 18 years. Whereas for the analysis, age, sex, tumor type, and diameter of the catheter complications related to placement
Results: 66 catheters were implanted, of these 59 met the study criteria, the mean age was 9.98. The sex ratio was F: M = 1: 1.565. Insertion site most frequently used was the right internal jugular vein (47.45%), followed by the right subclavian vein (35.59%). The Seldinger technique was used, checking with the use of fluoroscopy final location of the catheter tip 77.97%. The most frequent oncological diseases: Osteosarcoma (42.37%), neuroblastoma (10%) and Wilms tumor (8.47%). Twelve patients developed catheter-related complications: catheter related infection (6), Breaking system (2), Port rotation (3) and Pneumothorax (1), only infected catheters were removed suggested by the committee infections.
Conclusions: The use of a port-a-cath are associated with a low rate of complications, so it could be safely used in pediatric patients, these being more accepted by their comfort, however familiarization health team would help reduce complications.

P-0297

ASSOCIATION OF WILMS' TUMOR WITH A HORSESHOE KIDNEY

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Purpose/Objective: Nephroblastoma (Wilms' tumor) is the most common renal malignancy in childhood. Wilms' tumor with a horseshoe kidney is uncommon. It is extremely rare that the incidence of Wilms' tumor occurring in a horseshoe kidney were reviewed.
Materials and Methods: From 2000 to 2013, three patients were found to have a Wilm' tumor arising in a horseshoe kidney, and the diagnosis was admitted with an abdominal mass that had been noticed by routine ultrasonography and scans from computed tomography(CT). They records were reviewed retrospectively.
Results: We report three cases that we were able to identify. The first case was a 3-year-old boy with a huge tumor that connected the left flank toward the midline. The second case was a 1-year-old girl with occupied most of the retroperitoneum. The third case was a 7-year-old boy with a lower pole of horseshoe kidney and is the second case of Wilms' tumor having an associated esotropia and nasal hemangioma. These cases presented with a stage?-? Wilms' tumor in a horseshoe kidney. Those cases were treated with surgical resection followed by adjuvant chemotherapy. They are now 112 months, 44 months and 28 months postchemotherapy, respectively, and are symptom and recurrence free. A review of all reported cases of Wilms' tumor with horseshoe kidneys before Feb 2013 is presented.
Conclusions: We recommend treating this entity with protocols designed for Wilms tumor with a horseshoe kidney and to conduct further basic research to understand its biologic nature.

P-0298

CHRONIC INFLAMMATIONS AND PRE-CANCEROUS LESIONS IN CONGENITAL CYSTIC ADENOMATOID MALFORMATION OF THE LUNG: AN ALREADY WRITTEN HISTORY?

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Purpose/Objective: to evaluate the influence of chronic inflammation for the pathogenesis of pre-cancerous lesions in patients affected by Congenital Cystic Adenomatoid Malformation of the Lung (CCAML)
Materials and Methods: Specimens obtained from patients operated on CCAML were processed for routine histological examination to establish both the type of malformation according to Stoker's classification and the presence of Atipycal Adenomatoid Hyperplasia (AAH) or Atypical Goblet Cells Hyperplasia(AGCH), pre-cancerous lesions of bronchiolo-alveolar carcinoma. Additional immunohistochemical staining for CD3, CD68 and CD20 antigens was also performed to evaluate the presence/absence of chronic inflammation within the lesions and within the atypical cells.
Staining for Ki-67 was used to assess the proliferative index in the same areas.
Samples were considered negative when the staining was seen for ≤ 5 positive inflammatory cells. Positive inflammatory elements was semi-quantitatively categorised into: score 1 for < 20 positive inflammatory elements, score 2 for 20-50 positive inflammatory elements and score 3 for > 50 positive inflammatory elements. The Ki-67 proliferative index was assessed in all fields containing epithelial respiratory cysts as well in those with hyperplastic epithelium. The percentage reported was referred to the median value of Ki-67 in all cystic areas. Areas containing normal bronchus were used as control.
Results: Specimens were obtained from 32 patients (21 males * 11 females) diagnosed from February 2008 to March 2012. Type I CCAMLs showed expression of CD20 and CD68 elements in hyperplastic areas of the malformation, as well as a strong positivity of Ki-67 index compared to type II CCAMLs, which showed principally CD3 elements without evidence hyperplastic lesions and normal expression of Ki-67
Conclusions: Chronic inflammation may play a major role in pathogenesis of pre-cancerous lesions in type I CCAMLs, thus confirming indication for early surgical treatment of patients affected by those malformations.

P-0299

OXIDISED REGENERATED CELLULOSE GRANULOMA AFTER BIOPSY FOR ANAPLASTIC LARGE CELL LYMPHOMA

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Purpose/Objective: Anaplastic large cell lymphoma (ALCL) is a type of non-Hodgkin lymphoma. It is rare, affects children and young adults, more common in males. The diagnosis is made by biopsy of enlarged lymph nodes with pleomorphic pattern and could expresse positivity for CD 30, ALK+.

Different absorbable haemostatic methods can be employed in surgery. Oxidised regenerated cellulose (ORC) is commonly used and retention is rare.

We present a case of ORC granuloma after lymph nodule biopsy for retroperitoneal ALCL mimicking recurrent lymphoma.

Materials and Methods: A 15 year old boy underwent laparoscopy and laparotomy to take samples of enlarged retroperitoneal nodules.

The diagnosis was ALCL-ALK +.

ORC was used to achieve haemostasis. CT scan at 6 th month follow up revealed a 57×45 mm mass with contrast enhancement at the same location. Positron emission tomography suggested relapse. Fine needle aspiration of cervical nodules confirmed the diagnosis. The patient developed intestinal suboclusion and needed parenteral nutrition for 1 month, afterwards he was reoperated.

Results: The mechanical bowell obstruction was solved and the causative factor was found to be a pseudocapsulated gelatinous material mimicking a necrotic lymph nodule.

Histopathological examination: foreign material granuloma, solid fibers surrounded by inflammation and fibrosis.

Conclusions: In case of OR application, retention is a rare situation and surgical granuloma should be considered when it is close to the primary resection site.

Cellulose has a variable appearance on CT mimicking tumour recurrence, similar to a lymphoma in PECT if is not reabsorbed.

We advise caution with the use of hemostatic agents and location and use of this material should be noted in the surgical report. Such adverse reaction should be taken into account in oncology. Biopsy may be considered for definitive diagnosis.

P-0300

SURGICAL TREATMENT OF THE MALIGNANT NEOPLASM OF CALACNEUS IN CHILDREN. LONG-TERM RESULTS OF THE RECONSTRUCTION WITH THE ALLOGENIC FEMORAL HEAD GRAFT.

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Purpose/Objective: Malignant neoplasm of calcaneus are very rare in children and constitute 3% of all bone tumors. This report aims to present the method and the result of surgical resection and reconstruction of calcaneus using the allogenic graft of head and collum of femur.

Materials and Methods: Three patients with primary malignant neoplasm of calcaneus (Ewing sarcoma, Synovial sarcoma, Chondrosarcoma). In all pts after tumor removal the reconstruction of the defect was undertaken. The allogenic graft was modeled and it was connected with the tarsal bone using a metal clasp (arthrodesis). The Achilles tendon was sawn to the graft. The limb was immobilized in a plaster.

Results: Early post-operative complications were not observed, but marked edema of the surrounding tissues was always seen. The flexion and extension of the foot were partially maintained. Completeness of resection in all was confirmed microscopically (R0) in all pts. There was no case of graft rejection. Functionally all patients were ambulant without crutches. Oncological outcomes: 1pt died of distant recurrence, 2 are alive. No local recurrences were observed.

Conclusions: The implantation of a large allogenic graft of the head of femur after excision of the calcaneus can assure very good long-term functioning results.

P-0301

OVARIAN GERM CELL TUMORS: PRESENTATION AND MANAGEMENT IN PEDIATRIC AGE GROUP

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Purpose/Objective: To evaluate the presentation, treatment and outcome of the ovarian germ cell tumours in Pediatric age group.

Materials and Methods: All females presented with ovarian tumours between 2008-2012 in the Department of Pediatric Surgery, VM Medical College and SafdarJung Hospital. New Delhi. India, were included in study. They were reviewed for the Presentation, pathology, treatment protocol and outcome.

Results: Nine females with age ranging between 3 to 12 years had ovarian tumours. The most common presentation was lump abdomen ($n = 5$), followed by pain abdomen ($n = 3$) while one was incidental. The alpha feto protein was raised in 4(44%) patients, ranging from 800ng/ml to 2000 ng/ml. Unilateral salpingo-oophorectomy was done in all cases by laparotomy. 3(33%) had malignant germ cell tumours in which 1(11%) had mixed germ cell tumour and 2(22%) had yolk sac tumours. Mature teratoma was the finding in rest of the patients ($n = 6$). One cycle of pre-operative PEB (Cisplatin-Etoposide-Bleomycin) chemotherapy was given in a one patient who presented with abdominal lump and respiratory distress. Post-operative chemotherapy was given in all patients with malignant lesions, of which two responded well (Yolk sac tumour). Recurrence was noted in 1 patient.

Conclusions: Ovarian germ cell tumours are uncommon in pediatric age group and majority of them are benign. Tumour markers are valuable in both pre and post-operative period. Surgery suffices as a treatment in benign lesions, however malignant lesions require both surgery and chemotherapy.

P-0302

IMPLANTABLE CENTRAL VENOUS ACCESS DEVICES IN PEDIATRIC ONCOLOGY PATIENTS

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Purpose/Objective: Minimizing Catheter-Related Blood-Stream Infections (CRBSIs) amongst oncology patients with implantable central venous access devices remains the constant endeavor of every tertiary pediatric oncology unit.

This study aims to examine our unit's experience with placement of these devices and associated CRBSIs.

Materials and Methods: With IRB approval, clinical charts and electronic records of pediatric patients who had ports or Hickman lines placed for administration of chemotherapy between January 1, 2009 and July 31, 2011 were retrospectively reviewed. Data on patients' demographics, diagnoses, full blood counts, number of device-days and CRBSIs were collected and analyzed with the SPSS version 18. Each device placed was followed through still December 31, 2011.

Results: A total of 156 ports and 37 Hickman lines were placed during the study period, giving a total of 96,687 device days. Ninety-eight of these were in leukemic patients and 95 were in patients with pediatric solid tumors. The Absolute Neutrophil Count was 0-12,210/mm^3 (mean 1,631/mm^3) amongst the patients with leukemias and 0*13,980/mm^3 (mean 4,210/mm^3) amongst patients with solid tumors.

119 ports(76%) were placed by specialist surgeons and 37(24%) were placed by surgeons in training. The duration of placement ranged from 20*60 minutes.

The incidence of CRBSI was 0.2 episodes per 1000 device days. There was no significant association between the ANC at port placement and CRBSI. A platelet count of < 50K was however associated with a relatively higher incidence of CRBSI. Procedures that exceeded 40 min were also associated with a higher incidence of CRBSI although surgeon seniority was not a significant factor in predicting CRBSIs.

Conclusions: Our CRBSI rates are comparable to other tertiary institutions managing pediatric malignancies. While neutropenia does not predict for higher CRBSI rates, platelet counts of < 50K and prolonged procedural times were associated with higher incidence of CRBSI.

P-0303

DIFFUSE INFILTRATIVE LIPOBLASTOMATOSIS: A SHORT CASE SERIES

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Purpose/Objective: Lipomatous lesions in children occur as 9 disticnt categories, as described by WHO committee for classification for soft tissue tumors. Lipomas represent 50% or more of these lesions. Lipoblastoma is a rare benign mesenchymal tumor of embryonal white fat that occurs in infancy and early childhood of which about 70% are well-circumscribed and localized and most commonly occurring in the extremities. Those occurring in the retroperitoneum, perineum, intraabdominal and mediastinal are much rarer. 4 cases of diffuse infiltrating lipoblastomatosis occurring in various sites are presented here.

Materials and Methods: Retrospective analysis of children treated in the department of pediatric surgery between 2007 to 2012.

Results: 4 males with ages ranging from 1-4 years presented with painless progressive multiple lumps in various sites such as extremities 2/4, abdomen 2/4, Gluteal region $\frac{1}{4}$, upper back 1/4, mediastinal major vessel infiltration 1/4. Associated features were weakness of the lower extremity 1/4, right hydronephrosis $\frac{1}{4}$, abdominal distension 2/4. CT scan evaluation revealed diffuse infiltrating lesions in all. Surgical excision was undertaken in all but only incomplete excision was possible, of which 2 patients underwent surgical excision twice. 1 child was given chemotherapy as the tumor was causing neurological symptoms leading to

foot-drop of the right lower extremity and infiltration into the sciatic foramen causing sciatic nerve entrapment could not be dealt with surgically. Residual tumor is present in all children. Recurrence occurred in 2 patients in the lesions at the back and infraaxillary region, re-excision is awaited. The child with intrathoracic lesion underwent partial excision and later abandoned treatment as he switched to alternate medicine. Histopathology in all children revealed lipobastoma or lipoblastomatosis.. Genetic/chromosomal analysis is awaited.
Conclusions: Though lipoblastoma and lipoblastomoses is a benign condition and malignant transformation or metastases is not known, these infiltrative lesions cause significant morbidity in our experience.

POSTER SESSION: POSTER SESSION - RADIATION ONCOLOGY (PROS)

P-0304

FRACTIONATED REIRRADIATION (50 TO 54 GY) USING INTENSITY MODULATED RADIATION THERAPY (IMRT) FOR ISOLATED TUMOR BED RECURRENCE IN CHILDREN WITH EPENDYMOMA

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Purpose/Objective: To determine the outcome of children with isolated tumor bed recurrence after surgery and reirradiation for ependymoma
Materials and Methods: Fifteen children were treated with fractionated reirradiation (2RT) for isolated tumor bed recurrence from ependymoma. There were 9 males (60%) with a median age of 7.4 years (3.2-17 years) at 2RT. The most common location was posterior fossa in 11 (73%) while the most common tumor grade was anaplastic in 11 (73%). All patients underwent maximal safe resection followed by postoperative radiotherapy (1RT) for the initial tumor. The median radiotherapy (RT) dose for the initial tumor was 55.8 Gy (50.4-59.4 Gy). Gross total, subtotal and no resection was performed in 11, 3 and 1 patient prior to 2RT. Median time to 2RT was 43 months (22-74 months) after end of first RT course (1RT). Median 2RT dose was 54 Gy (50.4-54 Gy). For both 1RT and 2RT, intensity modulated radiotherapy (IMRT) was utilized. Median follow-up was 27 months (3-44 months).
Results: The 1-,2- and 3-year local control and overall survival rates after 2RT were 86.7%, 55.2% and 36.8% and 86.7%, 78.8% and 70% respectively. Nine patients (60%) relapsed after 2RT. The most common pattern of failure was local only in 4, local + distant in 4 and distant only in 1. Age at 2RT, gender, degree of resection, tumor grade, tumor location and time from 1RT to RT were not found to be prognostic for local control and overall survival. One patient developed transient visual field loss within a few weeks after 2RT which resolved on steroids. None of the patients had brain necrosis, myelopathy or secondary malignancy after 2RT.
Conclusions: Fractionated reirradiation using IMRT for locally recurrent ependymoma is feasible. Long-term local control is suboptimal but offers a possibility of prolonged survival. Disseminated disease was seen in approximately half of relapsed patients after 2RT.

P-0305

ADVANCES IN TARGETED RADIOTHERAPY FOR PEDIATRIC SARCOMA METASTASES

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Purpose/Objective: To overcome limitations of current therapeutic practices for metastases in pediatric sarcoma patients, we investigated the feasibility and tolerability of delivering focal, ablative radiotherapy (RT) using various stereotactic techniques. Specifically, we describe the use of stereotactic radiosurgery (SRS), spine SRS (SSRS) and stereotactic body RT (SBRT) on local control and palliation of brain, bone and lung metastases from sarcoma in this population.
Materials and Methods: A retrospective analysis was performed of patients
Results: Fifteen patients received stereotactic RT at mean age 17.4 y (range 12-24 y): 7 with lung SBRT, 3 with SSRS, 4 with SRS, and one with SRS + SSRS. Histology was osteosarcoma in 10/15 (66.7%), Ewing sarcoma in 3/15 (20.0%), and unclassified sarcoma in 2/15 (13.3%). Mean RT dose was 40.5 Gy (range 24-50 Gy) in 3-4 fractions lung SBRT, 25.5 Gy (range 24-27 Gy) in 1-3 fractions SSRS, and 18.3 Gy (range 12-20 Gy) in 1 fraction SRS. Four patients (26.7%) are alive at mean 14.25 mo (range 2.5-42 mo) from RT completion. Of 13 evaluable patients, 8 (61.5%) had durable LC, with the others demonstrating local failure at mean 5.2 mo (range 2.5-9 mo) after RT. None of 12 evaluable patients had $>/=$ grade 3 toxicity; 5 (41.7%) had grade 2 pain.
Conclusions: Stereotactic RT is an effective and well-tolerated treatment for improved local control and palliation of isolated metastases in pediatric sarcoma patients. Novel RT approaches using systemic delivery of bone-seeking radium-223 are currently being investigated at our institution for pediatric sarcoma patients with more diffuse metastatic disease.

POSTER SESSION: POSTER SESSION - RETINOBLASTOMA

P-0306

NATIONAL RETINOBLASTOMA (RB) REGISTRY IN INDIA

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Background: A national retinoblastoma registry was set up in India.
Materials and Methods: A descriptive study of all the new cases of the retinoblastoma from 11 centers in India using a common core proforma along with SOP, data entered into excel sheet, both internal/external Quality control done. Duplications removed. Stata 11 was used to analyze data. The survival analysis was done using Kaplan Meier curves.
Results: There were 1561 cases enrolled into the registry from Jan 1, 2009 to December 31, 2011. The median age was 19 months. There are 877 males and 684 females enrolled in the study. The first sign noticed was Leucocoria. The family history of retinoblastoma was seen in 2.56% of the cases. 54% of the cases of retinoblastoma occur before 2 years (SEER data 63% before 2 Years) and 92% of the cases occur before 5 years (SEER data 95%). The unilateral retinoblastoma was seen in 1043 cases (66.8%) and bilateral in 503 Cases (32.2%) cases. In less than 1 year old bilateral was seen in 47.1% and unilateral in 51.4% (SEER data 42% bilateral disease). The IIRS grouping showed 72.3% of the cases were in Group D and E. 30.7% were extraocular by Chantada Staging. The Intraocular retinoblastoma treatment was enucleation in 61.3%, where as extra ocular eyes the treatment was enucleation with secondary chemo-radiotherapy. The follow up was done in 89.6% of the cases with a median follow up of 13.1 months .The median survival time not reached. Both overall and disease free survival studies were done with respect to the age, sex, stage, extra ocular status, risk pathology, laterality and type of therapy.
Conclusion: The survival of 1561 cases of RB enrolled in the RB registry in India is reported.
Acknowledgements: The steering committee of RB registry is acknowledged.
The National Retinoblastoma Registry is a task force project funded by Indian Council of Medical Research IRIS ID NO.2007-0683
References
Retinoblastoma-SEER Pediatric Monograph, J.L. Young, seer.cancer.gov/publications/childhood/retinoblastoma.pdf

P-0307

SYSTEMATIC ANALYSIS OF CURRENT OUTCOMES OF RETINOBLASTOMA FROM INDIA

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Purpose/Objective: Retinoblastoma is highly curable in resource-rich nations. Outcomes are much poorer in resource-limited nations with advanced stage at presentation being a critical adverse factor. The management and outcome of retinoblastoma across India has not been previously described.
Materials and Methods: Electronic databases (Pubmed, Embase, Scopus, Web of Science) were searched to identify studies published from year 2000 onwards. SIOP (2000-2012), ASCO (2000-2012) and PEDICON (2007-2012) annual meeting abstracts were hand searched.
Results: Eleven studies (8 published papers, 3 scientific abstracts) with 2036 patients (range 8-1067) were selected from 829 unique studies. These included one population-based cancer registry (PBCR) report and 10 cohorts/case-series from 6 centers in 6 cities. Unilateral to bilateral disease ratio was 1-9:1. The median age of presentation was 2-3 years Males were 1.1 to 2 times more than females at different centers. Time to presentation ranged from 4.5-12 months and the disease was extraocular in 6-76% of patients.

Treatment strategies were not uniform although there was some stratification by stage. Enucleation was commonly employed in intraocular retinoblastoma. The 5-year overall

survival was 48% in a single population-based cancer registry report. The event-free survival for intraocular retinoblastoma was 77-100% (median 83%, 5 studies) and for regional extension retinoblastoma was 37-43% (median 41%, 3 studies) with variable follow-up. Mortality, progression/relapse rates and treatment abandonment rates were 0-57% (median 16%, 4 studies), 0-52% (median 32%, 5 studies) and 0-60% (median 32%, 7 studies) respectively.
Conclusions: Outcomes of retinoblastoma overall in India are poor with advanced stage at presentation leading to more intense treatment (toxicity), loss of eye/vision, higher relapse and treatment abandonment rates. For intraocular retinoblastoma, outcomes are much better but morbidity is high as eye salvage rates are still poor.

P-0308

RETINOBLASTOMA IN PAKISTAN: OUTCOME WITH LIMITATIONS AND CHALLENGES

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Purpose/Objective: Retinoblastoma is highly curable with survival rate more than 90% in developed countries. However, these cures are less than 50% in developing countries. Aim of this study is to look into clinicopathologic features and outcome of Retinoblastoma at Children Cancer Hospital, Karachi.
Materials and Methods: This is a retrospective chart review and prospective follow up of all cases of Retinoblastoma, who were registered at Children Cancer Hospital, Karachi, Pakistan over a 5 year period (July 2007 * June 2012).
Results: During the 5 years period, 93 cases of retinoblastoma were registered. Males were 55% and 45% were females. Most cases, 36% and 45% were diagnosed at age 1/2-2 years and 2-5 years respectively. Family history were positive in 5.4% cases. Leukocoria (72%), proptosis (34%), visual loss (29%) and squint (13%) were the common presenting complaints. Mean duration of symptoms before presentation were 6.8 month. 56% had unilateral while 43% had bilateral and 1% case had trilateral involvement. Most of our patients presented with extensive diseased eye (72%) and 13% patients had metastasis (CNS, 6%; Bone, 5%; Brain, 2%). 27% patients were managed with upfront enucleation, while another 12% patients eyes were enucleated after chemotherapy. Around 44% cases were left before or during treatment and/or lost to follow up. 56% cases were finally treated, 43% got active treatment while 13% were put on palliative care. 5% patients had progressive disease and 4% were relapsed on treatment. Overall, 36% of our treated patients were expired, out of 11% were palliative deaths. The overall survival including abandonment is 33% while without abandonment included it is 64%
Conclusions: Our data suggest that late and extensive disease at presentation, higher rate of noncompliance with therapy and/or lost to follow-up are the potential problems critically influencing the survival of retinoblastoma patients in our country.

P-0309

NATIONAL REFERENCE UNIT FOR RETINOBLASTOMA: A MODEL OF HIGHLY SPECIALIZED INTEGRAL MANAGEMENT

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Purpose/Objective: A national reference unit for retinoblastoma(RB) agglutinates a highly specialized multidisciplinary team that provides an individualized and integral management to affected patients(p) in order to offer the best opportunities of survival,preservation of visual function and ocular preservation.Our centre achieved the Spanish Health Ministry certificate as National Reference Unit for Retinoblastoma in November 2008. Organization and activity of our reference unit for RB is reviewed.
Materials and Methods: Descriptive analysis of the 60p attended between 1974-2013, established treatments and survival.Review of resources and relationship with another Pediatric Oncology Units.
Results: 60p,unilateral 32(53%)-bilateral 28(47%).New patients 49:1974-2006 13p(mean: $<$ 1/year);2007-2012 33 new p + 3 relapses referred from another hospitals(mean:6 p/year).From 2007-2102 9 children and adolescents+ 2 adults previously treated in other hospitals were referred for follow-up. Family history: 6p(10%):4 bilateral/2 unilateral.6p(10%) were referred from other parts in Spain(2) or Africa..RB1 gene analysis:57/60 (95%).Treatment:a)Enucleation indicated at our unit:45/49p(91%),6/28 bilateral(21%),ocular preservation rate 25%.b)Individualized chemotherapy: vincristine + carboplatin + etoposide for intraocular disease, cisplatine + cyclophosphamide + vincristine + etoposide for advanced disease.) Focal therapy:laser coagulation,cryotherapy and traspupillary thermotherapy.) External radiotherapy 6/49(12%);brachytherapy: 12/49(24%).d)Intrarterial chemotherapy:1p.Follow up:age adapted fundoscopy(+/ − general anesthesia);brain and orbitary MRI along four years in all constitutional RB1 gene mutation carriers;orbitary MRI for two years in patients with unilateral disease who undergo enucleation.3/49 treated patients(6%) died:1 fatal sepsis, 2 tumor progression.10/36p(28%) treated between 2007-2012 received shared attention in their local Oncology Unit for chemotherapy, support treatment or MRI exams. From march 2009 monthly retinoblastoma committee was stablished.Pediatric Mental Health Unit supports patients and families.All patients with bilateral disease and severe visual impairment are also referred to national blind organization.
Conclusions: A national reference unit for retinoblastoma offers and guarantees a highly specialized team for individualized and integral management in all p with RB in order to give the best opportunities for cure. Easy communication with local Oncology Units allows chemotherapy, support treatment and MRI exams, limiting patients attendance at our Reference Unit only when periodic fundoscopy is scheduled.

P-0310

SIOP-PODC RECOMMENDATIONS FOR GRADUATED-INTENSITY TREATMENT OF RETINOBLASTOMA IN DEVELOPING COUNTRIES

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Purpose/Objective: The aim was to develop a retinoblastoma guideline for developing countries since retinoblastoma remains incurable in many regions of the world due to delayed diagnosis, poor treatment compliance and lack of evidence-based recommendations for clinical management.
Materials and Methods: Under the sponsorship of the SIOP-PODC Graduated Intensity Treatment Guidelines Working Group, a dedicated working group for retinoblastoma was created. The participation to the group was open and moderated by a group leader. A series of internet meetings via www.cure4kids.org were scheduled. The proposal was presented at regional SIOP meetings for further discussion. Following a general guideline of the working group, recommendations for 3 different settings mirroring the situation in low, lower-middle income and higher middle income countries were proposed.
Results: Participants from 4 continents participated in the discussions, representing most major treatment groups in developing countries and support organizations. A consensus document was generated and levels of evidence were included in each proposal when available. Recommendations were provided for staging and treatment of unilateral and bilateral retinoblastoma and counseling of families for whom compliance is an issue. The committee has generated guidelines for the clinical management of retinoblastoma in developing countries and developed a classification system based on the resources available in those settings. A manuscript was submitted for publication.
Conclusions: A proposal of a graduated intensity therapeutic guidelines for retinoblastoma was generated by a multidisciplinary group of experts from developing countries. A tool for evaluating the impact of this guideline should be developed.

P-0311

INTRAOCULAR RETINOBLASTOMA: 20-YEARS EXPERIENCE OF A SINGLE CENTER

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Purpose/Objective: As the survival rate in retinoblastoma has increased, preserving vision has become an important issue. The aim of this study is to evaluate the demographic features, treatment, outcome, late effects of intraocular retinoblastoma cases treated in a single institution.
Materials and Methods: Patients with intraocular retinoblastoma treated during 1990-2010 in Istanbul University Oncology Institute and Ophtalmology Department by surgery ± adjuvant chemotherapy(CT) ± radiotherapy or chemoreduction and local opthalmologic therapies, were retrospectively evaluated. Until 2009, the chemotherapy

protocol OPEC (vincristine, cisplatin, etoposide, cyclophosphamide), since 2008, VEC (vincristine, etoposide, carboplatin) was used for 2-6 cycles, depending on response evaluated ophtalmologically after each CT cycle.
Results: 244 eyes of 180 patients (91 males, 89 females), median age of 18 months (2 months-15 years) were treated. 64 had bilateral, 2 trilateral retinoblastoma. Five had familial history. Median follow-up was 6.5 years (26 months-23 years). 124 eyes were group E, 50D, 22C, 31B, and 11 A. Enucleation was done in 138 eyes, 49 eyes required no further treatment. Chemotherapy was used in 62 enucleated eyes due to the choroidal ± optic nerve ± skleral involvement. Neoadjuvant CT was given to 124 eyes (50%) and 133 (%54) eyes were treated with local opthalmologic therapies (transpupillary thermotherapy, cryotherapy, plaque radiotherapy). External beam radiotherapy was administered to 55 eyes. Recently, intra-arterial chemotherapy was used in selected cases. Preserving vision in groups A-C was high. Femoral osteosarcoma was diagnosed 4 years later in a bilateral retinoblastoma. 2 osteosarcomas, 1 meningioma developed within the radiotherapy field in 3 patients after 14 and 11 years, respectively.
Conclusions: In the last decade, as the survival rate in intraocular retinoblastoma has increased, preserving vision has gained importance. Chemoreduction and local ophtalmic therapies enable preservation of vision in most group A-C and some group D tumors. Most group E tumors require enucleation. Intra-arterial chemotherapy may be promising in maintaining globe salvage.

P-0312

MULTIMODALITY TREATMENT FOR INTRAOCULAR RETINOBLASTOMA IN BEIJING CHILDREN'S HOSPITAL FOR 3-YEAR RESULTS

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Purpose/Objective: Beijing Children's Hospital (BCH) have good ophthalmologists and oncologists. We established a multidisciplinary program for intraocular Retinoblastomas (RB) in 2009. We summarized intraocular RB in BCH for 3-year results.
Materials and Methods: We retrospectively reviewed medical records of children with 129 children (180 eyes) presenting with clinically and/or histologically confirmed RB were treated at BCH between Nov 1, 2009 and Nov 30, 2011. Eligible eyes were classified according to the International Intraocular Retinoblastoma Classification (IIRC). Analysis of 180 eyes with intraocular RB managed with adjuvant chemotherapy using vincristine sulfate, etoposide phosphate, and carboplatin (VEC), follow up to Dec 31, 2012.
Results: There were 70 males and 59 females, with a median age of 17 months (range 2 to 84months)at diagnosis. Seventy-eight patients (60%) had unilateral RB. Fifty-one (40%) had bilateral RB, and was diagnosed at a younger mean age (15.8 months) than mean age at diagnosis in unilateral patients (23.2 months). 26 eyes of bilateral RB and 31 eyes of unilateral RB were classified as group E.

Total 127 cases were treated in BCH. With a mean chemotherapy course 5.2(range 1 to 11), seventy-six eyes were enucleated (42%). Thirty-two eyes with advanced intraocular disease were enucleated at the time of presentation. Enucleation was then recommended for 44 of those eyes. Ten enucleated eyes (13%) showed high-risk pathologic features. At the time of follow-up of 29 ((range 2 to 38) months. 8 Cases occurred event. 119 patients (93.7%) were alive. Overall, 50 eyes (42.3%) were successfully preserved without the need for enucleation.
Conclusions: Multimodality treatment for intraocular RB in BCH have a good 3-year results. Chemotherapy using VEC regimen was effective in preventing metastasis. Attempted salvage of eyes with advanced disease was justified, particularly in patients with bilateral disease. We were able to salvage almost half of these eyes.

P-0313

COMPARING THREE VERSUS TWO DRUG-SCHEMES IN INTRAOCULAR RETINOBLASTOMA TREATMENT

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Purpose/Objective: Retinoblastoma is the most frequent ocular neoplasm in pediatrics. Survival after enucleating is as high as 100%. The aim of this study is to compare carboplatin-etoposide (scheme A) versus carboplatin-etoposide-vincristine (scheme B) in patients enucleated with unilateral disease excluding those with positive optic nerve involvement at cut.
Materials and Methods: The retrspective study covers 20 years, registering age, sex,sataging, number of courses of chemotherapy administered, number of toxicity events and status at last visit.
Results: One hundred and seven patients were studied, 51 patients were treated with scheme A and 56 patients with scheme B. There were no differences in clinical variables and coroidal/cribrosa involvement ($p = 0.08$). A total of two hundred sixty seven courses were administered to patients in scheme A, with 7 toxicity events that required hospitalization, and with a 92% EFS. Patients in scheme B received two hundred sixty three courses with 20 toxicity events that required hospitalization, and with 83% EFS.
Conclusions: Despite that both groups of patients had similar clinical variables there were significant differences in toxicity and EFS.

Two drug scheme A (carboplatin-etoposide) presented with less toxicity events, better EFS and lower cost than the three drug scheme B (carboplatin-etoposide-vincristine), therefore we will establish the use of the former as a first choice standard regimen.

P-0314

MULTI-AGENT CHEMOTHERAPY WITH LOCAL TREATMENT SAVED ADVANCED STAGE INTRAOCULAR RETINOBLASTOMA WITHOUT INCREASING RISK OF TUMOR EXTENSION AND SECONDARY MALIGNANCY

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Purpose/Objective: This study is to evaluate the efficacy and complications of primary chemotherapy combined with local therapy in patients with advanced stage intraocular retinoblastoma.
Materials and Methods: We performed retrospective analysis of 132 eyes with intraocular tumors in 98 patients who received primary chemotherapy at Seoul National University Children's Hospital between 1988 and 2012. As a first line chemotherapy, patients received a combination of cyclophosphamide/vincristine/adriamycin/methotrexate, or etoposide/vincristine/cisplatin (or ifosfamide), or cisplatin (carboplatin)/doxorubicin/etoposide/cyclophosphamide (with/without vincristine) (CARDEC). Local treatments were given when regular exam under anesthesia was performed.
Results: The median duration of chemotherapy was 11 months. As a first regimen, CARDEC was administered to 47 patients (48%), and etoposide/vincristine/cisplatin to 39 patients (40%). Tumor control and eye-saving were achieved in 79 out of 132 eyes (59.8%); 42 eyes were salvaged with CARDEC, and 14 eyes with etoposide/vincristine/cisplatin. Eye-saving rate was 100% (14/14 eyes) in IIRC group A tumors, 61.4% (27/44) in group B, 58.8% (10/17) in group C, 58.8% (10/17) in group D, and 36.7% (11/30) in group E. Among 53 eyeballs which were not salvaged and enucleated, only 4 were pathologically classified as over pT3 by AJCC staging. Six saved eyeballs showed relapsed disease, and were enucleated. Two patients with refractory retinoblastoma died from infection during chemotherapy. Five patients with bilateral retinoblastoma and Rb1 gene mutation developed osteosarcoma, and three died during treatment of osteosarcoma. There was no other secondary malignancy during a median follow up of 7.5 years after chemotherapy. Ninety three patients were alive so that overall and event free survival rate in 98 patients was 91.4% and 86.3%, respectively. Six patients administered cisplatin or ifosfamide based regimens developed tubulopathy after treatment.
Conclusions: Primary chemotherapy with local treatment in intraocular retinoblastoma was effective in eye-saving even in group E tumors without increasing risk of tumor extension and secondary malignancy.

P-0315

INTRA-ARTERIAL MELPHALAN THERAPY FOR RETINOBLASTOMA: HACETTEPE EXPERIENCE

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Purpose/Objective: Supraselective injection of intraarterial melphalan (IACT) has been used for treatment of retinoblastoma to improve tumor control and prevent side effects of systemic chemotherapy (SCT). We aimed to report our experience with IACT in intraocular retinoblastoma.
Materials and Methods: Between January 2012 and January 2013 40 eyes of 32 consecutive patients treated with IACT were evaluated.
Results: Median age of 18 males and 14 females were 8 months (ranged 1-120 months-old) at diagnosis. Forty eyes received 79 procedures (1-4 for each eye). Ten newly-diagnosed eyes treated with IACT as first-line treatment and procedures for 30 eyes were performed after 5-16 cycles of SCT due to relapsed or refractory disease. There were 6, 3, 9, 15 and 6 eyes staged as groups A, B, C, D, and E tumors, respectively. At a median follow-up of 8.5 months (ranged 1.2-13.1 months) all patients were alive with complete or very good response in 50% ($n = 24$), stable disease in 25% ($n = 10$) and no response in 25% of eyes ($n = 10$). Eight of 10 nonresponsive eyes were enucleated (1 eye from fist-line IACT group and 9 from after-SCT group). The probability of enucleation-free eye survival (EnFS) was 65% (90% in newly

diagnosed patients, 56% in after-SCT group). Ocular and systemic complications were: ophthalmic artery occlusion in 2 patients and femoral hematoma in 4 patients. Red blood cell transfusions were needed in latter 4 patients. No cytopenia was noted.
Conclusions: The aim of IACT is to achieve complete tumor regression and to spare the eye from enucleation with no complication or disease progression. 21 of 30 heavily pretreated patients were spared enucleation for median 8.5 months with EnFS of 56%. IACT might be used for such patients effectively. It also might be an option for newly-diagnosed patients. Our results should be evaluated cautiously because of short follow-up period.

P-0316

PRELIMINARY RESULTS OF ORGANSAVING TREATMENT FOR INTRAOCULAR RETINOBLASTOMA IN CHILDREN WITH SELECTIVE INTRA-ARTERIAL CHEMOTHERAPY BY MELPHALAN.

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Purpose/Objective: To describe the direct efficiency of conservative management of retinoblastoma (Rb) using selective intra arterial chemotherapy by melphalan as alternative for external beam radiation (EBR) therapy and enucleation.
Materials and Methods: Eight children (10 eyes) had intraocular Rb and received selective intra - arterial chemotherapy (SIAC) since February 2011 till May 2012. SIAC was administrated after system chemotherapy in 4 (6 eyes) from 8 patients with a big residual tumor at indications to EBR therapy with clinical stages of T2a or group C ($n = 3$), T2b or group D ($n = 2$) and T2c or group E ($n = 1$) in the struck eyes; 2 (2 eyes: one with a stage of T2b or group D and another with a tumor of the central localization with a stage of T1b or group B) in 8 patients received therapy by SIAC in a complex with system chemotherapy for strengthening of antineoplastic effect, including to one child with the unique eye. t is carried out in a complex with system chemotherapy for strengthening of antineoplastic effect, including to one child with the unique eye. Last 2 of 8 patients were treated with SIAC as alternative to enucleation because of new retinal, subretinal tumors after initial treatment - systemic chemotherapy with laser treatment or in combination with EBR therapy. Seven of eight children SIAC it was combined with intravitreal introductions of melphalan in the presence of vitreous seeding and/or big vitreous tumor masses.
Results: It was possible to rescue 8 of 10 eyes with indications to EBR therapy or an enucleation. System complications of SIAC weren't observed. Ophthalmic complications were minimal, including lid edema and forehead hyperemia.
Conclusions: Direct results of SIAC with melphalan has shown high effectiveness. Research is necessary for continuing to reliably estimate the long-term results of treatment.

P-0317

RETROSPECTIVE ANALYSIS OF CLINICOPATHOLOGICAL FACTORS IN RETINOBLASTOMA

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Purpose/Objective: Retinoblastoma is the most common intraocular malignant tumor in children and it remains a therapeutic challenge for pediatric oncologists. Histopathological high risk factors (HRFs) are associated with a greater risk of orbital recurrence and distant metastasis and need adjuvant therapy. Therefore, the aim of the present study is to analyze histopathological and clinical parameters in a large series of primary enucleated retinoblastoma.
Materials and Methods: Retrospective analyses of primary enucleated retinoblastoma cases over a period of 3 years from January 2010 to December 2012 were included. All the clinical and histopathological data were retrieved from our medical and laboratory records. Haematoxylin and eosin stained sections were evaluated for tumor differentiation and histopathological high risk factors like choroidal invasion, optic nerve involvement, scleral, iris and ciliary body invasion.
Results: A total of 248 eyes were taken up for the study where age ranged from 2months to 10 years. There was a male preponderance (61.2%). Poorly differentiated (PD) tumors constituted 199 (80.2%) eyes. Extensive necrosis and calcification was found in 108/248 (43.5%) and 98/248 (39.5%) respectively. Histopathologically 61 cases (24.5%) had massive choroidal invasion, 109 (43.9%) had optic nerve involvement, 37 (14.9%) had iris and ciliary body invasion and 17 had scleral invasion. One or more than one histopathological high risk factor were present in 96/248 (38.7%) cases. Extensive necrosis was seen in 99/199 (49.7%) poorly differentiated tumors and in 9/49 (18.3%) well-differentiated tumors. On statistical analysis, PD tumors correlated significantly with necrosis ($p = 0.0001$) and massive choroidal invasion ($p = 0.0263$).
Conclusions: Histopathological high risk factors are present in a significant number of primary enucleated retinoblastoma patients. Presence of higher number of poorly differentiated tumors and histopathological high risk factors may represent tumor progression and need to be treated aggressively with adjuvant therapy and followed up for recurrence and metastasis.

P-0318

GERMLINE RB1 GENE MUTATIONS ANALYSIS IN 60 PATIENTS FROM A SPANISH NATIONAL REFERENCE UNIT FOR RETINOBLASTOMA

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Purpose/Objective: After achiving the Spanish Health Ministry certificate as National Reference Unit for Retinoblastoma (RB) in November 2008, our unit provides an integral management to all RB patients.This multidisciplinary attention includes the analysis of germline RB1 gene mutations that is carried out by an external reference research unit.The results of germline RB1 gene mutations analysis in 60 patients that were attended in our unit from 1974 to 2012 are reviewed.
Materials and Methods: Total patients 60:unilateral 32/60(53%) and bilateral 28/60(47%).Patients with a positive family history: 6/60 (10%), 4 bilateral and 2 unilateral.Molecular genetic testing of RB1 gene included sequencing of exons 1-27 and multiplex ligation dependent probe amplification (MLPA) performed on blood sample DNA.In those cases in which DNA analysis was negative,RT-PCR from mRNA was carried out to identify abnormalities in mRNA processing.
Results: Genetic analysis was completed in 57 out of 60 patients(95%). Molecular studies were not performed in 3 patients diagnosed in the 80s with lost follow-up (1 bilateral/2 unilateral).Overall, mutations were identified in 29/57 patients (51%).Mutations were identified in 25 out of 27 patients with bilateral disease (92%) and in 4 out of 30 patients with unilateral disease (13%).RB1 mutations were identified in all familiar cases (6/6).Analysis of white blood cell DNA identified the mutation in 93% of cases (27/29) while mRNA analysis allow us to detect aberrant mRNA processing in 2 cases,probably indicating deep intron mutations. Identified RB1 gene abnormalities will be described.
Conclusions: In our series 1 out of 2 patients are carriers of germline mutations in the RB1 gene.According to other series, germline RB1 mutations are most often identified in patient with bilateral RB although they can be also found in 13% of our patients with unilateral disease.mRNA testing allows to identify abnormalities in mRNA processing in those patients with bilateral disease or family history in which DNA analysis can be negative.

P-0319

CLINICAL SIGNIFICANCE OF HIGH LEVELS OF SURVIVIN AND TRANSFORMING GROWTH FACTOR BETA-1 PROTEINS IN AQUEOUS HUMOR AND SERUM OF RETINOBLASTOMA PATIENTS

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Purpose/Objective: To evaluate the diagnostic and prognostic value of survivin and transforming growth factor- beta1 (TGF-β1) expression in both aqueous humour and serum of retinoblastoma patients in comparison to the conventional retinoblastoma tumor marker lactate dehydrogenase (LDH) and possible relationship between them with the clinicopathological features of the disease.
Materials and Methods: The study included (28) newly diagnosed children with retinoblastoma in whom enucleation was indicated in at least one eye and (20) age matched children with ophthalmic conditions rather than tumors prepared for intraocular surgeries, served as controls. Seventeen patients who underwent enucleation were included as a follow up group. Histopathological analysis of the enucleated eyes was performed. Venous blood samples (2 mL) and aqueous humor samples (100*150 μL) had been obtained from all children to measure concentrations of survivin, TGF-β1 and LDH proteins before and six months after treatment.
Results: The expression of survivin, TGF-β1 and LDH proteins in serum and aqueous humor of retinoblastoma patients before treatment was statistically higher than the control group (P-values were < 0.01). The mean concentration of the three proteins in serum of retinoblastoma group was reduced after treatment and this reduction was highly statistically significant than the mean concentration before treatment (P-values were ≤ 0.01).A statistically significant positive correlation between aqueous survivin and the presence of optic nerve infiltration (P-value was ≤ 0.05). Meanwhile, there was highly statistically significant positive correlation between aqueous TGF- b1 and differentiation of the tumor (P-value was ≤ 0.01).
Conclusions: The high sensitivity, specificity and accuracy of serum and aqueous humor survivin and TGF-b1 proteins make them promising markers for early detection and follow up of retinoblastoma patients.

P-0320

DOES APOPTOTIC PROTEINS HAVE ROLE IN RETINOBLASTOMA?

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Purpose/Objective: PUMA (p53 up-regulated modulator of apoptosis) is the pro-apoptotic protein which initiates apoptosis by binding to regulatory sites on anti-apoptotic Bcl-2 proteins. They belong to the Bcl-2 protein family which has been proposed to play a key role in the control of apoptosis and in the initiation of the apoptotic pathways. Role of apoptotic proteins (PUMA and Bcl-2) in retinoblastoma (Rb) and its prognostic significance have not been reported in literature till date
Materials and Methods: Prospective analyses of 60 surgically enucleated primary retinoblastoma specimens were imunohistochemically assessed for PUMA and Bcl-2 expression and then confirmed by western blotting. Cytoplasmic staining was considered as positive and the expression was correlated with tumor differentiation and histopathological high risk factors like massive choroidal invasion, scleral invasion, optic nerve invasions etc.
Results: There were total of 45 (75%) cases with poorly differentiated retinoblastoma. Necrosis and calcification was found to be present in 37 and 17 cases respectively. Of the 60 eyes, 20 (33.3%) had massive choroidal invasion, 17 (28.3%) had retrolaminar and cut end optic nerve invasion, 9 (15%) had iris & ciliary body invasion and 5 (8.33%) had anterior chamber invasion. Expression of PUMA was observed in 39/60 (65%) cases whereas Bcl-2 was positive only in 18/60 (30%) cases. The western blotting results correlated with the immunohistochemical expression of PUMA (24kDa) and Bcl-2 (25kDa) proteins. Poorly differentiated tumors showed statistically significant correlation with both PUMA ($p = 0.0011$) and Bcl-2 ($p = 0.0253$). PUMA also correlated well with various histopathological high risk factors.
Conclusions: Both the pro-apoptotic and anti-apoptotic proteins correlated with tumor differentiation and histopathological parameters. Thus, apoptotic regulatory proteins may be useful as poor prognostic markers in patients with Retinoblastoma.

P-0321

EXPRESSION OF ISOFORMS OF POLO-LIKE KINASES IN RETINOBLASTOMA

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Purpose/Objective: Polo-like kinases (PLKs), a family of conserved serine/threonine kinases, are important regulators of cell cycle progression for maintaining DNA integrity. Both isoforms (PLK1 and PLK3) are frequently overexpressed in highly proliferating malignant tumors and this overexpression is associated with poor prognosis. However, the expression of PLK1 and PLK3 in patients with retinoblastoma is still not studied.
Materials and Methods: Prospective analyses of primary enucleated retinoblastoma cases over a period of one year were included. PLK1 and PLK3 protein expression was analyzed by immunohistochemistry in formalin fixed paraffin embedded sections and then confirmed by western blotting in fresh tissue. Expressions of these proteins were correlated with clinical and histopathological parameters.
Results: A total of 30 eyes were taken up for the study in which 9 (30%) eyes had bilateral involvement. There were 17 males and 13 females and their ages ranged from 3mnths-8yr. Poorly differentiated retinoblastoma (PDRB) was present in 22 (73.3%) cases. Necrosis and calcification was found in 16 (53.3%) and 6 (20%) cases respectively. Histopathologically 11 cases had massive choroidal invasion, 14 had optic nerve cut end and retrolaminar invasion, 2 each had scleral and anterior chamber invasion and 3 had iris and ciliary body invasion. Strong expression of PLK1 was observed in 20/30 (70%) cases whereas PLK3 was observed in 22/30 (73.3%). Out of 22 PDRB cases, 15 cases had PLK1 positivity and 16 had PLK3 positivity. PLK3 statistically correlated with massive choroidal invasion ($P = 0.0060$).
Conclusions: Overexpression of PLK1 and PLK3 was more frequent in PDRB cases and with one or more histopathological high risk factor in retinoblastoma. These proteins may serve as poor prognostic markers in retinoblastoma and their inhibitors could be used as future therapeutic target.

P-0322

AUTOPHAGY: A MARKER OF RETINOCYTOMA AND RELATED WITH ITS MALIGNANT TRANSFORMATION

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Purpose/Objective: Retinoblastoma (RB) is the most common childhood eye tumors, while retinocytoma (RC), a benign lesion of RB is rare and researches about it are scare and superficial. The mechanism underlying the malignant transformation from RC to RB is still puzzling and confused. The purpose of the study was to find whether there are some relationships between autophagy and the malignant transformation of RC.
Materials and Methods: We collected 21 specimens having both RB and RC regions from 215 formalin-fixed, paraffin-embedded blocks in recent 3 years. Comparing the discriminatory expression pattern of LC3b by IHC and detecting the autophagosome by electron microscope to confirm to the presence of autophagy. Furthermore analysis the correlation between LC3b and other autophagy related proteins, LC3b, Beclin, PTEN, p27, $p16^{INK4a}$, mTOR and BCL-2, to find the potential regulation mechanism of autophagy in RC.
Results: We found RC cell having lots of autophagic vacuole and high expression level of LC3B, a special autophagy marker. Further compare the expression of LC3B, Ki67, Beclin, PTEN, p27, $p16^{INK4a}$, mTOR and BCL-2 in both RB and RC regions, we revealed Beclin, PTEN, p27 had positive correlation with LC3, and $p16^{INK4a}$ had negative correlation.
Conclusions: Ours finding suggested autophagy play a key role in the malignant transformation of RC and autophagy related proteins could be ideal markers to distinguish RC from RB.

POSTER SESSION: POSTER SESSION - BRAIN TUMOURS

P-0323

A MULTI-CENTRED CLINICAL TRIAL OF CNS GERM CELL TUMORS IN HONG KONG

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Purpose/Objective: To evaluate the incidence and outcome of CNS germ cell tumors.
Materials and Methods: The Hong Kong Paediatric Haematology and Oncology Study Group reports the data on childhood cancers prospectively since 1994. A clinical treatment protocol was started in January 2008. Patients who were suspected to have germinoma received a biopsy, followed by 4 cycles of chemotherapy with carboplatin (600 mg per m^2 on day 1) and ectoposide (150 mg per m^2 per day, day 1 to 3), alternating with ifosfamide (1.8 mg per m^2 per day and etoposide (150 mg per m^2 per day, day 1 to 5), followed by RT. Patients with non-germinomatous germ cell tumors received operation to remove the tumor (if possible), chemotherapy as above for 6 cycles and cranio-spinal radiotherapy.
Results: From 1994 to 2011, there were 111 patients (22% of 504 brain tumor patients) with CNS germ cell tumors. Thirty one patients were treated with a uniformed treatment protocol from 2008. The male to female ratio was 2.9: 1. The median age and follow up period were 11.2 years of age (0.4 to 18.7) and 30.6 months (0.5 to 48.6) respectively. The main clinical presentations were endocrine dysfunction (48.4%), headache (38.7%), vomiting (29%), visual field impairment (19.4%), cranial nerve palsy (19.4%), hemi-plegia (3.2%), convulsion (3.2%) and others (19.4%). The pathology were germinoma ($n = 17$) and non-germinomatous germ cell tumors ($n = 14$). The locations of the tumors were suprasellar ($n = 8$), pineal gland ($n = 15$), bifocal ($n = 4$) and basal ganglia ($n = 2$) and others ($n = 2$). Two patients had spinal metastasis. Fifteen patients had elevated AFP (25.8%) and HCG (22.6%) levels in blood. Nine patients had elevated AFP (12.9%) and HCG (16.1%) levels in CSF. All patients achieved complete remission except 2 patients had partial response. All patients were alive.
Conclusions: With a multi-disciplinary approach, a good outcome is achieved.

P-0324

EVOLVING MANAGEMENT FOR INTRACRANIAL GERMINOMA IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS: REPORT OF 30 CASES

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Purpose/Objective: Combined chemotherapy and either focal-RT(40Gy) in localized or CSI(24Gy) plus boost(40Gy) in disseminated Germinoma(G) was applied in French-SFOP-

TGM90 and SIOP96-armB studies. Ventricular relapse-pattern evidenced after focal-RT led us to introduce, ventricular-fields(24Gy) plus boost(40Gy). We report our experience during the interim-period, before SIOP-CNS-GCT II protocol opening, that will include all age categories.
Materials and Methods: Between [2003-2012], 30 Germinoma patients, median age 17[6-29], 24 males, Pineal(14), Suprasellar(10), Bifocal(6), were referred to Institut-Curie. One patient demonstrated mixed Germinoma-Teratoma. 25 localized G received ventricular-RT plus boost; Proton beam therapy implemented in 2011, was delivered to 13/25. Five patients received Craniospinal-RT(CSI): for ventricular(3) axial(1) dissemination, or incomplete staging(1). Dynamic of specific care for AYA started in 2003.
Results: All 5 CSI were delivered in age group [18-23yrs]. With median follow-up 26mths[3-117], overall survival(OS) is 100%, only 1 local and leptomeningeal with elevated CSF-HCG relapse occurred, at 50mths, in a 19yrs old patient initially metastatic. Salvage treatment delivered conventional chemotherapy(VIP), followed by oral etoposide. Patient is alive at 85mths with stable disease. Non-compliance to follow-up was seen in 3 patients(19, 20, 25yrs). AYA specific psychological follow-up was initiated for 6 cases. Official AYA dedicated structure will open in 2013. Proton-beam delivery required gantry-room with large collimator. Patients dosimetric comparison of proton therapy versus IMRT showed similar conformity-index, lower heterogeneity and reduced isodose-volume at 15 and 10Gy offering better protection of brain parenchyma and cochlea; early tolerance was excellent.
Conclusions: More advanced disease and lower compliance to follow-up after 18yrs, suggests non-optimal medical awareness for young-adults symptoms and supports the need for developing AYA dedicated networks for earlier recognition and diagnosis. Whether optimised protection of normal tissues using proton-beams results in better long-term tolerance of this large and complex volume irradiation has to be documented. Long-term multidisciplinary management including quality of life is necessary.

P-0325

CLINICAL AND RADIOLOGICAL FEATURES OF DIABETES INSIPIDUS IN PAEDIATRIC INTRACRANIAL GERMINOMA

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Purpose/Objective: The pituitary bright spot (PBS) is acknowledged to indicate functional integrity of the posterior lobe. This radiological feature was reviewed along with the incidence and clinical characteristics of diabetes insipidus (DI) in patients with suprasellar (SS) and bifocal (BF) germinoma
Materials and Methods: A retrospective review of all children with intracranial germinoma treated in Toronto, from 2000 to 2012 was performed. Eligible cases had radiological or histological diagnoses of SS or BF germinoma. Data were collected from clinical notes, laboratory results and both diagnostic and most recent MRIs.
Results: Nineteen patients fulfilled inclusion criteria (11 SS, 8 BF; median age 12.5 years (range 6.2*16.8 years)). All patients were alive at a median of 3.3 years follow up (range 0.4 * 11.8 years) after receiving chemotherapy followed by radiotherapy (13 focal/ventricular, 4 whole brain, 2 neuraxis), with only one case of progression. All had DI symptoms at presentation, although desmopressin was commenced and maintained in 17/19 cases (89%). The symptom interval was greater than one year in seven cases (37%). The median diagnostic serum sodium level was 149 mmol/L (range 142 * 185 mmol/L). The PBS was lost in most cases, but was apparent in 6/17 (35%) interpretable cases at diagnosis. Four remained visible at last follow up (range 0.4 * 6.6 years), with three such patients still receiving desmopressin.
Conclusions: Protracted symptom interval for central DI may reflect poor clinical awareness. Explanations for persistence of the PBS in patients with symptomatic DI remain elusive. Evidence from our experience suggests treatment of DI seldom reverses clinical features such that it can be discontinued and does not cause PBS recovery.

P-0326

DOSIMETRIC RESULTS OF THREE TREATMENT PLANS FOR RADIATION OF INTRACRANIAL GERMINOMAS.

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Purpose/Objective: To compare the radiation dose distribution of three treatment plans in five child with intracranial germ cell tumors.
Materials and Methods: A CT scanner for dosimetry was performed and fused with initial pre-chemotherapy MRI. First part of treatment has been delivered in a 'whole-ventricles (WV) PTV'. This PTV included 'WV-CTV' plus 5-mm margin. CTV included WV delineated on CT scan and MRI plus 5-mm margin combined with initial tumor plus margins. The 'WV-PTV' received 24 Gy in 15 fractions of 1.6 Gy. A complement of irradiation was delivered in PTV of the initial tumors. CTV was GTV of initial tumors delineated on initial MRI plus 5-mm margin. This PTV received 16 Gy. Organs at risk were delineated on MRI or dosimetric CT scan.

Dosimetric plans were three-dimensional conformal radiotherapy (3D-RT), intensity-modulated radiotherapy (IMRT), or WV by IMRT and boost by dynamic conformal arc therapy (DCAT).
Results: After comparison of IMRT and 3DRT: for the whole brain, the average of the mean doses was decreased by 2.8 Gy with IMRT, for the temporal lobes by 7 Gy, for the brainstem by 4.3 Gy and for the cochlea by 15 Gy. The average conformality index (CI) was 1.7 vs 2.3 with 3D-RT. Homogeneity index (HI) were comparable.

After comparison of IMRT and DCAT: for the whole brain, the average of the mean doses was decreased by 0.3 Gy with IMRT, for the brainstem by 1,8 Gy and for the cochlea by 2.6 Gy. However, for the temporal lobes, it was increased by 1.5 Gy. The CI were slightly comparable, 1.7 with IMRT vs 1.6. HI was better with IMRT (0.05 vs 0.08).
Conclusions: IMRT leads to the best dose distribution. The spare of organs at risk is clearly improved. These results should convince radiation oncologist to use IMRT with the hope of the decreasing of late radiation-induced effects.

P-0327

VISUAL IMPAIRMENT AND INTRACRANIAL DYSGERMINOMAS

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Purpose/Objective: Dysgerminomas are usually located initially on midline. Localization to optic pathways (OP) have been described. We assessed the incidence of such localization.
Materials and Methods: A blinded central retrospective review of initial imaging and charts of 28 patients with intracranial germinomas was performed. 13 were pineal, 12 supraoptic (7 bifocal), 1 optic nerve, 1 corpus callosum and 1 brainstem.
Results: Among 11 patients that complained of decreased visual acuity (DVA), 6 did not have signs of intracranial pressure: 5 of them had an invasion of OP. Two had normal fundi, 3 abnormal fundi.

Three had a supraoptic mass with contiguous involvement of the chiasma. Another patient had DVA and endocrinological symptoms. The MRI showed pineal tumor. Biopsy revealed a germinoma. CSF bHCG were raised (90UI/L). This ''bifocal'' ''secreting' tumor was treated with chemotherapy and focal radiation on both primaries. He relapsed with a diffuse ventricular and meningeal dissemination. The review showed that the thickening of optic nerves with contrast enhancement was overlooked, and optic nerve wasn't included in the radiation field. The last patient had DVA. The MRI showed a chiasmatic and optic nerve tumor.

Among the 8 other patients with supraoptic germinoma and the 15 patients with others locations, 6 had DVA. Patients with abnormal fundi and/or DVA all had intracranial hypertension. MRI showed no involvement of OP.
Conclusions: Optic pathways involvement of germinoma is not rare and should be discussed in case of thickening of OP. DVA may be secondary to intracranial hypertension and/or to OP invasion. MRI exploring visual pathway is mandatory to adapt radiotherapy in any doubtful case.

P-0328

OUTCOME OF METRONOMIC ORAL ETOPOSIDE TREATMENT IN REFRACTORY AND RECURRENT CENTRAL NERVOUS SYSTEM GERM CELL TUMOURS

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Purpose/Objective: The outcome for patients with recurrent germ cell tumour is sometimes very poor, even with aggressive treatment with high-dose chemotherapy and/or re-irradiation. This is the retrospective analysis of eight patients treated with low-dose oral etoposide(VP-16) for the1st to 4th recurrence, refractory to previous treatments.
Materials and Methods: Eight patients(3 with germinoma and 5 with mixed malignant germ cell tumour) age 10 to 31 years were treated with VP-16 after neuroradiographic and clinical evidence of tumour progression. All had received prior irradiation and six of them received re-irradiation for recurrence. All had been pre-treated with a variety of chemotherapeutic agents and four of them had recurrent lesions after high-dose chemotherapy. VP-16 was administered orally as repeated 21-day course at 50 mg/m^2/d with 7- or 14-day interval between courses. In one patient the dose was reduced to 25/m^2/d for fungal pneumonia.
Results: The major toxicity of oral VP-16 was hematologic, with one patient requiring platelet transfusion due to thrombocytopenia. Though all patient developed treatment-related mild neutropenia, there was no need for support with granulocyte colony stimulating factor(G-CSF). There was no treatment-related death. Of 8 patients assessed, two demonstrated complete response(CR), two partial response(PR) and three stable disease(SD)

and one progressive disease(PD). Response in tumour marker(beta-HCG and/or AFP) was observed in seven. Progression free survival was >11months, >5months, 11months, 12months, 27months, >34months, >56months in each responders.
Conclusions: This demonstrates the good activity of metronomic oral etoposide in the treatment of heavily pretreated patients with recurrent germ cell tumors refractory to any kinds of treatment including craniospinal irradiation and high-dose chemotherapy. This treatment can have a new role in the earlier course of the treatment for recurrent tumours, possibly combined with other agents or modalities.

P-0329

ENDOCRINE COMPLICATIONS IN PAEDIATRIC INTRACRANIAL GERM CELL TUMOURS

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Purpose/Objective: Intracranial germ cell tumor (GCT) is much more prevalent in Asian population than the western world. They often arise around the hypothalamic-pituitary (H-P) axis. The cure rate has much improved but there are significant late complications, including growth and endocrine disturbances. We evaluated frequency and nature of endocrine complications in paediatric patients with intracranial GCT from 2008 to 2011 in Hong Kong.
Materials and Methods: The medical records of 31 patients with GCT were reviewed retrospectively for background, disease-related and treatment-related information. Endocrine dysfunction was determined by clinical and laboratory evaluation. The progression of hormonal deficiency was reflected by the drug dosage.
Results: Of 31 patients diagnosed intracranial GCT in the study period, 17 (55%) were germinoma and 14 (45%) were non-germinomatous germ cell tumors (NGGCT). The median age at brain tumor diagnosis was 11.2 years. The overall survival rate was 100%. Forty eight % (15) of all patients had pineal involvement, 26% (8) had suprasellar involvement and 13% (4) were bifocal (pineal and suprasellar).

Diabetes insipidus (DI) and hypocortisolism were two most common endocrine complications (both were 52%) on presentation, followed by hypothyroidism (45%). Twenty-nine % patients had hyperprolactinemia.

In germinoma, 70.6% patients had DI on presentation, followed by hypothyroidism and hypocortisolism (both 64.7%), hypogonadism and precious puberty (both 5.9%). 29.4% patients had late onset of any endocrine complications. 23.5% patients had at least one endocrine problems improved or resolved during/after treatment.

In NGGCT, 35.7% patients had hypocortisolism on presentation, followed by DI (28.6%), hypothyroidism (21.4%) and precocious puberty (14.3%). 42.9% patients had late onset of any endocrine complications. 14.3% patients had at least one endocrine problems improved or resolved during/after treatment.
Conclusions: Endocrine disturbances are common in intracranial GCT. Timely assessment and long term surveillance of endocrine functions are pertinent to minimize morbidity and benefit from early medical intervention.

P-0330

NEOADJUVANT CHEMOTHERAPY IN METASTATIC MEDULLOBLASTOMA: CHANGING PARADIGMS

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Purpose/Objective: Treatment-related morbidity is a major concern in medulloblastomas, particularly because of surgical complications. Preoperative chemotherapy may be useful to decrease morbidity and enhance the efficacy of surgery
Materials and Methods: Seventy one children were treated for a metastatic medulloblastoma in a single reference center. We retrospectively compared children treated with 2 strategies according to the refering neurosurgical wards. Tumor surgery was performed either at the time of the diagnosis (42 patients) or after neoadjuvant conventional chemotherapy with carboplatin and etoposide (29 patients). Hydrocephalus was usually treated with a ventriculocisternostomy before initiatiation of the chemotherapy. In all the 29 cases treated with neoadjuvant chemotherapy, diagnosis was confirmed by a biopsy either of a metastasis during ventriculocisternostomy or directly of the primitive tumor. Children were treated with different post-operative protocols combining chemotherapy, eventually at high-dose with stem-cell rescue and radiotherapy adapted to age. The current retrospective study was designed to define the correlations between the timing of surgery and the post-operatives complications, neuropsychological outcome, and survival.
Results: Chemotherapy decreased disease extension for 25 patients (86%) and delayed surgery allowed a complete tumor excision more often than with first-line surgery (100% vs 64%, $p = 0.002$). Differing the surgery did not have deleterious consequences on the local control of the tumor, on the rate of post-operatives complications and on patients' survival. Moreover, median IQ score was higher in the group 'delayed surgery' (88,5 vs 71,5), especially for children aged under 5 years at the time of the diagnosis ($p = 0,02018$). The IQ score was not associated with the dose of brain irradiation.
Conclusions: When treatment schedules are adapted to risk of disease and age, surgery-related risk factors then become critical for predicting intellectual impairment. Neoadjuvant chemotherapy significantly leads to more frequent complete tumor excision result and decreases the neuropsychological impairment.

P-0331

A SYSTEMATIC REVIEW OF CURRENT OUTCOMES OF MEDULLOBLASTOMA IN CHILDREN IN INDIA

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Purpose/Objective: To assess current treatment outcomes of children with medulloblastoma in India by a comprehensive review of the published and grey literature.
Materials and Methods: A search of Medline, Embase, Scopus and Web of science (2000 to June 2012) databases were undertaken. Hand searching of abstracts from 12 international and national scientific meetings was done.
Results: Nine studies (six published papers and three scientific abstracts; seven retrospective, two prospective) were selected from 1860 studies. These represent 560 patients (range 20-154 per study) from eight centres in six cities. There were no multi-centre or controlled studies. Median age was 8-12 years and male to female ratio was 1.3-4:1. 60-92% of patients had classic histology while data on staging was not available for most studies.

Treatment strategy was always with upfront surgical resection (+/− CSF diversion procedures) followed by adjuvant treatment which varied. Craniospinal radiotherapy with posterior fossa boost was generally used except when it was omitted/delayed in some studies in those <3 years age. Use of chemotherapy, usually after radiotherapy, was mostly reserved for those with high risk medulloblastoma or <3 years age.

Gross total/near-total resection was achieved in 49-100% of patients (median 78%) in these studies. Event free survival was 24-85% (median 56%) with variable follow-up. Outcomes were superior in average risk (73-85%) than in high risk (34%-70%). Information on late effects was sparse. There was a trend for improved outcomes in recently reportedly series. Molecular sub-grouping based analysis in 40 patients available from 1 centre revealed significantly superior EFS in WNT versus SHH and C group.
Conclusions: A little more than half of children with medulloblastoma in India are expected to get cured of their disease although data from recent prospective studies report outcomes closer to those seen in the Western literature. Prospective studies with protocol-based treatments asking focused clinical research questions should be promoted.

P-0332

HIGH-DOSE CHEMOTHERAPY AFTER RADIATION THERAPY IN CHILDREN WITH MEDULLOBLASTOMA OLDER THAN 3 YEARS OF AGE: MOSCOW NEURO-ONCOLOGY COOPERATIVE GROUP INTERIM RESULTS

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Purpose/Objective: Medulloblastoma (MB) is the most common malignant brain tumor in the childhood. Contemporary treatment regimens, used to treat MB led to improvement the overall and progression free survival. Nevertheless, outcome of high * risk MB is still poor. The purpose of our study, based on SJMB96 protocol, is to improve the progression free survival in high * risk MB group patients
Materials and Methods: From 2007 to 2012, we have enrolled 27 patients at the age of 3 to 18 with pathologically confirmed MB. After primary tumor resection and staging PBSC were mobilized and harvested. Risk stratification based on traditional criterias. Risk adapted radiotherapy (23.4 or 36 Gy CSI and local boost up to 54 Gy) followed One month after completion radiotherapy, all patients received four cycles of high dose chemotherapy that consisted vincristine 1 mg/m^2 two doses per cycle, cisplatin 75mg/m^2 per cycle and cyclophosphamide 2000 mg/m^2 two doses per cycle. At day 0 PBSC transfusion was performed. The average dose of CD34+ cells was $1.29*10^6$/kg (range 0.2 - $2.6*10^6$/kg) for

each cycle. All children received G-CSF until WBC reaches $>2*10^9$/L. Bone marrow recover observed on 12-15th day after transfusion of PBSC.
Results: All patients experienced grade III - IV hematologic toxicity and 59% (n = 16) encountered febrile neutropenia. Two patients developed liver toxicity with elevated hepatic enzymes. Treatment related mortality was observed in two patients (7.4%). The three year PFS for all group patients was 73 ± 10%. PFS for average risk patient was 82 ± 11%, for high-risk patients PFS was 67 ± 16%.
Conclusions: This interim results of our study shows that high * risk MB patients have worse outcome than average risk, and that future molecular stratification is warranted for better understanding of risk groups and outcome improvement.

P-0333

CRANIOSPINAL IRRADIATION USING DIFFERENT MODALITIES OF RADIOTHERAPY IN MEDULLOBLASTOMA PATIENTS

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Purpose/Objective: Treatment approach in meduloblastoma (MB) has changed through the years. The purpose of this study is to assess the prognostic factors for survival of craniospinal irradiation (CSI) with different modalities of radiotherapy (RT) in MB patients.
Materials and Methods: The study was conducted for patients with primary MB treated with CSI from August 1996 through May 2012. Inclusion criteria included no prior history of RT and minimum follow up of 6 months for alive patients. Thirty-four patients (standard risk, N = 21; high risk, N = 13) met such criteria. Median CSI dose was 36 Gy in 20 fractions. The tumor bed received 50-60 Gy at 1.5-2 Gy/fraction. RT technique used were two dimensional RT (N = 11), three dimensional RT (N = 15), volumetric modulated arc therapy (VMAT; N = 3), and tomotherapy (N = 5). Toxicity was scored using the Radiation Therapy Oncology Group (RTOG) scoring system. Univariate and multivariate analyses were performed to define predictors for survival.
Results: The median age at diagnosis was 8 years (range, 2-43) and the median follow-up for alive patients (N = 20) 56 months (range, 9-198). Two and three-year overall survival was 74% and 65%, respectively. Twenty patients underwent complete surgical resection whereas 14 underwent partial resection. Eleven patients received postoperative chemotherapy (CT). Nine patients had grade ≥3 hematological toxicity. Overall, 14 patients died. In the univariate analysis, leptomeningeal and cerebrospinal fluid spread at diagnosis, high risk stage, partial surgery, and CT before RT associated with higher risk of mortality ($p\ p\ =0.004$).
Conclusions: Several factors related to high risk MB patients, particularly cerebrospinal fluid spread at diagnosis, are associated with a higher risk of mortality. Further research is necessary to assess a better treatment approach in high risk MB patients in order to improve the outcome.

P-0334

IMPROVED SURVIVAL OF PATIENTS WITH RECURRENT MEDULLOBLASTOMA TREATED WITH A METRONOMIC AND TARGETED ANTI-ANGIOGENESIS THERAPY

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Purpose/Objective: Patients with relapsed medulloblastoma have a poor prognosis irrespective of salvage therapy used. We report on an updated and extended series of patients with recurrent medulloblastomas treated with an antiangiogenic combination therapy partly included in a previous publication (1).
Materials and Methods: From 11/2006 to 4/2011, nine consecutive children with recurrent medulloblastoma (6 first, 3 multiple recurrences) started treatment with an antiangiogenic multidrug-regime (bevacizumab, thalidomide, celecoxib, fenofibrate, etoposide, and cyclophosphamide) augmented with intraventricular therapy (etoposide and liposomal cytarabine) in seven patients. All patients had received craniospinal irradiation and prior multiagent chemotherapy, including HDCT in one. Median age at start of antiangiogenic therapy was 14 (range 7-24) years. For their current relapse four patients received antiangiogenic therapy only and five patients received some additional therapy (reoperation, local radiotherapy and/or chemotherapy)
Results: As of 2/2013, 5/9 patients are alive at a median of 50 (range 22 to 54) months. Three patients died of tumor progression 63, 27 and 10 months after their last recurrence. One patient died of an accident without signs of tumor progression on MRI 23 months after initiation of antiangiogenic therapy. The remaining five patients are alive for 54, 50, 50, 24 and 22 months, four of them off therapy for 36, 19, 15 and 2 months. Both OS and EFS after 6 months was 100%, after 12 months 88.9 ± 11%, and after 24 months OS was 76.2 ± 15% and EFS 64.8 ± 17%. Therapy was generally well tolerated, toxicities were manageable and quality of life was considered better regarding participation in daily life.
Conclusions: Our results suggest that antiangiogenic metronomic chemotherapy has clinical activity in recurrent medulloblastoma. Further investigation with a formal phase II study is in progress ((MEMMAT); ClinicalTrials.gov Identifier: NCT01356290) and will be extended internationally in 2013.
1 Peyrl et al., Pediatr Blood Cancer, 2011

P-0335

SYSTEMS BIOLOGY OF 10 MEDULLOBLASTOMA CELL LINES IDENTIFIES A MOLECULAR SIGNATURE ASSOCIATED WITH CHROMOSOME 17 ALTERATIONS

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Purpose/Objective: Molecular profiling of medulloblastomas identifies 4 main subgroups, increasingly recognised to be separate diseases. Two are driven by Wnt/β-Catenin signalling (WNT) and Sonic Hedgehog signalling (SHH). No clear molecular drivers have been identified for groups 3 and 4, although patients in these groups exhibit an isodicentric chromosome 17 characterized by 17p loss and 17q gain.
Materials and Methods: Using proteomics, we relatively quantified 3595 proteins in 10 human medulloblastoma cell lines and filtered transcriptomic data to validate significant protein/gene regulation in cell lines and patients with 17q gain or isodicentric chromosome 17.
Results: Six cell lines had a copy number profile consistent with an isodicentric chromosome 17. Two had normal chromosome 17 copy number profiles. Two had disordered chromosome 17. We identified 103 proteins consistently differentially regulated in the 6 cell lines with isodicentric chromosome 17 compared to those with a normal profile. Candidate biomarkers of group 3 and group 4 medulloblastomas included OTX2, TP53, CAV1 and markers of TGF-β pathway inhibition such as TGFB2, DAB2, COL1A2, TGFB1I1, FBN1, FKBP1A and HSPA5.
Conclusions: The protein correlates of the large-scale genomic and transcriptomic changes associated with each medulloblastoma subgroup are not yet defined. We have identified candidate proteins through which the isodicentric chromosome 17 may exert its biological effects.

P-0336

INTRACRANIAL XENOGRAFTING OF EXTRANEURAL DISSEMINATED ANAPLASTIC MEDULLOBLASTOMA IN IMMUNOCOMPROMISED MICE AND SUBSEQUENT IN VIVO BIOLUMINESCENCE IMAGING

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Purpose/Objective: Medulloblastoma (MB) represents the most common malignant brain tumor in children. Although survival has significantly improved within the last decades, prognosis for high risk patients still remains poor. To further investigate the biology of these 'high risk' cells, we established an xenogenic mouse model with the ability for bioluminescence imaging (BLI).
Materials and Methods: MB cells, transduced with a lentiviral vector coding for enhanced green fluorescent protein (eGFP) and firefly luciferase (FLuc), were evaluated by fluorescence microscopy, flow cytometry and in vitro BLI. For intracranial grafting transduced cells were injected i) infratentorially ii) supratentorially into the brains of immunocompromised mice. Tumor growth was evaluated by clinical surveillance and kinetic in vivo BLI. Tumors were histologically analyzed.
Results: After lentiviral transduction, expression of eGFP could be easily detected by fluorescence microscopy and flow cytometry. Analyzing FLuc activity by limited dilution assay and BLI revealed emission of 483 photons/second/cell. When implanting the cells into the brains of immunocompromised mice, there was a 100% penetrance. As few as 500 cells were capable to form tumors. BLI showed a continuously increasing signal after supra- as well as infratentorial grafting. Histology and immunohistochemistry revealed that tumors were identical to the primary tumor. They were anaplastic MBs and showed a high tendency to invade and spread through the cerebrospinal fluid.
Conclusions: We established a highly reproducible anaplastic MB model that closely resembles the morphological (i.e. anaplasia) and biological (i.e. dissemination) features of the primary tumor. Because of lentiviral transduction, noninvasive imaging of in vivo cell

growth is possible thus providing an ideal tool for monitoring tumor biology or treatment effects.

P-0337

GENOMIC ANALYSIS OF MEDULLOBLASTOMA USING CEREBROSPINAL FLUID-DERIVED TUMOR DNA

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Purpose/Objective: Medulloblastoma (MB) is one of the most common malignant brain tumors in children, and has a propensity for cerebrospinal fluid (CSF) dissemination.

This study aimed to assess the feasibility of using DNA from CSF for the detection and quantification of tumor-specific alterations, not only for the diagnosis of CSF dissemination, but also for molecular characterization of tumors, which might aid the assignment of patients into therapeutic regimens tailored according to their molecular genetic profiles.

Materials and Methods: For this purpose, frozen tumor samples, CSF at primary diagnosis and blood as germline control were collected from 30 MB patients. Currently, the DNA samples are being subjected to high-coverage next-generation sequencing together with the DNA from their matched primary tumor and blood samples.

This allows us to identify somatic mutations, which are present in both the primary tumor and metastasis, and, importantly mutations, which are unique to one tumor compartment.

Results: Initial results suggest that the majority of alterations in the primary tumor can also be identified in the CSF. Interestingly, however, several mutations were detected at high allele fraction in the CSF, while being restricted to only a minor fraction of the primary tumor. This may indicate that the cells being seeded into the CSF derive from a distinct subclone within the main tumor bulk, in line with recent reports in mouse models.

Conclusions: In summary, this study shows that genetic testing of CSF from MB patients as a non-surgical approach is feasible for the detection of tumor-specific genetic aberrations in cases, where CSF cytology indicates the presence of tumor cells. Additional post-treatment analyses may allow the monitoring of residual disease and histopathological progression. Thus, in addition to giving important new insights in the molecular dissemination of MB, this technique has the potential to facilitate optimization of tumor characterization and assignment to risk-stratified treatment protocols.

P-0338

MTOR PATHWAY IN THE ASPECT OF MEDULLOBLASTOMA PATHOLOGY AND TREATMENT

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Purpose/Objective: As mammalian Target of Rapamycin (mTOR) plays role in cellular protein synthesis and metabolism, mTOR pathway activation is involved in the pathogenesis of several type of tumors. Our aim was to elucidate its role in medulloblastoma in terms of prognosis and as a therapeutic target.

Materials and Methods: Members of activated mTORC1 pathway (phospho-mTOR and phospho-S6) were examined in cytoplasm by immunohistochemistry in formalin fixed paraffin embedded samples of 40 patients with medulloblastoma and results were compared to clinical features and survival of patients.

In proliferation assays Daoy and UW-228-2 medulloblastoma cell lines were tested by rapamycin (mTORC1 inhibitor) or NVP-BEZ235 (dual inhibitor of mTOR and phosphatidylinositide-3-kinase) in monotherapy and in combination with cytostatic drugs (cisplatin and etoposide). In Daoy and UW-228-2 cell lines components of mTORC1 and mTORC2 complexes were also examined.

Results: In our cohort, single expression of phospho-mTOR or pospho-S6 was observed in 32.5-32.5% of samples, and their coexpression was detected in case 22.5% of samples. Neither of their presence showed correlation with age, gender and histological subtype. Kaplan-Meier survival analysis showed inferior survival of patients with activated mTORC1 (3-year survival rate 55.6% vs 80.0%), which failed to reach significance possibly due to low case numbers. UW-228-2 cells had greater sensitivity to mTOR inhibitors than Daoy cells, possibly caused by its lower expression levels of mTORC1 marker proteins compared to UW-228-2. In both cell lines antiproliferative effect of cytostatic drugs was significantly enhanced with mTOR inhibitors ($P < 0.05$).

Conclusions: Based on our in vitro and clinicopathological studies mTOR inhibitors may have a role in the future treatment in a subset of medulloblastoma patient.

P-0339

PEDIATRIC MEDULLOBLASTOMAS AND NON-NEOPLASTIC CEREBELLUM PRESENT DIFFERENTIAL MICRORNA EXPRESSION: IDENTIFICATION OF PREDICTED PATHWAYS INVOLVED IN TUMORIGENESIS.

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Purpose/Objective: Medulloblastoma (MB) is the most frequent malignant brain tumor in children. Although several studies have been carried, the molecular mechanisms responsible for MB tumorigenesis are not completely known. The aim of this study was to analyze the expression profile of microRNAs is pediatric MB comparing to a pool of non-neoplastic cerebellum.

Materials and Methods: We analyzed 19 pediatric medulloblastoma (13 classic and 6 desmoplastic) samples at diagnosis and 2 non-neoplastic human cerebellum controls (a pool of human non-neoplastic cerebellum, catalogue 540007, Agilent; and a sample of human cerebellum) using the Human miRNA Microarray Kit (V3, 8×15K, Agilent), with 955 microRNA represented. The quality, normalization and statistics analysis of differential expression were analyzed using AgiMicroRna AFE R package with empirical Bayes corrected for multiple test comparison.

Results: Similar miRNA expression profile was observed between the 2 non-neoplastic controls. The comparison between MB with non-neoplastic cerebellum reveled 10 microRNA that were down-regulated in MB. The microT and mirPath (diana.cslab.ece.ntua.gr) algorithms showed that these microRNAs regulate genes involved on cell cycle and tumor development, including MAPK signaling, regulation of actin cytoskeleton, focal adhesion, Wnt signaling, ErbB signaling, TGF-beta signaling pathways.

Conclusions: Our finding suggests a potential role of several pathways in the medulloblastomas development.

P-0340

ALTERNATIVE TARGETS FOR MEDULLOBLASTOMA TREATMENT: POLO-LIKE KINASE 1.

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Purpose/Objective: Medulloblastoma is the most common solid malignant cerebellar tumor in childhood. Even though survival rates attain over 50%, current treatment strategies display long-term severe sequels on patients. Thus, alternative treatments are needed, especially for patients younger than 3 years old that cannot receive radiotherapy. Polo-like kinase 1 (PLK1) is a serine-threonine kinase involved in cell cycle progression that has already been associated with cell proliferation and tumor prognosis. The aim of this study was to evaluate the effects PLK1 inhibition by several specific inhibitors on medulloblastoma cell lines.

Materials and Methods: Here we tested and compared the *in vitro* antitumor activities of four different inhibitors of Polo-like kinase 1 (PLK1) (BI 2536, BI 6727, GW843682X and GSK461364), against UW402, UW473 and ONS-76 MB cell lines. Cells were treated at different concentrations during 24, 48 and 72 hours. Cellular viability, colony formation capacity, apoptosis and cell cycle dynamics assays were performed and results analyzed by one-way ANOVA.

Results: The inhibition of PLK1 with BI 2536, BI 6727, GSK461364 and GW843682X showed an efficient decrease (p

Conclusions: Here we showed that even though all drugs were efficient in their anticancer activity, GSK461364 was the best. These results emphasize the role for PLK1 as a possible potential target to improve medulloblastoma outcome and point to GSK461364 for new opportunities in future therapeutic intervention.

P-0341

RESULTS OF TREATMENT OF ATRT CENTRAL NERVOUS SYSTEM IN CHILDREN

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Purpose/Objective: ATRT is a malignant tumor withaggressive behavior, is more common in young children.
Materials and Methods: We evaluated the results of treatment of 43 patients with histologically confirmed diagnosis of ATRT, which were observed from 2005 to 2012. The median age was 22 months (range 2 months - 15 years). Dominated patients under 3 years - 28 (65%), patients older than 3 years were 15 (35%) patients. Infratentorial tumor location was found in 21 (48.8%) patients, in 2 patients (4.7%) the tumor was located in the kidney and infratentorial, supratentorial - in 20 (46.5%) patients. 24 (55.8%) patients were with M0 stage, 11 (25.6%) had initially metastases or tumor cells, in 8 (18.6%) patients the stage is not specified.

24 (55.8%) patients were treated according the protocol ATRT-2006, 8 (18.6%) patients * CWS, 4 (9.3%) * HIT-SKK, in 7 (16.3%) * non-protocol treatment.
Results: Alive 13 (30.2%) patients, 30 died (69.8%), 26 of them from PD, 4 patients from toxicity, 3 patients are alive with PD. 2 year PFS was 30% ± 0,06, OS was 38% ± 0,06. Median of survival was 18 months, median of PFS - 12 months, median of follow-up - 14 months (range 2-89 months). 2-year PFS was significantly better in patients older than 3 years compared with patients younger than 3 years old - 53% and 14%, respectively, $p = 0{,}004$. 2-year PFS in patients with infratentorial tumor was 44%, with supratentorial - 11% ($p = 0{,}74$). Best results in 2-year PFS is marked by total resection of the tumor - 55%, compared with subtotal - 31% and partial resection - 12% ($p = 0{,}15$).
Conclusions: Patients who received intensive multimodal therapy protocol ATRT-2006 had the best survival rate (43%) compared with other patients, treated with the protocol CWS (12%) and HIT-SKK (18%), $p = 0{,}01$.

P-0342

HIGH-DOSE CHEMOTHERAPY (HDCT) WITH AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (APBSCT) IN CHILDREN WITH ATYPICAL TERATOID/RHABDOID TUMORS (AT/RT): A REPORT FROM THE EUROPEAN RHABDOID REGISTRY (EU-RHAB)

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Purpose/Objective: AT/RT are highly malignant, prognostically unfavorable embryonal tumors predominantly affecting children below the age of 3 years. Long-term survival has been reported following intensive multimodality treatment including HDCT with APBSCT. It is still unclear whether conventional or HDCT offers the best results. A retrospective database analysis was performed to describe the outcome of HDCT in children with AT/RT registered within the EU-RHAB.
Materials and Methods: A total of nineteen patients (male, n = 15; median age at diagnosis 21 months) were included. Tumor location was supratentorial in 11 and infratentorial in 7 patients. One patient had a spinal AT/RT. Eight patients (42%) presented with metastatic disease at diagnosis. A partial or subtotal resection was performed in 11, a total resection in 5 and a biopsy in 3 patients. All patients received conventional chemotherapy prior to HDCT. Radiotherapy was performed in 14 patients (first-line, n = 10; following progression, n = 4). Conditioning included carboplatin (n = 18), thiotepa (n = 17), etoposide (n = 9), cyclophosphamide (n = 5) and melphalan (n = 2). Six patients underwent double APBSCT. Disease status before HDCT was complete remission (CR) in 6, partial remission (PR) in 8, stable disease (SD) in 2, and progressive disease (PD) in 2 patients (data missing, n = 1).
Results: With a median follow-up of 16 months (range, 8-82) 13 patients (68%) progressed. Estimated progression-free and overall survival at 2 years were 29% (± 11%) and 50% (± 12%), respectively. At last follow-up eight patients were alive (first CR, n = 5; second CR, n = 1; PR, n = 1; PD, n = 1). Eleven patients died of PD. Median time-to-progression was 14 months.
Conclusions: Despite HDCT with APBSCT prognosis is poor in AT/RT. Selected patients, however, might benefit from HDCT. The definitive impact of this treatment modality has to be evaluated prospectively in a larger cohort of patients. This will allow defining prognostic parameters in patients with favorable/unfavorable outcome.
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P-0343

A GENE SIGNATURE TO IDENTIFY LONG-SURVIVAL ATYPICAL TERATOID/RHABDOID TUMORS (AT/RT)

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Purpose/Objective: Atypical Teratoid/Rhabdoid Tumors (AT/RTs) are, highly aggressive CNS tumors that most often occur in young children. The outcome is very poor and survival is dismal despite surgery, aggressive chemotherapy and radiation. Although radiation therapy may improve the outcome, it results in devastating side-effects, especially in young children. Therefore, it should be avoided. Isolated reports describe cases of AT/RTs with long-survival with no correlation to age, clinical stage, cranial radiation or extension of surgical excision. We hypothesized that there is a class of AT/RT with a distinctive genetic profile that tends to present with long-survival.
Materials and Methods: We performed high throughput gene expression (GE) profiling using Illumina HumanHT-12 Expression Beadchip Arrays (Illumina, San Diego) of 15 pre-treatment frozen AT/RT samples obtained from 13 children (IRB#2009-13778). One of the patients presented disease-free-survival of over 8 years (99 months) despite incomplete surgical excision. After recurrence, the tumor rapidly progressed with patient's death within 13 months. We evaluated samples from the primary tumor, the relapse and the progression in order to investigate genetic characteristics that could identify long-survival tumors at the time of diagnosis for potential treatment stratification.
Results: Unsupervised hierarchical clustering grouped together the 3 events of the long-survivor (primary, recurrence after 8 years and progression 1 year after relapse) demonstrating its unique genetic profile. A gene signature was defined consisting of 148 genes (FC > 2, FDR < 0.05), whose expression remained unaltered throughout the 3 events of long-survival AT/RT, but significantly differs from short-survival tumors (p-value < 0.05).
Conclusions: Our results suggest that there is a subgroup of AT/RTs that presents potential for long-survival. We suggest a gene signature that, once validated, might be applied to newly diagnosed tumors for prognosis and therapeutic purposes.
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P-0344

ACTIVATION OF ERBB2-ERBB3 SIGNALING PATHWAY IN ATYPICAL TERATOID/RHABDOID TUMORS (AT/RT): POTENTIAL THERAPEUTIC TARGETS

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Purpose/Objective: Atypical Teratoid/Rhabdoid Tumors (AT/RT) are WHO grade IV embryonic CNS neoplasms that are among the most aggressive and lethal malignancies in pediatric oncology. Current treatment involves surgery, radiation therapy and combinations of multiple highly toxic chemotherapeutic agents to which tumors rarely respond. For this

reason, an effective and less toxic treatment is urgently needed. The purpose of this study was to identify new potential therapeutic targets for AT/RTs.
Materials and Methods: We analyzed the gene expression (GE) profiles of 6 AT/RTs and 6 Medulloblastoma (MB) frozen tissue samples (IRB#2009-13778) using Illumina HumanHT-12 Expression Beadchip Arrays (Illumina, San Diego). Fold changes (FC) were calculated and t-test was applied to assess the significance of differentially expressed genes between the AT/RT and MB. Ingenuity Pathway Analysis (IPA, www.ingenuity.com) was used to identify enriched biological functions among differentially expressed genes. Validation: selective genes by real-time PCR and protein expression by immunohistochemistry.
Results: Among the most differentially expressed transcripts between AT/RT and MB, ErbB2/HER-2/EGFR2 (FC = 5.14, p-value < 0.00001) was found to be significantly up-regulated in AT/RTs as well as ErbB3 and downstream genes to HerbB2-HerbB3: SHC (FC = 11.82), TYK2 (FC = 2.25), STAT3 (FC = 2.28), RRAS (FC = 3.2), MAP2K2 (FC = 2.19), c-Myc (FC = 4.94), FOX1 (3.89) and CCND1 (FC = 11.88) all with p-values < 0.05.
Conclusions: The ErbB family of transmembrane RTKs plays an important role in the pathogenesis of many cancers. ErbB2-ErbB3 heterodimers are potent complexes that signal through the RAS-ERK pathway for proliferation and the PI3K/AKT/PKB pathway for survival. It has been shown that using ErbB2 inhibitors provides a survival benefit for patients whose tumors express this receptor. Our findings suggest that ErbB2 and the ErbB2-ErbB3 downstream activated genes might function as new potential therapeutic targets for AT/RTs.

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P-0345

HIGH-DOSE METHOTREXATE IMPROVED SURVIVAL IN PEDIATRIC GLIOBLASTOMA: RESULTS OF HIT-GBM-D

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Purpose/Objective: Survival in pediatric glioblastoma has remained low as none of many single arm treatment high grade glioma protocols provided sufficient compelling outcomes, while sample sizes are too small and the heterogeneity of tumors too large to conduct conventional prospective single tumors randomized prospective trials.
Materials and Methods: The folate antagonist methotrexate (MTX) was tested as single agent in a phase III window study with pediatric glioblastoma. Patients were randomized to receive or not receive two cycles of MTX 5g/msqr over 24 hours, leukovorin at hour 42. All patients were further treated with induction therapy with radiation and simultaneous cisplatin etoposide vincristine and ifosfamide followed by maintenance chemotherapy with lomustine prednisone and vincristine.
Results: 39 pediatric glioblastoma patients were randomized in 29 institutions. 24 patients were male; the median age was 10.5 years (range 4.1 to 16.7). Tumor locations were: cerebral cortex 11, lateral ventricle 1, third ventricle and basal ganglia 8, pons 4, cerebellum 5, and spinal cord 1, and overlapping brain regions: 6. Three tumors were metastatic at presentation. Surgeries were classified as gross total resection 7, subtotal resection 13, partial resection 14, and biopsy only 5. 20 patients received methotrexate. The median overall survival was 1.1 years. The toxicity of the synchronous radio chemotherapy was not influenced by MTX given before. Survival was influences by previously known prognostic factors: Superior after gross total resection and inferior for pontine locations. Correcting for these factors using the COX multiple regression model showed superior outcome for patients that received MTX in both overall survival ($p = 0.009$ for OS and $p = 0.00033$ for PFS). Validation of the data in a larger but not randomized dataset of the cooperative group confirmed the finding.
Conclusions: We conclude that high dose methotrexate was beneficial for pediatric patients with glioblastoma. The benefit was small and may be increased by giving higher doses of more infusions.

P-0346

BRAIN STEM TUMOR TREATMENT RESULTS IN CHILDREN TREATED WITH RADIATION THERAPY AT THE CHILEAN NATIONAL CANCER INSTITUTE

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Purpose/Objective: Brain stem tumors (BT), because of their location, imply a high surgical risk, which is why diagnosis is most often done by imaging. In Chile BT are treated according to the PINDA protocol. All patients receive radiotherapy (RT) after diagnosis. The objective of this publication is to review the historical patient series of the Chilean National Cancer Institute (CNCI)
Materials and Methods: A retrospective review of every patient treated with BT at the CNCI was performed. We describe the patient population, clinical presentation, treatment received and overall survival. Prognostic factors were explored.
Results: Between November 1993 and December 2011 70 children were evaluated for RT with the diagnosis of BT, out of which 68 were treated. Median age at diagnosis was 7 years. At the time of analysis in June 2012 of the 70 patients 60 had died of disease progression. Median overall survival of patients who received RT was 8.5 months. Overall survival at 1, 2 and 3 years was 31,5%, 14,3% and 12,8% respectively. In univariate analysis high tumor grade in MRI ($p = 0.07$) and diffuse tumor pattern ($p = 0.025$) were negative prognostic factors. In multivariate analysis high tumor grade in MRI ($p = 0.011$) remained a significant negative factor and a higher RT dose was a positive prognostic factor ($p = 0.015$).
Conclusions: The poor results of the treatment of BT at the CNCI are similar with those reported in other centers. Exploration of new combined modality treatments remains and interesting area of research.

P-0347

IMPROVED SURVIVAL WITH CHEMOTHERAPY AS SECOND-LINE TREATMENT IN PATIENTS WITH TYPICAL DIPG AND INITIAL RADIOTHERAPY RESPONSE

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Purpose/Objective: Radiotherapy remains the cornerstone of treatment for children presenting with diffuse intrinsic pontine glioma (DIPG). However, after a transient period of symptom improvement, progression occurs. Several treatment options have been applied at disease progression. So far the efficacy of these second-line treatments remains unclear. The aim of this study is to determine the role of systemic treatment at the time of disease progression in a homogenous cohort of patients with typical DIPG.
Materials and Methods: A validated cohort containing 54 patients with typical DIPG (symptom duration ≤ 3 months, ≥ 2 symptoms of the neurological triad combined with well defined MRI criteria) was used (*Janssens et al. Int J Radiat Oncol Biol Phys 2013*). Poor responding patients, defined as progression within 3 months after the end of radiotherapy, were excluded. Chemotherapy, as second-line treatment compared to 'Best Supportive Care' (BSC) at time of progression was evaluated.

Kaplan Meier graph's were estimated to compare Progression Free Survival (PFS), Time from Progression to Death (TPD), and Overall Survival (OS) in both groups.
Results: Out of 54 patients (median age 7.3 years), 33 met our inclusion criteria: 16 children received BSC and 17 received chemotherapy (Temozolomide $n = 11$; other $n = 6$) at time of progression. Four children who received BSC died within one month after progression.

Between both groups, no difference was observed in median PFS from diagnosis ($P = 0.566$). A significant difference in median TPD (1.5 vs 3.3 months; $P = 0.017$) and OS (8.8 vs 10.5 months; $P = 0.024$) was observed between children who received BSC and chemotherapy, respectively.
Conclusions: Children with typical DIPG and initial response on radiotherapy, had a median OS benefit of 7 weeks when receiving second-line treatment. However, the significant number of patients in the BSC group dying within one month after progression, implies patient selection for chemotherapy indication. (Acknowledgement: Stichting Semmy)

P-0348

PRIMARY GLIOBLASTOMAS OF CHILDREN AND ADULTS AND NON-NEOPLASTIC WHITE MATTER PRESENT DIFFERENTIAL MICRORNA EXPRESSION PROFILE

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Purpose/Objective: MicroRNAs (miRNAs) are small non-coding RNAs able to regulate gene expression at a posttranscriptional level. Alterations in the expression profiles of many miRNAs have been described in several human tumors including central nervous system tumors. The present study aimed to evaluate the miRNAs signature in glioblastomas (GBM).
Materials and Methods: We investigated the global expression of miRNAs in microdissected samples at diagnosis from 28 primary GBM, being 20 adults (10 MGMT methylated and 10 non-methylated) and 8 children compared to 12 non-neoplastic white matter samples using the Human miRNA Microarray Kit (V3, 8×15K, Agilent), with 955 microRNA represented. Changes in miRNA expression levels were detected by microarray analysis using empirical Bayesian approach corrected by FDR (False Discovery Rate), using a $P < 0.05$ and fold-change $\geq |2|$ as cut-off and further *in silico* prediction of targets were made using bioinformatics tools to identify predicted miRNA target genes.
Results: A significant modulation of the expression was found in 38 microRNAs (25 up- and 13 down regulated) in GBM compared to non-neoplastic samples. These miRNAs have predicted target genes involved in cell cycle, apoptosis and cell adhesion molecules and several signaling pathway including VEGF, ErbB e p53. Differences were also found between miRNA expression of GBM from adults versus children (14 up- and 2 down regulated) with the main involved predicted pathways those associated with ErbB, Insuline, mTOR, p53, GnRH, VEGF; GBM from adults with MGMT methylated versus non-methylated (15 up- and 4 down regulated) involved with mTOR, TGFB, ErbB, Wnt, VEGF e Notch pathways; and pediatric patients with GBM and giant cells GBM (35 up- and 2 down regulated) involved in Wnt, p53, Axon Guidance, NOTCH, TGFB pathways
Conclusions: Our findings suggest a potential role of miRNAs in tumorigenesis and progression of GBM, which can contribute to a better understanding and management of this tumor.

P-0349

PRECLINICAL STUDIES OF PEGYLATED- AND NON PEGYLATED LIPOSOMAL FORMS OF DOXORUBICIN AS RADIOSENSITIZER ON ORTHOTOPIC HIGH-GRADE GLIOMA XENOGRAFTS

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Purpose/Objective: Pediatric highgrade glioma (HGG) patients have a grim prognosis. Doxorubicin (DXR) has a marked cytotoxicity against HGG cells in vitro. However, its brain exposure is hindered by the blood*brain barrier. Encapsulation of DXR in liposomes is known to reduce toxicities and to improve brain tumors exposure to DXR. To date, no study compared the biodistribution or the efficiency of nonpegylated (Myocet) and pegylated (Caelyx) liposomal DXR in vivo on HGG. To evaluate the potential radiopotentiation of these agents, we performed a study comparing for the first time the biodistribution and efficiency of Myocet and Caelyx, given at equitoxic doses, on orthotopic HGG xenografts (U87).
Materials and Methods: Treatments started when a tumor was observed on MRI. Mice were randomly assigned into ten groups: control, Myocet or Caelyx alone using 4 or 6 injections for 2 consecutive weeks; Radiotherapy (RT: 2 Gy, once daily, 5 days/week x 2); Myocet and Caelyx groups + RT. DXR biodistribution was assessed by HPLC. Antitumor efficacy was investigated by tumor volume measurements and mice survival.
Results: The Myocet MTD (15 mg/kg) was 37% of the Caelyx MTD (24 mg/kg). Encapsulation ensured a preferential deposition of DXR in tumoral tissue in comparison with normal brain tissue with best tumor/normal tissue AUC ratio of 5.9 for Myocet and 3.6 for Caelyx. Administered alone, both Myocet and Caelyx improved mice survival of 25 and 32% respectively; the difference with the CTRL group is statistically significant only for Caelyx ($P = 0.01$). A supra-additive effect was observed only with the Myocet + RT group ($P = 0.03$), however, the difference in efficiency between Myocet and Caelyx combination with RT is not statistically significant.
Conclusions: A radiosensitizing effect without toxicity of this combination is demonstrated on the U87 human malignant glioma orthotopic xenografts which depends on the liposomal form and schedule.

P-0350

PEDIATRIC MYXOPAPILLARY EPENDYMOMA IS ASSOCIATED WITH A SIGNIFICANT INCIDENCE OF DISSEMINATED OR RECURRENT DISEASE BUT AN EXCELLENT OVERALL SURVIVAL.

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Purpose/Objective: Myxopapillary ependymomas (MPE) are rare in children. Treatment is maximal excision with no consensus on requirements for adjuvant therapy. Specific studies of pediatric MPE are needed to guide decisions.
Materials and Methods: We performed an IRB approved retrospective review of children treated at Dana-Farber/ Children's Hospital Cancer Center between 1982 and 2013. All pathology and available imaging was centrally reviewed. Clinical details including presenting symptoms, treatment and outcome were documented.
Results: 18 patients with confirmed spinal cord MPE were included. Median age was 14 years (range 8-21), and median time of follow up was 7 years (4 months * 29 years).

Presenting symptoms included back pain, leg weakness and sphincter disturbance. Tumors were commonly located within the thoracolumbar spine, contrast enhancing and T2 hyperintense.

Nine children (50%) had disseminated disease at presentation (most commonly within the thecal sac). Dissemination above the primary occurred in 3 patients.

14 children had gross total resection of the primary. 3 received radiotherapy immediately post-operatively. Tumor recurrence was noted in 9 patients, of which 2 had received adjuvant radiotherapy. The most common treatment for recurrence was surgery and/or radiation therapy. Two children received chemotherapy however had significant toxicity.

Ten year EFS was 26% ($\pm$ 14.8%) and OS was 100%. Children with metastatic disease at presentation had lower EFS, with 10 year EFS of 12.7% ($\pm$ 11.9%) in those with metastasis and 57% ($\pm$ 24.9) in children with localized disease ($p = 0.07$). Median time to progression was 2 years (2 months-9 years).
Conclusions: Although children with MPE have a significant incidence of disseminated and recurrent disease, the overall survival is excellent. Treatment should aim to reduce long-term tumor and treatment morbidity and radiation therapy at diagnosis should be avoided. Adjuvant therapy should be reserved for the setting of symptomatic progression where resection is not feasible.

P-0351

DOSE-LEVEL RESPONSE RATES OF MTOR INHIBITION IN TUBEROUS SCLEROSIS COMPLEX (TSC) RELATED SUBEPENDYMAL GIANT CELL ASTROCYTOMA (SEGA)

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Purpose/Objective: TSC is an autosomal dominant multisystem disease that may involve any organ system. Brain lesions affect 95% of individuals with TSC. SEGAs are benign brain lesions that shrink in response to mTOR inhibitors but re-grow once medication is discontinued.
Materials and Methods: Through this retrospective case series, an attempt was made to discover the minimum mTOR inhibitor dose needed to maintain radiological response of SEGA in 6 paediatric patients treated at SickKids since 2007. This study reviews medication doses and blood levels as related to SEGA size on MRIs at 3-month intervals. Blood levels were monitored every 3 months and 2 weeks after dose adjustment, aiming for therapeutic level of 10-15 ng/ml initially. Total dose reduction by 25% was considered after SEGA shrinkage was maintained on at least 2 consecutive MRIs. Further 25% stepwise total dose reduction was executed if subsequent MRI documented stable SEGA size.
Results: All 6 patients demonstrated SEGA shrinkage greater than 50% when treated with mTOR inhibition at therapeutic doses (4-5 mg/m^2). Majority ($n = 5$) were treated with Sirolimus and 1 with Everolimus. When Sirolimus doses were weaned in 2 patients by 50% resulting in levels as low as 8.5 and 1.4 ng/ml, SEGAs regrew by 66% and 32% respectively. In 2 patients, responses have been maintained with 25% decrease in Sirolimus dose and blood levels at 5.6 ng/ml and 10.6 ng/ml respectively. One patient underwent SEGA resection. The patient on Everolimus remains on therapeutic dose.
Conclusions: mTOR inhibition at therapeutic doses is effective in shrinking SEGAs. In this limited experience, doses of < 2 mg/m^2 were insufficient to maintain response, while doses between 2-3 mg/m^2 maintained response in 2 cases. Further investigations to identify optimal dose response relationship will be beneficial in regards to a potential lifelong medication and long-term risks.

P-0352

LONG-TERM OUTCOME OF 3945 CHILDREN DIAGNOSED WITH PEDIATRIC LOW-GRADE GLIOMAS: AN ANALYSIS OF THE SURVEILLANCE EPIDEMIOLOGY AND END RESULTS (SEER) DATABASE

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Purpose/Objective: Children with pediatric low-grade gliomas (PLGG) are known to have improved survival rates compared to adults, however the long-term outcomes of pediatric low-grade gliomas is unknown. We identified patients diagnosed with PLGGs diagnosed between 1973 and 2008 through the Surveillance Epidemiology and End Results (SEER) database to examine outcomes in adult survivors of PLGG.
Materials and Methods: 3945 patients with PLGG and 5952 patients with adult low-grade gliomas (ALGG) were identified and outcome data were retrieved. Variables recorded for each patient included age, year of diagnosis, race, sex, location of tumor, histological diagnosis and grade of tumor, extent of surgery, and whether they received radiation therapy. Outcome data, alive or dead, and time of last follow up (or death) and cause of death were recorded. Cox regression multivariate analysis was performed to identify prognostic factors and Kaplan Meyer survival curves were generated to examine outcome data.
Results: PLGGs have a distinct natural history compared to ALGGs. Adult survivors of PLGG have excellent overall survival, with 30 year survival rates for PLGG of 82.3% compared to 24.4% in ALGG (p value < 0.0001). Strikingly, there were very few deaths after patients transitioned to adulthood, with an overall survival at 30 years of 93 +/− 1.7% after the patients' 23rd birthday suggesting that PLGGs become stable and do not undergo malignant transformation. Histology (fibrillary astrocytoma or LGG not otherwise specified) and treatment with radiation therapy were associated with poorer outcome. Location and extent of surgical resection was not prognostic in multivariate analysis.
Conclusions: While ALGGs have a propensity for ongoing growth and subsequent malignant transformation, PLGGs appear to become stable and do not cause death in adult survivors. Treatment strategies for pediatric tumors should therefore aim for disease control during childhood and adolescence with an emphasis on minimizing long-term toxicities.

P-0353

DIENCEPHALIC SYNDROME IN THE NON-IRRADIATION ERA: A 15 YEAR INSTITUTIONAL EXPERIENCE

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Purpose/Objective: Diencephalic syndrome (DS) is widely considered an adverse prognostic factor in children with hypothalamic/chiasmatic (HC) low-grade gliomas (LGGs). This feature was reviewed along with clinical characteristics, biological correlations, weight recovery and metabolic response to treatment.
Materials and Methods: A retrospective institutional review of children with DS from 1997 to 2012 was performed. Eligible patients had HC lesions and met pre-defined failure to thrive parameters. In selected cases, metabolic rate was assessed using open-circuit calorimetry. Tumour tissue was analysed for *BRAF* fusion and V600E mutation, using reverse-transcription polymersase chain reaction and fluorescence *in situ* hybridisation. Outcomes were compared with an age-matched institutional cohort of 42 non-DS children with HC LGGs.
Results: Nine patients fulfilled inclusion criteria (median age 1.49 years, range 0.55 * 2.69 years), including two Neurofibromatosis Type I (NF1) positive children who were older ($p = 0.005$), and one case with neuraxial disease dissemination. Nystagmus was a common accompanying clinical feature (5/9, 56%). Eighty percent of tumours analysed exhibited *BRAF* fusion. All children received chemotherapy upfront upon DS diagnosis. Importantly, all gained weight shortly after initiating therapy, documented after only six months in eight cases (89%). Although DS patients had an inferior progression-free survival (PFS) when compared to the non-DS cohort (five year PFS: 11% versus 36%; $p = 0.048$), all DS patients remain alive at a median follow up of 5.0 years (range 1.2 * 14.6 years). Furthermore, none of the DS children received radiotherapy. Long-term sequelae included pituitary dysfunction, visual impairment, learning difficulties (4/9, 44%) and excessive weight gain (3/9, 33%).
Conclusions: DS in young children with HC LGGs, irrespective of NF status, appears responsive to chemotherapeutic strategies without radiotherapy. Whilst multiple lines of therapy may be required to overcome disease progression, excellent survival rates can be achieved. Continued surveillance is mandatory to prevent obesity and support affected children with long-term clinical sequelae.

P-0354

DIFFERENTIAL MICRORNA PROFILING IN PEDIATRIC PILOCYTIC ASTROCYTOMA AND NON-NEOPLASTIC WHITE MATTER SAMPLES

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Purpose/Objective: Pilocytic astrocytoma (PA) is the most common tumor of the pediatric central nervous system. Neurofibromatosis type 1 (NF1) is an important inherited tumor predisposition syndrome in which approximately 20% of the patients develop PA. Specific genetic alterations have been described in PA, but the pathogenesis remains poorly understood. MicroRNAs (miRNA) have been found to play an important role in cancer, including NF1 associated tumors, thus the aim of this study was to evaluate the miRNAs signature in samples from pediatric patients with PA and non-neoplastic white matter controls.
Materials and Methods: We investigated the global expression of miRNAs in 16 microdissected samples of pediatric PA (13 sporadic and 3 NF1-associated) and 12 non-neoplastic human white matter samples using the Human miRNA Microarray Kit (V3, 8×15K, Agilent), with 955 microRNA represented. Changes in miRNA expression levels were detected by microarray analysis using empirical Bayesian approach corrected by FDR (False Discovery Rate), using a $P < 0.05$ and fold-change $\geq |5|$ as cut-off and further *in silico* prediction of targets were made using bioinformatics tools to identify predicted miRNA target genes.
Results: We found 16 miRNAs down regulated and 9 up regulated in the group of patients with pilocytic astrocytoma compared to non-neoplastic samples. These miRNAs have predicted target genes involved in cell adhesion molecules, apoptosis process and in several signaling pathway including TGFB, JaK-STAT, ErbB, mTOR, VEGF, insuline, MAPK, Wnt and P53. We observed also 29 miRNA down-regulated in NF1-associated PA when compared to those without NF1 with the main pathways predicted as involved ErbB, MAPK, mTOR and TGFB.
Conclusions: Our findings suggest a potential role of miRNAs in the tumorigenesis of the pilocytic astrocytomas, including NF1-associated, which can contribute to a better understanding and management of these tumors.

P-0355

METASTATIC CHOROID PLEXUS PAPILLOMA IN THE SIOP CHOROID PLEXUS TUMOR 2000 AND 2009 STUDIES

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Purpose/Objective: The Choroid Plexus Tumor (CPT) * International Society of Pediatric Oncology (SIOP) 2009 study has enrolled one patient with metastatic choroid plexus papilloma (CPP). An analysis of data from the CPT-SIOP 2000 study was used to guide prognosis.
Materials and Methods: CPT-SIOP 2000 was an international registry and clinical trial for children and adults with tumors of the choroid plexus. Data from the 2000 study was used to determine how many participants had metastatic CPP. We compared survival rates for patients with metastatic CPP versus no metastases at presentation in the 2000 study to be able to provide direction on a patient currently enrolled on the 2009 study.
Results: Our patient was diagnosed with CPP located in the posterior fossa in 2010 and a spinal tumor in the thecal sac in 2011. Both were resected in 2010 and 2011 respectively. In 2012, he was found to have metastatic lesions bilaterally in the internal auditory canals. He was then enrolled on CPT-SIOP 2009 and treated with chemotherapy and radiation. Of 241 patients in the CPT-SIOP 2000 study, 4 patients with CPP had metastatic lesions at presentation. The mean survival for patients with metastatic CPP at presentation was 4.2 years ($\pm$ 3.1 SE) versus 4.4 years ($\pm$ 0.8 SE) with no metastases at presentation.
Conclusions: Little is known about the behavior of metastatic CPP due to small numbers. International clinical trials may be used to help determine prognostic factors in these rare presentations. An effort to enroll more patients internationally is needed for the CPT-SIOP 2009 study to yield meaningful information.

P-0356

CEREBRAL METABOLIC ASYMMETRY IN CRANIOPHARYNGIOMA PATIENTS AFTER SURGERY AND BEFORE PROTON THERAPY

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Purpose/Objective: To identify regions of injury by fluorodeoxyglucose positron emission tomography (FDG PET) in children with craniopharyngioma after surgery and prior to proton therapy.
Materials and Methods: Between 8/2011 and 2/2013, 22 patients were enrolled on a prospective trial for craniopharyngioma with serial imaging and neurocognitive assessment.

Surgical approach included transsphenoidal resection in 6 patients and open craniotomy in 14. One patient had both and one did not have surgery. Using HERMES Brain Analysis software, left-right asymmetry of the tracer uptake in each of 63 anatomical regions was computed. Regional asymmetry was deemed significant when its Z score exceeded two standard deviations of normal population. Twelve control children with non-CNS related diseases and normal cerebral FDG PET scans were analyzed to verify findings.
Results: Median patient age at diagnosis was 9 years (range, 3-18 years). Time from resection to baseline PET studies ranged from 7 to 227 days (median, 78 days). Significantly decreased glucose uptake occurred mainly in right frontal gyrus (superior and medial), right caudate nucleus, right putamen, and right thalamus corresponding to the surgical approach. It was observed in 6 of 12 craniotomy patients with Ommaya insertion and/or ventriculostomy, in 1 of 3 craniotomy-only patients, and in none of the 6 patients undergoing transsphenoidal surgery only or no surgery. None of the aforementioned uptake asymmetry was significant in control subjects. Patients with significant uptake asymmetry had an average ten-point lower standard score than their counterparts in visual motor integration ($p = 0.054$).
Conclusions: Postoperative FDG PET of craniopharyngioma patients indicated metabolic abnormalities in the right frontal lobe, striatum, and thalamus corresponding to the corridor and extent of surgery. Our results support differences in normal tissue injury based on surgical approach and care to avoid exacerbating pre-existing injury should be considered in the proton therapy treatment planning.

P-0357

PAEDIATRIC CRANIOPHARYNGIOMA: A 30 YEAR RETROSPECTIVE ANALYSIS OF THE WEST OF SCOTLAND EXPERIENCE

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Purpose/Objective: This study aimed to ascertain presenting features, symptom duration, treatment received and the incidence of immediate and long term complications.
Materials and Methods: Retrospective case note analysis from children diagnosed with craniopharyngioma over the last 30 years in the West of Scotland.
Results: Between 1981 and 2010, 27 patients (15 males) aged < 16.0 years were diagnosed. Median age at presentation was 8.5 years (IQR 5.5-10.1). Median symptom duration was 3 months (IQR 1.8-6.0). Mean height, weight and BMI SDS at diagnosis were -1.31, 0.41, 1.71 respectively. Clinical presentation was highly variable - common signs and symptoms included headache 81.4%, lethargy 70.3%, visual disturbance 51.9%, hydrocephalus 50%, weight loss 11%, weight gain 11% and vomiting 18.5%.

Most patients ($n = 22$) were treated with surgery and 11 required further surgery and/or radiotherapy for recurrence. Common long term sequelae included growth hormone deficiency (77.7%), hyperphagia (40.7%), memory problems (33.3%)and visual problems (70% post-treatment compared with 54% pre-treatment). Some patients ($n = 5$) were lost to follow up.
Conclusions: Clinical presentation of craniopharyngioma and symptom duration in our population was highly variable. The majority presented with headaches, cranial nerve palsies and reduced visual acuity. There were significant endocrine, neurological, neurocognitive and ophthalmological morbidities at presentation and in the long term. Recurrence rates are high. It is difficult to compare outcomes over time due to changes in management during the 30 year period. All children with craniopharyngioma require lifelong surveillance to manage disease and treatment related complications and monitoring for potential late effects. This should be in a multidisciplinary paediatric craniopharyngioma clinic which has been successfully established in our institution.

P-0358

MORBIDITY ASSOCIATED WITH MANAGEMENT OF PEDIATRIC CRANIOPHARYNGIOMA PATIENTS:TEN YEARS OF EXPERIENCE IN A DEVELOPING COUNTRY

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Purpose/Objective: To describe the morbidity associated with management of Craniopharyngioma and its effect on quality of life.
Materials and Methods: Retrospective review of pediatric patients
Results: Sixteen patients were identified (nine females). Median age was eight years (3.3-16.5 years). Main presenting symptoms were vision impairment in twelve (75%), headache and vomiting in ten (63%), delayed puberty in two (13%) and one patient had focal neurological deficit. Six patients (38%) had their first surgical resection before referral. Eventually, six (38%) had gross total resection (GTR), and ten (62%) had subtotal resection (STR). Five patients (31%) received focal radiotherapy (> 50Gy) and three received intracystic Interferon for cystic progression.

At a median follow up of 50 months (4-111 months), one patient lost for follow up and two were dead; one after post operative cerebral infarction and the other following status epileptics. At their last evaluation, three of thirteen (23%) had cystic progression. All patients, except one, needed hormonal supplements. Six (46%) had near normal vision, four were blind in one eye, and three had poor vision in both eyes.

Three patients were overweight and two were obese (31%) before any intervention. At their last follow up, one was overweight and seven were obese (50%). One patient had gastric bypass surgery. Three obese patients had abnormal lipid profile tests and four had liver ultrasound showing diffuse fatty infiltration. One patient had esophageal varices and underwent multiple banding procedures and two had elevated HbA1C.

Nine patients (69%) are attending regular schools; only one of them has near normal vision and appropriate weight. Two attended special-needs schools while the other two had left school due to behavioral problems
Conclusions: Morbidity is significant in Craniopharyngioma. Multidisciplinary care is needed to optimize treatment choices in order to decrease complications and improve quality of life.

P-0359

EXPRESSION OF FABP5 AND CRABPII IN CRANIOPHARYINGIOMA AND INHIBITION OF CRANIOPHARYNGIOMA CELLS BY RETINOIC ACID

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Purpose/Objective: Tumor cells undergo proliferation with high level of FABP5 and apoptosis with high level of CRABPII. We aim to study on FABP5 and CRABPII expression in craniopharyngiomas, effect of pharmacological dose of retinoic acid on craniopharyngioma cells, and to improve *in vitro* craniopharyngioma cell cultures.
Materials and Methods: Expression of FABP5 and CRABPII in craniopharyngioma tissue was studied using immunohistochemistry, RT-PCR and Western blot. Tumor specimens were categorized into primary and recurrent group, and into adamantinomatous and papillary groups. Expression of the two molecules was compared. Primary craniopharyngioma cell cultures were established using tissue explants method. Success rate, cell growth curve and cell metabolism were compared to those established using enzyme digestion method. Craniopharyngioma cells were treated using various concentrations of all-trans-retinoic acid(0, 1, 10, 30μM), and cell growth curve, metabolism, morphological change, apoptosis index, expression of FABP5, CRABPII and NFκB were compared in different treatment groups and the control group.
Results: FABP5/CRABPII ratiao was significantly higher in admatinomatous group than that in papillary group, and higher in recurrent group than that in primary group($p < 0.05$). Tissue explant method had higher success rate compared to enzyeme digestion method($p < 0.05$), but cell growth curve and metabolism were similar in successfully established cell cultures($p > 0.05$). Pharmacological level retinoic acid inhibited cell growth and induced cellular apoptosis in dose dependent manner ($p < 0.05$), and apoptosis index in cells treated with 30μM retinoic acid for 12 hours was 38.9%. Also, retinoic acid at pharmacological concentration up-regualted CRABPII, and down-regulated FABP5 and NFκB in craniopharyngioma cells ($p < 0.05$).
Conclusions: High FABP5/CRABPII ratio is correlated to craniopharyngioma recurrence irrespective of pathological type. Tissue explants method is preferred for morphological study of craniopharygnioma with is higher success rate. Retinoic acid at pharmacological level induced craniopharyngioma cell apoptosis via enhancing RAR signaling pathway and inhibiting NFκB signaling pathway.

P-0360

CRANIOPHARYNGIOMA CELL GROWTH CAN BE PROMOTED BY GH AND INHIBITED BY TAMOXIFEN: INVOLVEMENT OF GHR AND IGF-1R

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Purpose/Objective: Hormone replacement therapy is common in postoperative management for patients with craniopharyngiomas. There is concern whether hormonal replacement therapy could increase tumor recurrence. Our aim was to study expression patterns of GH related receptors on the tumor, and to test effect of GH and its mediator IGF-1, as well as tamoxifen on cranioharyngioma cell lines in vitro.
Materials and Methods: Primary cell lines were established from fresh tumor specimen. Expression of GHR and IGF-1R was studied using immunohistochemistry and RT-PCR. Cell lines were treated with various concentrations of recombinant GH(10, 100, 1000ng/ml), IGF-1(100ng/ml) and tamoxifen(0.5, 5, 50μg/ml). Cell growth promotion or inhibition was

studied using Trypan blue dye exclusion test. Expression of GHR, IGF-1R, P-Akt and Akt after treatment was studied using Western blot assay.
Results: Cell lines of 29 specimens from 36 patients were established. There was significant over expression of GHR and IGF-1R on tumor tissue compared to neural tissue. Promotion of cell growth by GH was most prominent at 100ng/ml, while inhibition by tamoxifen was prominent in concentration dependent manner. IGF-1 was most effective in IGF-1R positive cell lines, and it could increase phosphorylation of Akt protein.
Conclusions: Primary cell lines can be established in over 80% of all craniopharyngioma specimens. GH and its endogenous mediator, IGF-1, increase craniopharyngioma growth in cell model, while tamoxifen inhibits its growth. Our study shows that GH replacement bears risk of promoting tumor recurrence, for which chemotherapy may be an option.

P-0361

A TWO-STAGE MODEL FOR IN VIVO ASSESSMENT OF BRAIN TUMOUR PERFUSION AND ABNORMAL VASCULAR STRUCTURE USING ARTERIAL SPIN LABELLING

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Purpose/Objective: The ability to assess brain tumour perfusion and abnormalities in the surrounding vascular structure *in vivo* could provide significant benefits in terms of lesion diagnosis and assessment of treatment response. Arterial Spin Labelling (ASL) is an MRI-based technique for the non-invasive assessment of perfusion. We present a novel 'two-stage' model for processing dynamic ASL data, which offers improved fitting to the 'abnormal' perfusion signal observed in the tumour environment, compared to established 'single-stage' models.
Materials and Methods: ASL was performed in 9 paediatric brain tumour patients (3xgangliogioma, 3xpilocytic astrocytoma, 1xmeningioma, 1xdysembryoplastic neuroepithelial tumour, 1xoptic nerve glioma). Measurements were made at 12 'inflow times', up to 2.4s. The data were fit to the single- and two-stage models. The latter splits the ASL signal into an initial stage arising from non-exchanging arteries (with volume fraction *aBV*, and transit time *aTT*), and a second, exchanging stage in the capillaries (volume fraction 1-*aBV*).
Results: Dynamic ASL data in the tumour environment often displayed 'bi-phasic' behaviour, which could only be captured using the two stage model, and Bayesian Information Criteria was used to confirm the two-stage model was the preferred model in the tumour environment. Across the cohort, the median *aBV* was higher in tumour tissue *cf.* healthy contralateral tissue (0.39, tumour vs. 0.24, healthy), and median *aTT* was longer (1.22s, tumour vs. 1.15s, healthy; both comparisons $p < 0.01$, two-tailed paired t-test).
Conclusions: Hyper-intense regions of *aBV* and *aTT* were observed in the majority of patients, within and around the tumour region. This offers a novel contrast which is not visible using established single-stage ASL models. The increase in *aBV* and *aTT* is likely to represent the dilated and tortuous vascular structure around the tumour, and as such, this methodology provides a means for measuring tumour perfusion and vascular structural abnormalities in a fully non-invasive manner.

P-0362

APPARENT DIFFUSION COEFFICIENT IN PEDIATRIC BRAIN TUMOR GRADING

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Purpose/Objective: Brain tumor grading is essential for making therapeutic decisions and assessing prognosis. Tumor characterization based on MRI morphology alone has been insufficient. Our objective was to determine whether calculated apparent diffusion coefficient (ADC) value correlates with pathologic grade of pediatric brain tumors and therefore allows more accurate tumor characterization.
Materials and Methods: 100 pediatric hospital patients with recently diagnosed primary brain tumors of all histologic cell types who underwent preoperative conventional MRI and diffusion weighted images (DWI) were included in this study. All brain tumors analyzed were either solid-mass lesions or had a solid component suitable for region-of-interest analysis. The average ADC obtained from the solid component of each tumor was compared with the histological tumor grade according to the WHO classification of brain tumors.
Results: We found a signi?cant negative correlation between average ADC and brain tumor histopathologic grade ($P < 0.001$, $r = *0.8$): the higher the tumor grade, the lower the ADC value. The mean ADC values were $1.6 \pm 0.3 \times 10^{*3}$ mm^2/ sec (mean $\pm$ SD) for grade I tumors, $1.32 \pm 0.4 \times 10^{*3}$ mm^2/ sec for grade II tumors, $0.89 \pm 1.8 \times 10^{*3}$ mm^2/ sec for grade III tumors, and $0.66 \pm 1.6 \times 10^{*3}$ mm^2/ sec for grade IV tumors.
Conclusions: ADC values provide an accurate, sensitive, and non-invasive means of grading pediatric brain tumors. A priori tumor grading is useful in timing and treatment planning, especially for tumors in eloquent or surgically inaccessible regions of the brain.

P-0363

CHALLENGES FOR THE FUNCTIONAL DIFFUSION MAP IN PAEDIATRIC BRAIN TUMOURS

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Purpose/Objective: The functional diffusion map (fDM), or parametric response map, has been suggested as a tool for early detection of tumour treatment efficacy. The method consists of a voxel-wise comparison of pre- and post-treatment apparent diffusion coefficient (ADC) maps in tumour areas. We hypothesize that areas of necrosis, tumour grade and tumour change in size may act as confounding factors in the fDM.
Materials and Methods: 34 paediatric patients (19 male, 15 female, aged 4 months to 16.5 years, mean 7.8 years) with brain tumours and who had diffusion-weighted imaging, an MRI modality, as part of their clinical imaging, were enrolled in a retrospective study that examined the fDM. The fDM implemented in MATLAB, was used to analyse the three confounds. A qualitative analysis was carried out to classify tumour response and compare fDM findings to clinical image reports.
Results: Results show that the fDM in areas of necrosis do not discriminate between positive treatment outcome and tumour progression. Furthermore tumour grade alters the behaviour of the fDM: while a decrease in ADC is a sign of tumour progression in high grade tumours, it is a sign of tumour treatment success in low grade tumours. In tumours undergoing a large change in size, our results show that an increase or decrease in ADC outside the tumour overlap region is a reflection of a decrease in ADC to normal tissue, or an increase in ADC to areas of CSF and this should be taken into account in identifying treatment response.
Conclusions: Interpretation of fDM results needs to take into account various factors as well as the underlying biology, of both the tumour and healthy tissue. Areas of necrosis, tumour grade and change in tumour size need to be all taken into consideration when carrying out fDM analysis and interpreting results.

P-0364

18F−FLUOROETHYLCHOLINE (FECH) PET/MRI FUNCTIONAL PARAMETERS IN PAEDIATRIC BRAIN TUMOURS.

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Purpose/Objective: Integrated PET/MRI technology now allows simultaneous functional imaging with two complementary modalities to better characterise of both biology and treatment response of brain tumours in children.
To investigate whether simultaneous ^{18}F-fluoroethylcholine [FECH] PET/MRI with functional semi-quantitative parameters (SUVmax/mean and ADCmean) is a viable option for diagnosis and treatment response assessment, in children with histologically confirmed astrocytic and intra-cranial germ cell tumours
Materials and Methods: Eight children were injected with 250 MBq 18 ^{18}F -Choline and 40 minutes later, transferred onto the PET/MR scanner for a diagnostic work-up before starting chemotherapy and/ or radiotherapy. Four patients also underwent a second PET MRI scan after completing treatment. PET data were acquired simultaneously with the MR sequences. Maximal Standardized Uptake Value (SUVmax) and mean SUV (SUVmean) and Apparent Diffusion Coefficient (ADC) max and mean of the whole tumoural Region of Interest were recorded.
Results: Combining all tumours, mean SUVmax and SUVmean were 1.9 and 1.3 respectively. The mean ADC value was 1179 mm2/s. The areas of ^{18}F- FECH uptake corresponded to areas of contrast enhancement and of restricted diffusion.
There was a significant negative correlation between SUV mean and ADC mean (r: -0.7069 [95%CI]; $p < 0.0567$).
Four patients had response assessment scans 6 weeks after chemo-radiotherapy. In three patients (along with a reduction in tumour size at follow up) there was a decrease in SUV max and mean but an increase in the values of ADC mean. In one patient, while tumour volumetric dimensions were stable, there was a reduction of both SUV max and mean as well as the ADC max and mean.
Conclusions: The results suggest that fluoroethylcholine PET combined with functional MRI has a high degree of sensitivity and specificity may be a better tool for response assessment when compared to conventional cross sectional MRI alone.

P-0365

POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY (PET/CT) IS AN IDEAL OPTION FOR THE DIAGNOSIS OF PEDIATRIC INDIVIDUALS WITH BRAIN TUMORS

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Purpose/Objective: The aim of this study is to investigate the clinical diagnostic effectiveness of ^{18}F-FDG-PET/CT in pediatric patients with brain tumors.
Materials and Methods: According to the diagnoses thirty-five children included in this study were divided into tumor group and non-tumor group. All of them underwent the brain ^{18}F-FDG-PET/CT scan. We reviewed and compared the results of PET/CT scan and standard uptake values (SUV) between two groups. All data were conducted by SAS 8.0.
Results: There were 18 and 17 cases in the tumor group and non-tumor group, respectively. Fifteen cases in tumor group presented as high uptake of lesions after the PET/CT scan. In contrast, majority of cases (15/17) in non-tumor group presented as low uptake. There was statistical difference between groups (P
Conclusions: PET/CT is an ideal optional device for the diagnosis of pediatric individuals with brain tumors. SUV after PET/CT scan suggests the grade of intracranial tumors.

P-0366

TREATMENT OF REFRACTORY TUMORS OF THE CENTRAL NERVOUS SYSTEM (CNS) WITH MONONUCLEAR CELL FRACTIONS INTRODUCED INTO THE SUBARACHNOID SPACE VIA EPIDURAL IMPLANTABLE ACCESS SYSTEMS

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Purpose/Objective: Recurrent, metastatic and chemotherapy-resistant cancer management is one of the unsolved problems faced by oncologists. A promising treatment option is the introduction of mononuclear cell fractions (lymphocytes and monocytes) into the subarachnoid space.
Materials and Methods: From 2006 to 2013 17 patients (aged 2 to 18 years) with different types of CNS tumors (anaplastic ependymomas and glioblastomas) had injections of mononuclear cell fractions introduced into the subarachnoid space. The mononuclear cell fractions were derived from the peripheral blood. Prior to blood withdrawal, the donors * mainly parents of the patients * were treated with G-CSF. Two patients underwent epidural access system implantation. The procedure included a lumbar puncture between the lumbar vertebrae L_4-L5 followed by insertion of a catheter into the subarachnoid space. Because of the long-term application of the system, the catheter was inserted no deeper than 1.5 cm to prevent spinal nerve root injury. After the implantation procedure the catheter placement was confirmed by x-ray. The port was implanted into the soft tissues above right ribs 10-12. The catheter was threaded through the subcutaneous tunnel up to the port. Cells were injected into the subarachnoid space once every 2 weeks during the first 3 months and once a month following that.
Results: 8 patients (47%) achieved remission with no cancer foci detected. 3 patients (17.6%) are currently alive with complete remission and finished treatment. One of them had cancer recurrence 76 months after therapy. He underwent 12 additional cell injections into the subarachnoid space and has been in remission for 18 months. 9 patients (52.9%) died due to cancer progression.
Conclusions: Intrathecal immunotherapy of the CNS tumours by means of mononuclear cell fractions injection is a novel treatment option whose mechanism is not fully understood for now. Epidural implantable access systems aid doctors in providing such treatment and reduce the number of lumbar punctures.

P-0367

MUTATIONAL SCREENING OF MIR-17-92 CLUSTER AND MIR-34A ONCOMIRS BY DNA SEQUENCING METHOD IN CHILDHOOD HIGH-GRADE BRAIN TUMORS

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Purpose/Objective: MicroRNAs are small RNAs acting in physiological cell regulation by controlling gene expressions at translational levels. There are proven associations between different cancers and microRNA mutations/polymorphisms resulting in altered and/or dysregulated expression. Our study aimed to screen DNA mutations/polymorphisms of the oncomir miR-17-92 cluster and tumor suppressor mir-34a coding sequences in childhood high-grade CNS tumors.
Materials and Methods: There were 53 patients (age 0-18 years, 29 males, 24 females) with high-grade CNS tumor, which treatment and follow-up exams were carried out in the Department of Pediatric Oncology, Gazi University Faculty of Medicine. The control group consisted of 27 healthy volunteers with a similar age and gender of the patient group. Genomic DNAs of paraffin embedded tumor tissue ($n = 53$) and peripheral blood samples ($n = 15$) of the patient group and peripheral blood samples of the control group were extracted and analyzed for mutations/polymorphisms of miR-17-92 cluster and mir-34a coding sequences by DNA sequencing method.
Results: There were 44 cases with neuro-epithelial tumors (17 glial, 3 mixt glial-neuronal, and 24 embryonal), and 9 cases with CNS tumors originated from different tissues. Recurrence rate was 41,7% while overall and event-free survival rates were 42% and 17%, respectively. No mutations/polymorphisms (copy number alterations, amplifications, deletions, insertions, duplications, rearrangements, single nucleotide mutations and polymorphisms) were detected in miR-17-92 cluster and mir-34a coding sequences in the peripheral blood and tumor tissue DNAs of the patients and controls.
Conclusions: According to our study results, miR-17-92 and mir-34a expression alterations in high grade CNS tumors proven by many different studies are not the result of the mutations /polymorphisms of the coding sequences of these miRNAs. The expression alterations of these miRNAs can possibly be explained by transcription errors, epigenetic changes or defects in the microRNA biogenesis machinery.

P-0368

SERUM AND CEREBROSPINAL FLUID CHEMOKINES LEVES IN PEDIATRIC PATIENTS WITH BRAIN TUMORS

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Purpose/Objective: Chemokines were originally identified as mediators of the inflammatory process and regulators of leukocyte trafficking. Subsequent studies revealed their essential roles in leukocyte physiology and pathology. Thus, chemokines are crucial for cancer-related inflammation, which can promote tumor development and progression. In this context we aimed to investigate expression of several chemokines in peripheral blood as well as in cerebrospinal fluid (CSF) in children with Central Nervous System (CNS) tumors.
Materials and Methods: Fifty-six children with primary brain tumors were included in the study, while 32 children with non-malignant hydrocephalus served as controls. Determination of the chemokines EGF, Eotaxin, FGF-2, FLT-3 ligand, Fractalkine, IL-8 and MCP-1 as well as of the cytokines IL-6 and TNF-α and the angiogenic factor VEGF-A, was performed by using the chemokines-cytokines map-array Luminex technology.
Results: The main results of the study showed that: a) CSF levels of EGF and Eotaxin were increased significantly in patients with choroid carcinoma ($p < 0.01$), while CSF levels of Fractalkine, IL-8, IL-6 and TNF-α were increased significantly in patients with xanthoastrocytoma, and MCP-1 was increased significantly in patients with glioblastoma and xanthoastrocytoma ($p < 0.01$), b) we found increased serum levels of EGF in patients with craniopharyngioma, glioblastoma and rhabdoid tumors; Eotaxin in craniopharyngioma and oligodendroglioma; FGF2 in oligodendroglioma and xanthoastrocytoma; FLT3-Ligand in ;craniopharyngioma; IL-8 in oligodendroglioma, ependymoma and rhabdoid tumors and finally in glioblastoma, craniopharyngioma and rhabdoid tumors ($p < 0.05$).
Conclusions: Our findings showed for the first time that in pediatric patients with CNS tumors several chemokines are upregulated, possibly playing crucial roles in cancer-related inflammation and repair procedures.

P-0369

RESULTS OF HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF PEDIATRIC BRAIN TUMORS

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Purpose/Objective: Central nervous system (CNS) tumors are the second most common pediatric malignancies with an about 30% 5-year overall survival rate in high-risk group. The aim of this study was to assess the effectiveness of single or tandem high-dose chemotherapy (HDCT) with autologous hematopoietic stem-cell transplantation (auto-HSCT) in this patient group.

Materials and Methods: From October 2006 to December 2012, 31 pediatric patients with high-risk or relapsed medulloblastoma (N = 16), supratentorial PNET (N = 5), germinoma (N = 4), pineoblastoma (N = 2) and atypical teratoid rhabdoid tumor (N = 3), choriocarcinoma (N = 1) received HDCT with auto-HSCT after induction chemotherapy, radiotherapy and surgical treatment. At the moment of HDCT 13 patients were in complete remission (CR), 15 patients were in partial remission (PR) and 3 patients had stable disease (SD). The conditioning regimen for single auto-HDCT consisted of cisplatin, etoposide, and ifosfamide, or carboplatin, etoposide and thiotepa, or thiotepa and temozolomide. In tandem HDCT, the first conditioning regimen was carboplatin and etoposide with intraventricular/intrathecal metotrexat, the second was thiotepa and cyclophosphamide with intraventricular/intrathecal metotrexat.
Results: The median follow-up is 15 months (range, 2*85). All patients with SD at the moment of auto-HSCT died of disease progression. The following therapy toxicity was observed: liver toxicity grade 2-3 (N = 22), skin toxicity grade 3-4 (N = 6), severe mucositis grade 3-4 (N = 16), nausea/vomiting grade 3-4 (N = 10), infectious complications grade 3-4 (N = 18). Overall survival (OS) in all groups was 52% and disease free survival (DFS) was 45%. OS was significantly better among high-risk patients in 1st CR compared to patients in 2nd or following CR: 69% and 30%, respectively (p = 0,05). The same correlation was observed in DFS: 56% and 26%, accordingly (p = 0,04).
Conclusions: HDCT with auto-HSCT in pediatric patients with high-risk CNS tumors may be a feasible option for patients in CR or PR after induction chemotherapy. It is ineffective as a salvage therapy in refractory patients.

P-0370

CANCOL-BRAIN-KIDS: COLLABORATION BETWEEN CANADA AND COLOMBIA FOR PEDIATRIC CNS TUMORS.

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Purpose/Objective: Pediatric Neuro-oncology in developing countries has many unaddressed challenges including late diagnosis, lack of imaging and lack of specialization and guidelines. In Colombia, a middle-income country, there is no data for incidence and outcomes of central nervous system tumors. Despite widely available resources including imaging facilities, pediatric intensive care units in every major oncology centre, and top of the line radiation facilities, treatment of pediatric brain tumors in Colombia remains suboptimal.
Materials and Methods: Major pediatric hematology oncology centers in the capital, Bogota, were visited; facilities and resources were evaluated and in discussion with local colleges, a needs assessment was completed.
Results: In Colombia, with a population of 47,000,000, there are roughly 2,000 new diagnosis of childhood cancer per year, cared for by 65 pediatric oncologists. Out of 400 primary brain tumors, approximately 50% are managed by neurosurgery only; referral to a pediatric oncologist is frequently delayed and multimodal treatment as standard of care is not in place. Therefore, most of them receive radiotherapy as the only treatment. In some institutions, multidisciplinary tumor boards are in place but without participation of essential team members including neurosurgery or radiation oncology. No formal long-term follow-up programs exist.
Conclusions: Significant gaps were identified in the care of neuro-oncology patients in Colombia. The pediatric neuro-oncology team from McMaster Children's Hospital in Canada and members of the Colombian Pediatric Hematology Oncology Association (ACHOP), have established a monthly teleconferenced multidisciplinary tumor board that will provide scientific support and ultimately will enhance patient care.

Discussed cases will populate a database leading to the development of national treatment guidelines.

P-0371

BRAIN TUMORS OF CHILDREN < 18-MONTH-OLD: A POPULATION BASED STUDY

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Purpose/Objective: Objectives: Neoplasms in children
Materials and Methods: Methods: We reviewed our local pediatric brain tumors database obtained prospectively since 1994. Two sets of standard data entry sheet (1994-1999 & 1999-2011) had been used and data entry was performed by data managers. It was crosschecked with the Hong Kong Cancer Registry which collected all local pathology reports of cancer.
Results: Results: From Jan 1994 to Dec 2011 (18 yrs), a total of 504 cases of childhood brain tumors were diagnosed. 51/504 (10%) are children
Conclusions: Conclusion: In our Chinese children population, the 4 commonest brain tumors found in older children were also more common in our patients

P-0372

UNCOMMON TYPES OF BRAIN TUMORS AMONG CHINESE CHILDREN

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Purpose/Objective: Objectives: Pediatric brain tumors are the second commonest group of neoplasm in childhood. We reviewed the epidemiology of the relative uncommon forms of childhood brain tumors in a Chinese population.
Materials and Methods: Methods: It is a population based assessment based on prospective collection of childhood pediatric brain tumors data since 1999. Almost all pediatric oncology patients are admitted to 5 public hospitals in our locality. Standard data entry sheet was used and data entry was performed by full time data managers. It was crosschecked with the Hong Kong Cancer Registry which collected all local pathology reports of cancer.
Results: Results: From Jan 1999 to Dec 2011 (13 yrs), a total of 415 cases of childhood brain tumors were diagnosed. Astrocytoma (including brainstem), PNET (including medulloblastoma), germ cell tumors, ependymoma all together account for 84% (348/415) of all brain tumors cases. The rest of the tumors were divided into uncommon and rare groups. For the uncommon group, their respective incidence/million children (£15yrs)/year were 0.77 for craniopharyngioma; 0.63 for the 3 tumors including atypical teratoid rhabdoid tumor (ATRT); choroid plexus tumors (CPT) and oligodendroglioma; and 0.56 for ganglioglioma. Craniopharyngioma was commonly presented as headache, visual impairment or stunting growth. ATRT & CPT were mainly found in infant or young children and often presented with signs & symptoms of increase intracranial pressure. Oligodendroglioma and ganglioglioma were more common in older children and frequently presented as seizure. For the rare group, they all have an incidence of
Conclusions: Conclusion: Uncommon brain tumors in our Chinese patient cohort can be further divided into uncommon and rare group. They have unique characteristics and future studies on these brain tumors have to be through an international collaborative effort.

P-0373

FOLLOW-UP OF CHILDHOOD BRAIN TUMORS AT MAHAK PEDIATRIC CANCER TREATMENT AND RESEARCH CENTER (MPCTRC), TEHRAN, IRAN

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Purpose/Objective: As Central Nervous System tumors account for second most common childhood malignancies, improving treatment modalities can lead to increase the survival rate of patients. The epidemiological investigations make a large-scale database of analysis for prognostic features of this group. In this study, we examined the epidemiology, treatment and follow-up of childhood brain tumors in patients who referred to MAHAK's Pediatric Cancer Treatment and Research Center (one of the main national referral centers for childhood malignancies in Iran).
Materials and Methods: This cohort (simple sampling) study consisted of 198 children less than 15 years old with CNS tumor who referred to MAHAK's Pediatric Cancer Treatment and Research Center since 2007 to 2010. The unique checklist contained epidemiological features and kind of treatment filled for each individual separately. Data analyzed by SPSS version 19 with Kolmogorov-Smirnov and Chi square tests.
Results: There were 198 children eligible for the study. Out of enrolled patients 125(63.1%) were male and 73 (36.9%) were female. The majority of the tumors were infratentorial (n = 134), and the rest were supratentorial (n = 60) and spinal (n = 4) cases. The mean age was 6.11 ± 3.65 years old. Medulloblastoma (n = 66), low-grade glioma (n = 52) and High-grade glioma (n = 40) were the most common tumors. The most clinical findings were vomiting, headache and impaired vision respectively. Thirty-one (15.7%) patients had relapsed. At the time of this analysis there were 105 (53%) children alive off therapy, 82 (41.4%) deaths, and 11 (5.6%) lost for follow up. The five years survival rate was 78% ± 0.46.
Conclusions: According to the similar previously studies, the epidemiological features are same as worldwide ratio but the survival rate in this investigation was lower. Therefore,

cautious interpretation in the future's investigations is undesirable. Brain tumor-based approach can lead to determine better treatment modalities for increasing cancer burden in pediatric malignancies.

P-0374

POOR OUTCOME OF CHILDHOOD BRAIN TUMORS IN A RESOURCE POOR COUNTRY: INSTITUTIONAL REVIEW FROM CHILDREN CANCER HOSPITAL, PAKISTAN

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Purpose/Objective: To study clinic-pathological features and outcome of childhood brain tumors at Children Cancer Hospital, Karachi, Pakistan.
Materials and Methods: The study includes review of 100 children from October 2009 to January 2013, referred to our facility with diagnosis of brain tumor on histopathology and imaging in case of brain stem glioma. Variables include frequency, age, sex, site, histopathology, resectabilty, chemotherapy, radiotherapy. Final outcome were also measured.
Results: Charts of 100 children with Brain tumor were reviewed. Mean age at diagnosis was 7.5 years age range, (1 month to 18 years).Male to Female ratio was 1.5:1. 70% of the tumors were supratentorial and 25% were infratentorial, 5% were arising from spinal cords. Supratentorial HGG comprises 24% of all childhood tumor followed by posterior fossa Medulloblatoma(18%).Posterior fossa was the most frequently involved site(31%). 37% were lost to follow up before or during treatment, 40% children were put on supportive and comfort care due to very advanced diseases. Neurosurgeons were able to succeed in gross total Resection in 15% of all patients. Radiotherapy was given to 28% of children either with palliative or curative intent. 9% got chemo along with XRT/Surgery. Overall survival in the whole cohort is 19%. Overall survival in actively treated patients (excluding abandonment and palliation) is 29%.
Conclusions: The outcome of brain tumors in this study is dismal. The major reasons are advanced stage disease, high rate of abandonment, lack of surgical expertise and inco-ordination between neurosurgeons, Radiation and Pediatric oncologist

P-0375

VERBAL MEMORY DEFICITS AFTER PEDIATRIC BRAIN TUMOUR TREATMENT

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Purpose/Objective: A majority of children returning to school after brain tumour treatment experience significant learning difficulties after some years. Our purpose is to report a study of four aspects of verbal memory in a group of brain tumour survivors: learning capacity, interference, retention and recognition.
Materials and Methods: 35 children (14 males and 21 females) tested with the Swedish version of the Rey Auditory Verbal Learning Test were selected from our records of patients. Their age at diagnosis varied between 1 and 16 years (mean, 8.0 years; standard deviation, 4.0 years). The tumour was in the posterior fossa in 18 cases and in the cerebrum in 17 cases. 33 children underwent surgical operation, 22 chemotherapy and 21 radiation therapy. The data were analyzed using accepted norms by means of a one-sample t-test for standard scores. The impact of gender, age at diagnosis, time since diagnosis, tumour location, radiation, and hydrocephalus were analysed by means of t-test for independent samples.
Results: Children treated for brain tumour demonstrate significant impairments on the four aspects of verbal memory: they show a low immediate memory span ($p < 0.0001$), learn fewer words and need more repetitions compared with same-aged children ($p < 0.0001$); they report few words from an interference list ($p < 0.0001$), especially after radiation ($p = .047$) and they are sensitive to retroactive interference ($p < 0.0001$), especially when the tumour is situated in the cerebrum ($p = .021$), indicating disruption of memory by the interference list; children exhibit weak recall immediately after interference ($p < 0.0001$) as well as after some delay ($p < 0.0001$), indicating a impaired retention capacity; finally, they recognize fewer words from the learning list ($p < 0.0001$) and the interference list ($p = .024$), indicating an impaired storage capacity.
Conclusions: Child brain survivors demonstrate significant impairments in the four areas of verbal memory suggesting pathology in the hippocampus as well as in the prefrontal-striatal areas. The implications for rehabilitation are discussed.

P-0376

OBESITY AND IMMUNITY IN SURVIVORS OF CHILDHOOD BRAIN TUMORS: A PRELIMINARY REPORT

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Purpose/Objective: Survivors of childhood brain tumors are at higher risk of developing obesity which is not completely understood. Obesity is associated with immune system activation and chronic low-grade inflammation. It has been reported that obese children have higher monocyte and neutrophil counts and this correlates with their inflammatory state. There are no data to document this in survivors of childhood brain tumors. The aim of this study is to investigate the natural history of obesity in survivors of childhood brain tumors and to measure immune system activation and its correlation with BMI Z-Scores.
Materials and Methods: This study included survivors of childhood brain tumors up to 5 years post diagnosis. BMI Z-Score was calculated at diagnosis and annually afterwards (lean = BMI Z-Score $\leq 85^{th}$ percentile; overweight/obese = BMI Z-Score $\geq 85^{th}$ percentile). Correlations were obtained using Spearman rho correlation, and linear regression was used to define correlations of cell counts between lean and overweight/obese survivors.
Results: We included 66 children (low-grade glioma, optic glioma, medulloblastoma, other; 44% female, mean age 8.2 $\pm$ 4.7 years). The majority (83%) had surgery, 34% chemotherapy, and 37% radiotherapy. At diagnosis, 30% of children were overweight/obese, and this rose gradually to 68% by year 5. BMI Z-Scores at diagnosis strongly correlated with BMI Z-Scores for the subsequent years ($P = < 0.001$ for first 4 years and 0.015 for year 5 post diagnosis) regardless of the tumor type. There were no differences between lean and obese children in terms of total white cell count, neutrophil, or T-lymphocytes. Monocyte count at diagnosis correlated negatively with BMI Z-Scores (Correlation coefficient -0.433, $P = 0.005$).
Conclusions: BMI Z-Scores at diagnosis of pediatric brain tumors predict ongoing BMI Z-Scores in survivors. There appears to be a state of reduced inflammation at diagnosis in obese patients. Patients with high BMI Z-Score at diagnosis require more intensive intervention to control weight gain.

P-0377

PHYSICAL FUNCTIONING IN PEDIATRIC SURVIVORS OF CHILDHOOD POSTERIOR FOSSA BRAIN TUMORS

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Purpose/Objective: Survival rates for children diagnosed with posterior fossa brain tumors (PFBTs) have improved significantly over the past several decades and long-term functioning assessments have become priorities. These evaluations have occurred frequently in adults, but only rarely in children. This study describes a cross-sectional assessment of physical functioning in *pediatric* survivors of PFBTs using the Bruininks-Osteretsky Test of Motor Performance (2nd Edition) (BOT-2).
Materials and Methods: Primary analyses compared BOT-2 scores to normative data using one-sample t-tests for each gross motor subscale (Bilateral Coordination, Balance, Running Speed/Agility, Strength) and motor-area composite (Body Coordination and Strength and Agility). Second, the cohort was stratified by diagnostic or treatment variables. Group differences, and groups versus norms, were evaluated using independent two-sample and one-sample t-tests, respectively.
Results: Mean age of 30 participants was 11.4 years (range: 4.9-18.2 years) and mean time from diagnosis was 6.1 years (range: 1.1-16.7 years). Cerebellar astrocytoma (43.3%) and medulloblastoma (40%) were the most common diagnoses. As a group, significantly decreased functioning, compared to norms, in Balance ($p < 0.001$) and Running Speed/Agility ($p = 0.005$) was observed. Specifically in Balance, 21 (70%) participants performed below or well-below average. Participants with a non-astrocytoma performed significantly lower than norms in all areas, independent of age at diagnosis. Survivors with tumors infiltrating the vermis demonstrated significantly lower Body Coordination than norms ($p < 0.001$).
Conclusions: Pediatric survivors of PFBTs demonstrated decreased physical functioning, most notably in balance. These data underscore the need for further research and the implementation of physical activity programs aimed specifically at approaches to minimize physical limitations.

POSTER SESSION: POSTER SESSION - OTHERS

P-0378

A SINGLE-CENTRE EXPERIENCE OF CENTRAL VENOUS LINES IN PAEDIATRIC HAEMATOLOGY/ONCOLOGY PATIENTS OVER 5 YEARS

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Purpose/Objective: Safe central venous access is required for the management of paediatric patients with solid and haematological malignancies. We have retrospectively reviewed our central venous lines (CVL) experience over a five-year period (2007-2012) to determine the prevalence of line-associated complications and predisposing factors for premature line removal.
Materials and Methods: All patients had either a single or double lumen external catheter (Hickman) or Portacath inserted. The choice of catheter for each patient is individualized. The Lothian Surgical Audit System, TRAK, iLAB and case notes were reviewed for patient demographics, surgical details of line insertion, line-associated complications and reasons for removal of line.
Results: 140 patients underwent 213 line insertions, with 80 (57.1%) patients experiencing a line-associated complication (total number of episodes n = 145). Proven infection was the most common complication (77 episodes, 53.1%), followed by blockages (43 episodes, 29.7%), dislodgement (12 episodes, 8.3%), fracture (7 episodes, 4.8%), kinking (2 episodes, 1.4%) and migration (1 episode, 0.7%). The median (range) number of catheter days for single CVL was 309.5 (9-1357) days for Portacaths and 82.5 (15-218) days for Hickman lines. The median catheter duration for double CVL was 198.5 (1-582) days and 112 (0-882) days for Portacaths and Hickman lines respectively. Single Hickman lines had the highest rate of premature removal (42.9%), followed by double Hickman lines (42.6%), double Portacaths (35.7%) and single Portacaths (22.9%). The presence of severe thrombocytopenia ($< 50 \times 10^9$/L) and severe neutropenia ($< 0.5 \times 10^9$/L) at insertion were associated with higher rates of premature removal due to infection (20.0% and 19.6% respectively), compared with CVL with platelet count $\geq 50 \times 10^9$/L and neutrophils $\geq 1.0 \times 10^9$/L (18.3% and 18.2% respectively).
Conclusions: Single Portacaths are the longest surviving central venous lines. The presence of thrombocytopenia and/or neutropenia at the time of insertion may be associated with an increased risk of line sepsis and premature removal.

P-0379

DEVELOPMENT OF GAMMADELTA T-CELL RECEPTOR REPERTOIRE AFTER TCR-ALPHABETA /CD19 DEPLETED HAPLOIDENTICAL STEM CELL TRANSPLANTATION IN CHILDREN

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Purpose/Objective: Recent advances in stem cell manipulation techniques have allowed to optimize cellular composition of HLA-mismatched haploidentical stem cell grafts. TCR-alpha-beta-depletion of haploidentical stem cell graft (father -> child; mother -> child) represents the latest development in processing techniques for the purpose of overcoming HLA-barriers in the absence of an HLA-matched donor.
Materials and Methods: We analyzed immune and haematopoietic reconstitution in 4 children transplanted with TCRalphabeta/CD19-depleted haploidentical stem cell grafts with a special emphasis on gammadelta-T-cell reconstitution by FACS anlysis and spectratype/immunoscope analysis.
Results: Grafts consisted of $8.5 \times$ 10e6 CD34/kg, $8.8 \times$ 10e4 CD3TCRab+/kg, $8.8 \times$ 10e6 CD3TCRgd+/kg, and $17.5 \times$ 10e6 CD16+CD56+/kg BW. Haematopoietic reconstitution was rapid in all patients. T-cell counts reached $> 100/\mu$l after a median of 34 days, 75% of these expressing the gd-TCR. The predominance of gd-T-cells decreased and by day +100 50% of T-cells were positive for the gd-TCR and 46% for the ab-TCR. Gd-TCR Immunoscope analysis revealed the molecular composition of the gd-population: the Vg9-chain was expressed by a median of 54%, Vg2 by 17.6% of gd-T-cells, the remaining Vg-chains by less than 10%, respectively. Vd4-expressing subclones made up 53% of the whole gd-TCR-repertoire, followed by 33.4% Vd2+ subclones. Distribution of gd-subclones was relatively stable over time, so that the contraction of the gd-T-cell population could not be attributed to the disappearance of specific Vg- or Vd families.
Conclusions: These data provide new insight into the rapid T-cell reconstitution kinetics after TCRab/CD19-depleted transplantation.

P-0380

STUDY ON MALIGNANT TRANSFORMATION OF HUMAN UMBILICAL MESENCHYMAL STEM CELLS

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Purpose/Objective: Human umbilical mesenchymal stem cells(HUMSCs) have a relatively high proliferation rate and low immunological rejection as compared with bone marrow mesenchymal stem cells(BMCs). Therefore, clinical application of HUMSCs has been considered promising among other adult stem cells. However, the recent reports of stem cells undergoing malignant transformation spontaneously in vitro and hypothesis of cancer stem cell origin indicate that HUMSCs may risk possibly mutating in vitro. Our research aims to confirm the possible malignant transformation of HUMSCs, seek for a noval mode that can evaluate the security of its clincial application and explore effective methods to prevent HUMSCs from malignant transformation.
Materials and Methods: Primary HUMSCs was isolated and expanded by tissue adherent culture. Secondary passages were treated with 5 ug/ml 3-methycholanthrene (3-MCA) in culture medium for a week. Then the medium was changed twice weekly. Transformed cells were tested for malignancy by the observations of morphological change and proliferation data on an inverted microscope. Transformed cells were injected subcutaneously into immune-deficient mice. Tumor tissue sections were analyzed by histology and immunochemistry to identify tumor types.
Results: About three month after treatment with 3-MCA, the cells demonstrated properties of malignant transformation including morphologic changes, rapid growth, anchorage independence loss of contact inhibition and loss of polarity. After two month tumor was formed in immune-deficient mice. According to histological characteristics and immunochemical data, this tumor derived from transformed HUMSCs by Karyotypic analysis was divided into sarcoma or tumor of poor differentiation.
Conclusions: Our results indicate that HUMSCs which treated with 3-MCA can lead to malignant transformation. It might also represent a potential source of malignancy in vivo. Because of malignant possibility of HUMSCs, its security of clinical application is still need to be verified.

P-0381

CLINICAL STUDY OF POST-TRANSPLANTATION LYMPHOPROLIFERATIVE DISEASES IN CHILDREN WITH ACQUIRED APLASTIC ANEMIA AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Purpose/Objective: To study the epidemiology, clinical characteristics, diagnosis, treatment and prognosis of post-transplantation lymphoproliferative diseases (PTLD) in children with acquired aplastic anemia (AAA) after allogeneic hematopoietic stem cell transplantation (allo-HSCT).
Materials and Methods: The clinical data of children who underwent allo-HSCT with AAA at the institute of Shanghai Children's Medical Center from July 2002 to May 2012, were analyzed. The conditioning regimen included fludarabine, cyclophosphamide and rabbit-antithymocyte globulin with or without total body radiotherapy, and graft-versus-host disease prophylaxis mainly consisted of cyclosporine and methotrexate. For those patients who were monitored by EBV-DNA copies in peripheral blood mononuclear cells after allo-HSCT, a preemptive treatment with anti-CD20 monoclonal antibody rituximab was given when EBV-DNA copies rose persistently. Once PTLD was diagnosed, reduction or withdrawal of immunosuppression was administered.
Results: The incidence of PTLD for children with AAA after allo-HSCT was 4.2% (3/71). All the PTLD patients were presented with persistent fever with no reaction to any antibiotics, progressive antiadoncus and lymphadenectasis. Two of the three PTLD patients were monitored by EBV-DNA copies after allo-HSCT, and both had persistent high level of EBV-DNA copies before the diagnosis of PTLD, also after the first course of rituximab. After therapies, two of them were cured and alive till now; however, another one had no effect to the therapy and died 34 days after the diagnosis of PTLD.
Conclusions: PTLD is a rare and potentially fatal complication for children with AAA after allo-HSCT. Dynamic monitoring of EBV-DNA copies was important for early diagnosis and treatment of PTLD. The preemptive treatment with rituximab can reduce the incidence and mortality of PTLD.

P-0382

COMPARABLE OUTCOME AMONGST HAPLOIDENTICAL FAMILY DONOR TRANSPLANT WITHOUT IN VITRO T CELL DEPLETION, AND MATCHED SIBLING AND UNRELATED DONOR TRANSPLANTS IN CHILDREN

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Purpose/Objective: In this study, we analyzed the feasibility of allogeneic transplant from a haploidentical family donor (HFD) by comparing the results of HFD transplant to matched sibling donor (MSD) and unrelated donor (UD) transplants done during the same period.
Materials and Methods: 122 patients (Male 65; Female 57) who received either MSD (N = 27), UD (N = 75) or HFD transplant (N = 21) from August 2010 to June 2012 were included in the cohort. Underlying disease included malignancy in 81 patients, and non-malignant disease in 41 patients. All patients in the HFD group received peripheral blood stem cells. The HFD group received T cell depletion with rabbit ATG (2.5mg/kg/day for D-4 to D-1) during conditioning.
Results: Engraftment of neutrophils ($\geq$ 1,000) and platelets ($\geq$ 50,000) occurred at a median of 12 and 18 days for HFD transplants. Cumulative incidence of grades II-IV acute GVHD was significantly greater for HFD transplant (15/21, 71.4%)($P = 0.001$), although the disparity was less for grades III-IV GVHD ($P = 0.068$). Incidence of chronic GVHD was

also greater for HFD transplant (10/21, 59.6%) than either MSD (5/27, 19.3%) or UD transplant (17/75, 24.1%)($P = 0.023$). No difference in transplant-related mortality (TRM) was found among the 3 transplant groups (HFD 1/21, 4.8%; MSD 1/27, 3.7%; UD 1/75, 1.3%)($P = 0.599$). For the 81 patients who received transplant for malignant disease, no significant difference was found in relapse incidence among the three groups, although the incidence for HFD transplant was lower (4/15, 28.3%). For the overall cohort, event-free survival was similar among the three groups (HFD 15/21, 67.3 ± 11.2%; MSD 17/27, 62.0 ± 9.5%; UD 51/75, 64.1 ± 6.3%)($P = 0.815$)
Conclusions: With short-term follow-up, HFD transplant without *in vitro* T cell depletion resulted in outcomes that were comparable to MSD and UD transplant. Rates of TRM were similarly low for the three groups, although incidence of chronic GVHD was significantly greater for HFD transplant.

P-0383

EFFICACY AND SAFETY OF TREATING WITH MICAFUNGIN IN 75 CHILDREN WITH INVASIVE PULMONARY FUNGAL INFECTION

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Purpose/Objective: To analyze and evaluate the clinical efficacy and safety of Micafungin in children with invasive pulmonary fungal infection (IPFI).
Materials and Methods: Seventy-five children with hematological diseases and primary immunodeficiency disease were suspected with invasive pulmonary fungal infection and treated with Micafungin for 14 days to 4 weeks at a dose of 2.5-5mg /(kg.d) by intravenous administration over 1 h, once daily. Accesses the effects by follow-up thoracic high resolution CT scan and the organ index monitoring.
Results: A total of 75 children including 30 males (40.0%) and 45 females (60.0%) were enrolled to assesse efficacy and adverse events. The main underlying diseases were acute myeloid leukemia (21.0%), acute lymphoblastic leukemia (49.3%), primary immunology disease (8.0%) and hemophagocytic lymphohistiocytosis (6.7%). Sixty-three patients (84.0%) had undergone chemotherapy, 10 (14.3%) had undergone HSCT, and the remaining 2 (2.7%) had received immunosuppressive therapy. Based on the clinical observations and laboratory tests, we evaluated the efficacy of Micafungin for suspected IPFIs. Five cases were cured, 62 cases were improved and 4 cases were ineffective. The total effective rate was 89.3%. Two patients died and the mortality was 2.7%. No severe adverse effects were found in this group of patients.
Conclusions: Early diagnosis of invasive pulmonary fungal infection among high risk patients and empiric anti-fungi treatment is very important for therapy success. And Micafungin is effective and safe for empirical antifungal therapy in pediatric patients.

P-0384

IMMUNOHISTOCHEMICAL STAINING OF PEDIATRIC SMALL BLUE ROUND CELL TUMORS - A DEVELOPING WORLD EXPERIENCE

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Purpose/Objective: Small blue round cell tumors (SBRCTs) are highly malignant tumors which need support form ancillary studies to diagnose, particularly immunohistochemistry (IHC). In resource-poor countries, extensive panel of immunohistochemical staining is not always possible due to availability and cost issues. We report our experience in approaching IHC for SBRCT in a developing world setting.
Materials and Methods: Data from 133 children diagnosed with extra-cranial SBRCT between 2007 and 2012 were retrospectively analyzed. Clinical findings and pathological specimens were reviewed. Those for whom immunohistochemistry staining was done were included in this series. A sequence of immunohistochemical markers was used based on tumor location and clinical presentation to arrive at a diagnostic conclusion. Additional immunostaining was done wherever appropriate.
Results: Forty-seven children with NHL/ALL (n = 20), neuroblastoma (n = 16), rhabdomyosarcoma (n = 7), peripheral primitive neuroectodermal tumors (PNET, n = 3) and malignant rhabdoid tumor (n = 1) were included. The other 86 cases had either very classic presentation or typical histological features, which did not warrant further immunohistochemistry. Tumors mostly presented as abdominal masses. Other sites of presentation included chest, middle ear, skull, maxillary sinus and testes. All neuroblastomas tested for NSE were positive (specificity-33.3%) and 80% were positive for synaptophysin (specificity-80%). Although neural markers were helpful in diagnosing neuroblastomas, other studies like urinary catecholamines (sensitivity-66.6%, specificity-100%) and MIBG scanning were needed to distinguish neuroblastoma from PNET. All NHL/ALL were LCA-positive (specificity-100%). Myogenin was expressed in all rhabdomyosarcoma specimens tested (specificity-100%), while desmin was positive in 85.7% (100% specificity). CD99 lacked specificity, as it was positive in all PNETs, 50% of RMS, 50% of NHL/ALL and 25% of neuroblastomas.
Conclusions: Muscle markers and LCA are first line markers helpful in diagnosing rhabdomyosarcoma and NHL respectively. The distinction between neuroblastoma and PNET may be difficult when based only on neural markers. More specific immunohistochemical markers for PNET tumors need to be identified.

P-0385

PEDIATRIC SOFT TISSUE AND BONE TUMORS: DETERMINISTIC FACTORS FOR SAFETY AND ACCURACY OF IMAGE-GUIDED PERCUTANEOUS CORE-NEEDLE BIOPSIES

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Purpose/Objective: Percutaneous core needle biopsy (PCNB) of soft tissue and bone tumors is a minimally invasive technique with lower complications than open biopsy which can provide early and definitive diagnosis and guide decisions on management. This study was to assess lesion-related and technical factors that affect diagnostic yield and safety in image-guided PCNBs of pediatric soft tissue and bone tumors.
Materials and Methods: This was an institution review board approved retrospective study of 150 PCNB procedures of soft tissue ($n = 80$) and bone ($n = 70$) tumors performed at our institution from January 2003 to December 2012. The medical records and the radiological data of these patients were reviewed. Radiological features of tumors like location, size, extent, nature, enhancement pattern and associated abnormalities were recorded. Procedural details of the biopsy such as the approach, biopsy needle, image-guidance modality, number and length of specimens were noted. Procedure related complications, inability to obtain samples and repeat PCNBs due to poor or non-diagnostic yields were recorded. Pathological reports for findings, comments and diagnosis were reviewed.
Results: Diagnostic yield was 82% for all lesions. The diagnostic yield was more for lesions of the soft tissues $>$ 2cm, had well defined margins and demonstrated solid component. Increased diagnostic yield was also achieved with increase in number of specimens($>$ 5), use of larger needle gauges ($>$ 16 gauge) and in longer specimens ($>$ 2mm). Ultrasound guidance was the most common modality to provide real time guidance and reduce radiation dose.
Conclusions: Image guided PCNB is a safe, effective and accurate technique in the diagnosis of pediatric soft tissue and bone tumors.

P-0386

DISTRIBUTION OF CHILDHOOD CANCERS IN SUB SAHARAN AFRICA

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Purpose/Objective: Childhood cancer is a relatively rare disease on the African continent but the real incidence is not known. However African continent counts more than 410 million children and a calculated incidence of 50-60.000 new cases of childhood cancer is expected yearly.

In the absence of registries, the aim of the study was to analyze the distribution of childhood cancer in Sub Saharan Africa.
Materials and Methods: Childhood cancers were defined as those below the age of 15 and were classified according to the International Classification of Childhood Cancer.

Data obtained were analyzed using EpiInfo and Statistica 10 software.
Results: There were 21 centers included in the study from 19 Sub SaharanAfrican countries. The data analyzed differed from center to centre and included cases from 1985-2011.

The proportion of childhood cancer out of all cancers ranged between 1.4% in Ghana to 10.0% in Rwanda.

In Southern Africa, Kaposi sarcoma was the most common malignancy in children in Mozambique (15.8% of all cases) and the second most common in Zambia (15.6%) and in Malawi (12.4%).

In Eastern Africa, Uganda recorded Kaposi sarcoma as the most common tumor in children (22.0%) while 2 Kenyan centers reported mainly Burkitt lymphoma (25.1% and 37.1% respectively).

In Western Africa, Non Hodgkin lymphoma was the most common in Ghana (53.6%), in Ivory Coast (73.6%) and in Mali (32.7%).

Nephroblastoma remains of the most common solid tumors in Africa exceeding 10% of total pediatric cancers in many countries (Rwanda 26.0%, Ivory Coast 14.5%, Mali 17.6%, Congo 15.5% etc)
Conclusions: Unlike developed countries, lymphomas, nephroblastoma and Kaposi sarcoma were the most common pediatric tumors in Africa. The need for cancer registries in Africa remains a priority.

P-0387

CROCIN ATTENUATED CISPLATIN-INDUCED LIVER INJURY IN MICE

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Purpose/Objective: The protective activity of crocin (a main water-soluble carotenoid of the saffron extract) against cisplatin- induced acute liver injury in mice
Materials and Methods: Crocin was administered to Kun-Ming mice once daily for 7 consecutive days at the doses of 6.25 and 12.5 mg/kg body weight orally.
Results: On day 1, a single intraperitoneal injection of cisplatin was given at the dose of 10 mg/kg body weight. Crocin treatment significantly improved the cisplatin-induced hepatic damage as indicated by the serum marker enzymes (AST, and ALT). Parallel to these changes, Crocin also prevented cisplatin-induced oxidative stress by reducing MDA levels and restoring the levels of antioxidant enzymes (SOD, CAT, and GPx), and GSH. In addition, liver histopathology indicated that crocin alleviated cisplatin-induced inflammatory infiltration and focal necrosis. Crocin also significantly decreased phospho-p38MAPK, p53, and caspase-3 protein expressions by immunohistochemical staining and western blotting. Meanwhile, crocin significantly decreased mRNA expression of p53 and caspase-3.
Conclusions: The results of the present study suggest that the protective effect of crocin against cisplatin-induced hepatoxicity was related to attenuation of oxidative stress, and downregulation of phospho-p38MAPK, p53, and caspase-3.

P-0388

PAEDIATRIC ONCOLOGY DATA BASED NETWORK (POND) REGISTRY INITIATED IN BANGLADESH

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Purpose/Objective: 1. To register definitive diagnosis of all new cases of childhood cancer in order to develop a useful and informative cancer registry using POND database (www.POND4Kids.org)
2. To monitor disease patterns, treatment refusal/ abandonment and outcome of all childhood cancers at BSMMU, Dhaka (the largest referral centre) in Bangladesh.
Materials and Methods: Bangladesh had no population or hospital based cancer registries to estimate reliably childhood cancer incidence. This prospective study was performed from January 2012 to December 2012. All newly diagnosed children with cancer aged under 16 years attending our department were enrolled using the POND4Kids registry (supported by a World Child Cancer Twinning Program). Data was registered by a dedicated data manager supervised by departmental consultants and a medical officer. The registry captured a complete summary including; patient demographics, tumor type and site, clinical status, initial investigation profiles, disease status,and treatment refusal or abandonment. At six monthly intervals each patient registered has a review in the clinic or by phone to confirm current status.
Results: 455 newly diagnosed childhood malignancy patient were registered from January 2012 to December 2012. Haematological malignancies comprise 82% of cases (ALL-58%, NHL-11%, AML-10%) and solid tumors 18% (Neuroblastoma-5%, Wilms' tumor-2%, RMS-2%, Hepatoblastoma-3%). 58% started treatment, 43% families refused and/or discontinued treatment after diagnosis mostly due to financial constraints. Among the children who started treatment 71% are continuing, 17% discontinued, 12% patient died during treatment.
Conclusions: ALL comprises more than half of the childhood cancer. High treatment refusal, abandonment and toxic death are the major obstacles in treating childhood cancer in Bangladesh. The register is enabling us to not only record outcome for each patient but reliably record workload, changes in incidence and define whether our attempts to reduce the obstacles to curability are working year on year.

P-0389

ISOLATION OF MESENCHYMAL STEM CELLS (MSCS) FROM HUMAN PALATINE TONSIL

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Purpose/Objective: Although mesenchymal stem cells (MSC) from human palatine tonsils (tonsillar MSC, T-MSC) have been isolated, whether T-MSC isolated from multiple donors are feasible for cell banking has not been studied
Materials and Methods: T-MSC before or after the standard protocol of cryopresevation-and-thawing were subjected to assess several basic characteristics, including colony-forming unit-fibroblast features, MSC-specific surface antigen profiles, and inhibition of alloreactive T cell proliferation. In vitro mesodermal differentiation potentials to adipocytes, osteocytes and chondrocytes were detected by stainings with cell-specific dyes after incubation with each appropriate differentiation medium. Expression profiles of endoderm-specific genes were also identified by reverse transcription polymerase chain reaction. The feasibility of T-MSC in future engraftment was tested by short tandem repeat (STR) analysis using genomic DNA randomly isolated from 3 independent subjects.
Results: Both fresh and cryopreserved-and-thawed T-MSC showed similar high proliferation capacity and expressed primitive cell surface markers. Hematopoietic cell markers, HLA-DR, co-stimulatory molecules, and follicular dendritic cell markers were not detected. In addition to mesodermal differentiation, fresh and cryopreserved-and-thawed cells also underwent endodermal differentiation, as evidenced by expression of endoderm-specific genes including FoxA2, Six1, and CCL21. Both cells significantly decreased phorbol 12-myristate 13-acetate (PMA)-induced T cell proliferation. T-MSC from 3 independent donors formed chimerism in STR analysis.
Conclusions: Our results demonstrate for the first time that T-MSC are a potentially good source for MSC banking.

P-0390

CLINICAL OBSERVATION OF 96 CASES OF CHILDREN HEMATONOSIS AND ONCOSIS WITH INVASIVE PULMONARY ASPERGILLOSIS(IPA)

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Purpose/Objective: Explore the clinical features of children hematonosis and oncosis with IPA, and analyze the efficacy and safety of different antifungal medicines.
Materials and Methods: Some high risk factors, clinical and imaging features, and reactions were investigated. Three groups were proposed in terms of the antifungal medicines used: Voriconazole (40 subjects), Amphotericin B (30 subjects) and Caspofungin (26 subjects).
Results: The differences of three groups in age, gender, underlying disease and diagnosis of fungal infection are not statistically significant. 78 subjects are in lack of neutrophils, the rest are mainly caused by basic pulmonary diseases and previous application of glucocorticoid. Fever, cough, and tachypnea are common clinical symptoms with no difference. The chest CT appearances show segmental pulmonary consolidation and Single or multiple nodules shadows. The nodules, formation of lung consolidation shadow with holes and air-crescent sign are common traits of IPA and halo sign appeared in early stage. Overall effectiveness rate is 85.4%, with that of Voriconazole, amphotericin B and Caspofungin being 95%, 86.7% and 69.2% respectively. The effectiveness rate of Voriconazole and amphotericin B are statistically higher than Caspofungin($p < 0.05$). Compared to amphotericin B, the adverse reactions such as hyperpyrexia, shiver, hypokalemia and hepatic dysfunction (elevation of transaminase) are statistically lower in Voriconazole and Caspofungin($p < 0.01$). The average defervescence time for Voriconazole(1.5 days) is statistically shorter than that of Caspofungin(7 days).
Conclusions: The period of bone marrow suppression after chemotherapy for malignant blood tumor and the long-term use of glucocorticoid children are high-risk groups of IPA whereas both diagnosis and treatment are difficult. Close attention to high resolution lung CT dynamic monitoring and earlier pre-diagnosis of IPA are the keys to successful treatment. Voriconazole could be used to treat blood basic diseases combined with IPA with remarkable curative effect and high safety and the defervescence time is relatively shorter.

P-0391

SINGLE CENTER ANALYSIS OF CASES WITH CHILDREN SOLID TUMOR FROM 2009 TO 2011

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Purpose/Objective: Single center analysis of cases with children solid tumor from 2009 to 2011
Materials and Methods: To investigate epidemiologic and clinical features of childhood solid tumor in our hospital from Jan. 2009 to Dec. 2011.
Results: Clinical and pathological data, including patient gender, age, manifestations, imaging investigations, tumor histology, therapeutic measures and prognosis of childhood solid tumors confirmed by pathological biopsy, were retrospectively collected and analyzed. Tumor classification was performed according to WHO tumor classification and diagnostic criteria. Results 983 cases of childhood solid tumor were enrolled including 721(73.35%)benign tumors and 262(26.65%) malignant tumors(2.8:1).

Pathological type: the top five benign tumors were vascular, calcifying epithelioma, mature teratoma, chondroma and fibroma and the top five malignant tumors were neuroblastoma, lymphoma, Wilm's tumor, germ cell and hepatoblastoma.

Original site: the top five benign tumors were skin and soft tissue, craniofacial and neck, bone tumors, abdominal tumors and thoracic tumors. The top five malignant tumors were abdominal tumors, intracranial tumors,craniofacial and neck tumors, skin and soft tissue tumors and pelvic tumors.

Most common malignant tumors were embryonal tumors(171 cases,65.3%), followed by tumors containing similar ingredients(57 cases,21.8%)and lymphoma(34 cases,13.0%).

There was statistically significant differences in terms of age of onset distribution between benign and malignant tumor groups ($P < 0.05$). Benign tumors in gender distribution was not statistically significant($P = 0.396$),while malignant tumors was meaningful($P = 0.003$).

Solid tumors were much more prevalent in infants and toddlers($P = 0.003$). The different types of malignant tumor in different age stages were different distribution($P \leq 0.001$).

29/262 cases(11.1%)in infant were massive malignant tumor and 26 of them(89.7%)were from abdominal.

Conclusions: Childhood malignant tumors are different from that in adults, with regards to histological types, age at onset and gender distribution.

Childhood malignant tumors commonly occur in the abdominal cavity with embryonic tumors as the predominant histological types.

Neuroblastoma and Wilm's tumor are the primary tumor presenting with huge tumor mass in children under 4 years old.

P-0392

COMPARISON OF PRESENTATION AND OUTCOME IN CHILDREN WITH CANCER BETWEEN ASSIUT (EGYPT) AND COLOGNE (GERMANY)

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Purpose/Objective: To compare the outcome of pediatric oncology patients between two large institutions, one in a developing country (Egypt), and the other in a developed country (Germany).

Materials and Methods: Retrospective review of all available data of newly diagnosed children with cancer started treatment between 2006 and 2010 in the departments of pediatric oncology in South Egypt Cancer Institute ($n = 502$) and University Hospital of Cologne ($n = 238$) including age, sex, diagnosis, travel time from home to treatment center, time interval from initial symptoms to admission and from admission to start of treatment, response to initial course of therapy, treatment related severe adverse events, compliance and outcome.

Data were analyzed using SPSS version 20 for Kaplan-Meier survival estimates and multivariate regression analysis.

Results: Diagnoses in Assiut were commonly leukemia (48.7%), lymphomas (24.1%), solid tumors (24.8%) and rarely brain tumors (1%) compared to (22.3%), (19.3%), (26.4%) and (28.6%) in Cologne respectively.

In comparison to Cologne, patients from Assiut were younger (6.70 ± 4.44 versus 8.89 ± 5.47 years, $P = 0.001$), lived farther (1.27 ± 0.06 versus 0.43 ± 0.06 hours, $P < 0.0001$), received therapy earlier (7.57 ± 0.6 versus 12.08 ± 1.1 d, $P < 0.0001$), showed less compliance (85.1%versus 97.1%, $P < 0.0001$) and relapsed earlier (10.14 versus 13.4 months, $P = 0.02$). Deaths in Assiut were significantly higher (47.4% versus 18.1%), related to farther patient home, complications and non-compliance and caused mainly by infection 59.7% (6.98% in Cologne), while in Cologne mainly by progressive disease 41.86% (15.5% in Assiut).

Conclusions: This direct institutional comparison of pediatric cancer patients may help to identify and overcome factors associated with poorer outcome in developing countries to meet their right for better health care.

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P-0393

BASIC FIBROBLASTIC GROWTH FACTOR LEVELS IN INFANTILE CAPILLARY HEMANGIOMA

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Purpose/Objective: The defects that occur during angiogenesis are thought to play a major role in the pathogenesis of capillary hemangiomas. The purpose of this study is to determine the importance of serum basic Fibroblastic Growth Factor (bFGF) levels in infants with capillary hemangioma.

Materials and Methods: Between April 2012-February 2013, 44 patients, who were diagnosed as capillary hemangiomas, were enrolled into the study. As the control group, 18 age matched healthy children were included. Twenty-nine were females, 15 were males with an age range of 1 month - 3 years (median: 4 months). After obtaining the signed informed consent from the families, peripheral blood samples were drawn and sera were collected from the patients and the healthy control.. and kept at-20°C till the study day. Serum bFGF levels were measured by ELISA (R&D) technique.

Results: Serum bFGF levels in patients (n:44) with capillary hemangioma were found to be higher (3.07 ± 4.53 pg/ml) than the healthy control group (n:18) 7.88 ± 7.47 pg/ml. The difference was statistically significant ($p = 0.013$).

Conclusions: Capillary hemangiomas are the most common benign soft tissue tumors of infancy and childhood, yet the etiology is not fully understood. Although more than 20 stimulant and 30 inhibitors of angiogenesis have been discovered in humans, bFGF appears to be essential for vasculogenesis and angiogenesis. BFGF, which is also called as FGF-2, is the most intensively studied of the 22 mitogenic proteins of the FGF family. Therefore, in our study, we aimed to measure the serum levels of bFGF in patients with capillary hemangiomas comparing the results of normal healthy control group. Elevated serum bFGF levels in capiilary hemangioma patients, can be taken into consideration for targeted therapies in the future, especially for the resistant cases with disfiuring leisons.

P-0394

CLINICAL OBSERVATION OF 68 CASES OF CHILDREN WITH EBV-HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (EBV-HLH) BASED ON HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS-04 PROTOCOL

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Purpose/Objective: Evaluate the efficiency of HLH-04 reform protocol(etoposide decrement 50mg/m2-75mg/m2)on children with EBV-HLH according to clinical features, treatment and prognostic risk factors.

Materials and Methods: The clinical features, laboratory analysis, rates of therapeutic response and prognosis of 68 children with EBV-HLH were investigated.

Results: All the 68 EBV-HLH patients had pyrexia, 92.3% of patients were persistent hyperpyrexia, hepatomegaly, splenomegaly, lymphadenectasis, jaundice, ascites and pleural effusion also with high occurrence rate. Liver function damage the most outstanding (100%), which focus on zymology change i.e. LDH, AST, ALT, GGT and hypoalbuminemia. Also hemophagocytosis in bone marrow was accounts for 85.78%. 94.23% of the natural killer cell was decreased, while 5.77% was increased. According to the HLH-04 protocol, the total survival rate of EBV-HLH was 69.12%. The survival rate of 26 EBV-HLH patients which used 150mg/m2 of etoposide was 53.85%, while 42 patients decreased to 50mg/m2-75mg/m2 of etoposide was 78.57%. Compared to therapeutic protocol was based on the HLH-04 protocol, the differences of two groups in age, gender, EB viral, liver function, bilirubin, lactic dehydrogenase, albumin, IFN-γ,IL-6, serum ferritin, fibrinogen, platelet count, natural killer cell were not statistically significant ($p > 0.05$). The effectiveness rate of etoposide decrement were statistically higher than etoposide standard dose ($p < 0.05$). There were lower of bilirubin, lactic dehydrogenase, albumin, IFN-γ,IL-6 and higher of fibrinogen and platelet count in remission group compared with the death group ($p < 0.01$), which could act as a reference indicator to evaluate prognosis.

Conclusions: Children with EBV-HLH varied in clinical manifestations, while EB viral, bilirubin, lactic dehydrogenase, albumin, IFN-γ,IL-6, fibrinogen and platelet count might be helpful to the assessment of prognosis of EBV-HLH. Etoposide decrement according to the HLH-04 protocol could be used to treat EBV-HLH with remarkable curative effect and high safety and less adverse reactions.

P-0395

IS IT POSSIBLE TO SPARE THE ADRENAL GLAND AT RADICAL NEPHRECTOMY IN CHILDREN DIAGNOSED OF WILMS' TUMOR?

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Purpose/Objective: Wilms' tumor is most common renal neoplasm in children. Radical nephrectomy is the generally recommended treatment of choice as a part of multi-disciplinary therapy. However, there is no definite clinical guideline for ipsilateral adrenalectomy when performing radical nephrectomy for the treatment of Wilms' tumor. Therefore we aimed to confirm whether patients with Wilms' tumor could be treated with ipsilateral adrenal sparing

Materials and Methods: Between 1992 and 2010, 51 patients with histologically confirmed Wilms' tumor undergoing radical nephrectomy were analyzed in this study. Patient age, clinical symptom, size and laterality of tumor, and adrenal invasion of tumor on abdominal computed tomography (CT) or ultrasound were reviewed as preoperative data and pathologic stage, renal capsule invasion, adrenal invasion, lymphovascular invasion, and complete resection were reviewed postoperatively.

Results: Of the 51 patients, 27 (53%) were male and 24 (47%) were female. The mean age was 39 months and the mean follow up duration was 73.7 months. Preoperative clinical symptoms included abdominal palpable mass (62.7%), abdominal discomfort (9.8%), and gross hematuria (27.5%). Tumor involved unilaterally in 49 and bilaterally in 2. The mean size of renal mass was 10.1cm on preoperative CT (74.5%) or ultrasound (25.5%). Six patients (11.8%) who had pulmonary metastasis received neoadjuvant chemotherapy (Vincristine, Dactinomycin, and Cyclophosphamide). Pathologic stage was: I-25 (49%), II-8 (15.7%), III-7 (13.7%), IV-9 (17.6%), and V-2 (4%). Renal capsule invasion in 13 and lymphovascular invasion in 4 were observed, but adrenal invasion was not identified in all nephrectomy specimens. Complete resection rate was 80% and adjuvant chemotherapy was performed following radical nephrectomy in all 51 patients.

Conclusions: Adrenal involvement is not likely in patients with Wilms' tumor, and adrenalectomy is unnecessary in all cases eventually. These results suggest that unconditional

ipsilateral adrenalectomy during radical nephrectomy for the treatment of Wilms' tumor could be avoided.

P-0396

FACTORS LEADING TO DELAYED DIAGNOSIS OF CANCER IN EGYPTIAN CHILDREN

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Purpose/Objective: Despite the tremendous importance of early diagnosis of cancer in children, little have been published in this aspect in Egypt. Early diagnosis allows timely management while the disease is still in its earliest stages. Our objective was to investigate delays in diagnosis of childhood cancers in Egypt, and factors that leads to these delays.
Materials and Methods: A retrospective study was performed on 172 child with cancer reported to two pediatric oncology units in Egypt. The interval between the onset of symptoms and the final diagnosis for each child was estimated and correlated to the sex, age at diagnosis, type and site of malignancy, family residence, socioeconomic status and parental education level using univariate and multivariate analysis.
Results: The median total diagnosis delay was 51 days. This was due to patients/parents 8 days and due to diagnosis 27 days. Misdiagnosis was recorded initially in 37% of cases. Infants below one year showed significant delay to diagnosis than older children. Lower parental education and socioeconomic status was significantly associated with delayed diagnosis. The malignancy and site of tumor ($P = 0.001$) significantly affected the time to diagnosis. Lowest median value appeared with Germ cell Tumors, Leukemia, and the highest with brain tumors. On the other hand, gender, residence and family sizes were not significantly related to delayed diagnosis.
Conclusions: Delayed diagnosis of childhood cancer was related to age, cancer types and sites and family socioeconomic status. Every effort should be carried to develop effective steps to eliminate the possible contributing factors and to find best methods of interventions.

P-0397

ABANDONMENT OF CHILDHOOD CANCER TREATMENT IN KENYA

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Purpose/Objective: The main aim of this study was to interview parents and/ or care takers of children who had abandoned cancer treatment so as to explore the reasons for abandonment and also to establish the condition of the children.
Materials and Methods: Home visits were conducted to interview families of childhood cancer patients, diagnosed between January 2007 and January 2009, who had abandoned treatment according to their medical record.Families were contacted by phone or by visits to their place of residence as per the information available in the medical records. A semi-structured questionnare was used during the interviews and the famiy's living conditions were also observed.
Results: Between January 2007 and January 2009, 222 children were newly diagnosed with a malignancy at MTRH. Treatment outcome was documented in 180 patients. Of these 180 patients, 98 (54%) children abandoned treatment. From December 2011 till August 2012, 53 (54%) of the 98 families were contacted. Due to lack of contact information 45 families were untraceable. From the 53 contacted families, 46 (87%) families agreed to be interviewed. Reasons for abandonment were reported by 26 families. Reasons were complex and diverse. Most common reasons were: financial difficulties (46%), inadequate access to health-insurance (27%) and transportation difficulties (23%). Most patients (72%) abandoned treatment after the first 3 months had been completed. Of the 46 children who abandoned treatment, 9 (20%) were still alive: 6 (67%) of these children looked healthy and 3 (33%) ill. The remaining 37 (80%) children had passed away
Conclusions: Prevention of childhood cancer treatment abandonment requires improved access to health-insurance, financial support, proper parental education, psycho-social guidance and ameliorated communication skills of health-care providers.

P-0398

CHILD'S PERCEPTION OF HIS/HER ABILITY VERSUS A QOL ASSESSMENT SCORE IN A COHORT OF CHILDREN TREATED FOR OSTEOSARCOMA

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Purpose/Objective: Quality of life is an individual's perception of their status in terms of physical, psychological and social function. There are many scoring systems available, which are tailored for various sociocultural groups. We used an indigenously prepared, pretested questionnaire to check QOL in a cohort of children treated for osteosarcoma and compared it with child's perception of his/her ability in relation to their peers.
Materials and Methods: 33 children aged 12-18 years, completed treated for osteosarcoma were recruited to assess their QOL using a scoring system based on their daily activities of life such as eating, dressing, bathing, and mobilization within and outside their house as well as social activities. The score ranged from 1 to 27 they were divided into four groups based on this. Each child was then asked to rate his ability compared to their peers; upto 25%, 26-50%, 51-75% or 76-100%.
Results: 27 children had lower limb tumours, 4 had upper limb and 2 had axial skeletal tumours. Of the 31 with limb osteosarcoma, 16 underwent limb salvage surgery (LSS) and 14 had amputation. Overall, 27/33 children scored 75% or more in the QOL assessment and the remaining 50-75%. There was no significant difference between those who had LSS vs amputation. When asked to rate their overall ability compared to their peers, only 2/33 scored above 75% and 9 children scores less than 50%.
Conclusions: It is interesting to note that while 81% of study population scored $> 75\%$ on a QOL scoring system, only 6% felt they were as able as their healthy peers. Though QOL scoring helps in assessing and planning interventions to improve quality of life in children treated for osteosarcoma, child's own assessment of his/her ability compared to their peer group cannot be ignored. Larger group studies are required to validate this assumption.

P-0399

THE IMPACT OF COUNTRY ECONOMIC CLASSIFICATION ON NUTRITION PRACTICE IN PAEDIATRIC ONCOLOGY HOSPITALS: A REPORT FROM THE INTERNATIONAL PEDIATRIC ONCOLOGY NUTRITION GROUP

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Purpose/Objective: While much has been published describing the impact of a country's economic status on provision of medical and nursing care, little is known about its impact on the delivery of nutrition services. International efforts are ongoing in providing education and standards of care to augment nutrition practice in low income countries (LIC) however a comprehensive understanding of all of the facilitators or barriers to the provision of nutrition care remains largely unknown. The aim of this study was to investigate the impact of a countries economic classification on nutrition practice in pediatric oncology sites.
Materials and Methods: A survey of nutrition practice in pediatric oncology treatment centers was conducted between 2011 and 2012. Surveys were distributed to members of paediatric oncology hospitals and through cure4kids to members from LIC. Responses were analyzed using Chi-squared analysis (SPSS ver 21).
Results: One hundred and forty-two surveys from 69 countries were included in analyses. Surveys were divided by the World Bank classification of the world's economies. Thirty-two percent of surveys were from high income countries, 35% from higher middle income, 27% from lower middle income and 6% from low income countries. Economic classification influenced access to dietician ($p > 0.000$), provision of patient nutrition education ($p = 0.01$), and availability of parental nutrition ($p = 0.008$) and oral nutritional supplements ($p = 0.01$).
Conclusions: This survey has highlighted some important considerations in developing nutrition management standards. The focus of nutritional management for LIC needs to be on educating the doctors and nurses as access to dieticians is limited, providing patient nutrition education and including alternative nutritional suggestions to replace oral supplements and parental nutrition in nutritional management algorithms. By considering the needs of LIC when planning standards of nutritional care, the International Pediatric Oncology Nutrition Group can ensure that optimal nutritional care can be provided to all children undergoing treatment for cancer.

P-0400

HAPLOIDENTICAL RELATED DONOR STEM CELL TRANSPLANTATION WITHOUT IN VITRO T-CELL DEPLETION COMBINING WITH CORD BLOOD TRANSFUSION RESULTS IN RAPID ENGRAFTMENT, LOW GVHD, AND DURABLE REMISSIONS

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Purpose/Objective: Recent advances in HLA-mismatched/haploidentical transplantation allow for the use of HSCT in many patients without an HLA-identical donor or who urgently require transplantation. In this study, we accessed the clinical outcome of Haploidentical

related donor stem cell transplantation without in *vitro* T-cell depletion combining with cord blood transfusion in consecutive 6 childhood patients.
Materials and Methods: Six patients were enrolled from August until November 2012, including 2 cases of ALL, 2 cases of AML, 1 case of CML, and 1 a case of SAA. Median age was 10 years; weight was 40kg. G-CSF*mobilized BM and peripheral blood stem cells at median of total nucleated cells of 14×10^8/L(range, 9.5 to 20) were used as a graft resource. Cord blood was infused 4 hours earlier than BM stem cells and one more day than peripheral blood stem cells. The conditioning regimen was a modification of BU/CY (busulfan/cyclophosphamide) and antithymocyte globulin (ATG). All transplantation recipients received cyclosporine A (CsA), mycophenolate mofetil (MMF), and short-term methotrexate (MTX) as GVHD prophylaxis. Chimerism was determined by STR and FISH.
Results: The median time to engraftment (absolute neutrophil count $> 0.5 \times 10^9$/L more than 3 days and platelets $> 20 \times 10^9$/L more than 7 days) was 11.8 (range, 10-15) and 14.2 (range, 12-16) days. The median time of STR $>95\%$ which is considered as complete engraftment was 18 (14-21) days. No case showed acute grades III/IV GVHD. All the patients had CMV reactive after ANC reconstitution. Three cases was diagnosed as BK infection accompanying with hemorrhagic cystitis around day 35. Two cases were diagnosed as invasive fungal pneumonia. The median of follow-up was 106.7 (range, 59-171) days, only one case with SAA died of interstitial pneumonia on day 138.
Conclusions: Haploidentical related donor stem cell transplantation without in vitro T-cell depletion combining with cord blood transfusion results in rapid engraftment, low GVHD, and durable remissions.

P-0401

THE IMPACT OF HIGH RESOLUTION TYPING OF HLA ON CLINICAL OUTCOME OF UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANTATION IN PEDIATRIC PATIENTS WITH HEMATOLOGIC DISORDERS

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Purpose/Objective: Donor-recipient human leukocyte antigen mismatch level affects the outcome of unrelated cord blood transplantation (UCBT). The purpose of this study was to assess the role of high resolution typing of HLA on clinical outcome in 10 consecutive childhood patients receiving transplants with UCB graft composed of 1 (n = 5) or 2 (n = 5) units.
Materials and Methods: Ten patients were enrolled from April 2011 until January 2013 with different diseases. Human leukocyte antigen (HLA) matching at enrollment was 6/6 (n =2), 5/6 (n =3), 4/6 (n =5) by low-resolution HLA-A, -B, and high-resolution (HR) DRB1. Retrospectively, 10 pairs were HLA typed by HR. The median precryopreservation total nucleated cell (TNC) dose was 4.5×10^7 TNC/kg (range, 3.6-8.3) infused. Conditioning regimens were modified on the basis of BuCy depending on specific diseases. Graft-versus-host disease (GVHD) prophylaxis included cyclosporine A and mycophenolate mofetil. Engraftment syndrome was controlled by methylprednisolone. Chimerism was determined by quantitative analysis of informative microsatellite sequences of DNA (STR) of peripheral blood and BM samples.
Results: UCB was engrafted in 10 patients and 7 patients showed engraftment syndrome. The median time to engraftment (absolute neutrophil count $> 0.5 \times 10^9$/L more than 3 days and platelets $> 20 \times 10^9$/L more than 7 days) was 22 (range, 15-30) and 44 (range, 21-96) days. The median time of STR $>95\%$ which is considered as complete engraftment was 14 days. Acute grades III/IV GVHD by day 100 was 4 in 10 cases. HR mismatching with HLA-DRB1 and HLA-DQB1 showed close relation with severe acute GVHD. HLA matching sites more than 5/10 (HR) is the minimal requirement for engraftment considering cases received 2 units of cord blood. TNC dose plays the dominant role in engraftment.
Conclusions: HR HLA typing is helpful in selecting UCB unit to increase engraftment while decrease the severe aGvHD. UCBT is an effective treatment for childhood hematologic disorders.

P-0402

HOLISTIC CARE MODEL FOR CHILDREN WITH CANCER IN DEVELOPING COUNTRY; SOUTHERN CHILDHOOD CANCER NETWORK THAILAND 3-YEARS EXPERIENCE

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Purpose/Objective: Songklanagarind Hospital is a tertiary hospital in southern Thailand. It serves approximately 100 newly diagnosed pediatric cancers in region each year. Abandonment and lack of education caused delayed diagnosis and poor treatment outcome. Treatment abandoned often caused by low socioeconomic status and could not access to health care services. A project to improved quality of life of children and family during cancer treatment has been developed.
Materials and Methods: In 2010, the holistic care program has been established with funding support from Union International Cancer Control(UICC) under ''My Childs Matters'' program. Southern Childhood Cancer Network has been established by collaborating with National Health Security Office (NHSO). The 3-years project was run to improved quality of life for children with cancer in region.
Results: Temporary buidling had been arranged for children with cancer who need out-patient treatment or during radiotherapy (occupancy 14 beds). Most children entered this program live in other provinces and cannot afford transportation or accomodation cost during treatment.The program could improved treatment adherence and decreased financial constraint of family.

Childhood cancer netwoking has been establised in southern Thailand included 14 hospitals and 44 health care personnel. Annual meeting and education workshop was held to discuss treatment strategies & problems among network hospital. Guideline for safe chemotherapy administration, referral guideline and oncologic emergency was developed and distributed. A network website www.cure2care.org has developed. 5 Chemotherapy regimen has been switched from in-patient to out-patient service at local hospitals.This program decreased admission visit in 131 patients without any major complication.
Conclusions: The holistic care model could improved treatment adherence and quality of life for children with cancer. The networking program could decreased travel cost and time therefore improved quality of life for family of children with cancer in southern Thailand. The holistic care program is needed in developing country with limited treatment resources.

P-0403

CLINICAL SUMMARY OF 691 CASES WITH LYMPHANGIOMA OF B ULTRASOUND GUIDED LOW CONCENTRATION PINGYANGMYCIN INJECTION TREATMENT

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Purpose/Objective: To investigate B ultrasound lead low concentration pingyangmycin injection in treating the effectiveness of pediatric lymphangioma.
Materials and Methods: 691 patients were treated by B ultrasound-guided Pingyangmycin percutaneous injection. Large and small cystic lymphangioma were injected pingyangmycin 0.4mg/mL in cyst. Cavernous lymphangioma and mixed lymphangioma were injected by multi-point with concentration of 0.33mg/mL. single maximum dose was School-age children no more than 8mg, young children no more than 4mg, baby no more than 2mg, 2-3month one cycle, totally 1-10 cycles. The longest follow-up for nine and a half years.
Results: of all 691 patients, the effect of large cystic lymphangioma were all complete remission (CR), multi-small cystic lymphangioma were CR or very good partial remission (VGPR), small cystic and cavernous mixed lymphangioma were VGPR or partial remission(PR), 80% of cavernous lymphangioma were VGPR or PR and 20% were micro remission (MR), effect of 8 cases of diffuse lymphangioma were MR. None of patients appeared acute bleeding, acute infection, local skin necrosis, and pulmonary fibrosis and other complications. There were delayed bleeding in 16 patients and delayed infection in 5 patients.
Conclusions: The method used anaesthesia and B ultrasound-guided percutaneous injections of local lymphangioma, accurate positioning, drugs injected directly into the tumor endothelial wall cavity after pumping clean cyst fluid. The low concentration pingyangmycin was able to achieve satisfactory result, and can do puncture and injection treatment in deep and hidden location and complex important structure, and reduce complications.

P-0404

HLA-HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANT WITH HIGH-DOSE,POST-TRANSPLANT CYCLOPHOSPHAMIDE FOR CHILDREN HEMATOLOGIC MALIGNANCIES

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Purpose/Objective: To evaluated the safety and efficacy of HLA-haploidentical hematopoietic stem cell transplant((HSCT) for children hematologic malignancies using high-dose post-transplant cyclophosphamide (Cy)
Materials and Methods: We retrospectively analysed the data of 26 patients with high-risk acute lymphoblastic leukemias (n = 13), acute myeloid leukemia (n = 9), chronic myeloid leukemia (n = 1), or lymphoma(n = 3) from June 2009 to December 2012. These Patients have received HLA-haploidentical HSCT with high-dose, post-transplant Cy. All donors were from $\geq$2 HLA mismatched first-degree relative (parent and sibling). All patients received conditioning therapy brie?y consisted of busulfan, Cy, thiotepa, with or without total body irradiation. After transplant patients received Cy 50 mg/kg i.v. on day 4 (n = 4), Cy 40 mg/kg i.v on days 3 and 4 (n = 10) or Cy 50 mg/kg i.v on days 3 and 4 (n = 12).
Results: The median follow-up time was 15 months. Donor chimerism was $\geq$95% on day $\sim$28. The median time to neutrophil and platelet engraftment were 23 and 20 days

respectively. The cumulative incidences of grade?-? acute GVHD (aGVHD),grade ?-? aGVHD,and chronic GVHD was 34%,4% and 11% respectively. In addition, there were 3 patients with garde ?-? aGVHD after donor lymphocyte infusion because of relapse.The cumulative incidences of relapse and non- relapse mortality were 23% and 34% respectively. The cumulative overall survival(OS)and event-free survival(EFS)at 3 years are 31% and 29% respectively.
Conclusions: HLA-haploidentical HSCT with high-dose, post-transplant Cy for children malignancies hematopathy is a viable treatment because of acceptable rates of graft failure and severe aGVHD or cGVHD.

P-0405

IMPACT ASSESSMENT OF THE EARLY DIAGNOSIS PROGRAM: DOES BUILDING CAPACITY OF PRIMARY HEALTH CARE WORKERS HAVE AN IMPACT ON REFERRALS FOR SUSPECTED PEDIATRIC CANCER?

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Purpose/Objective: As in Brazil the time between symptoms and diagnosis (lag time) of pediatric cancer is long and many patients are referred to treatment at advanced stages, NGO Instituto Ronald McDonald (IRM) developed the Early Diagnosis Program to build capacity of primary health care workers and improve patient care flow from primary care to treatment hospitals. Since 2008, the Program has run in 86 cities in 12 Brazilian states, providing training for 14,553 health professionals. So, the objective is EVALUATE THE ADEQUACY AND IMPACT OF THE EARLY DIAGNOSIS PROGRAM.
Materials and Methods: Longitudinal retrospective multicenter study, involving 9 referral hospitals. The analysis was based on a comparison before and after the 2010 intervention, stratified by regions which had or not received the Program. The adequacy indicators were: attendance at the capacity building training; and Program material available. The impact indicators were: children referred for suspected cancer; and lag time. The data were collected from medical records, interviews (with nurses and patients' families), and the database of the Program.
Results: Of the physicians and nurses registered in the program in 2010 ($n = 621$), 80% achieved the expected attendance rate (75%) and 54% reported that the program material is used in their practice. A total of 1,797 medical records were analyzed. A before/after comparative assessment showed a 23% rise in the number of children referred. The median lag time fell after the Program by 61% in the regions which received the Program (from 13 to 5 weeks).
Conclusions: The Program was carried out as anticipated, and the targets were achieved. The impact can be inferred from the increased number of referrals for suspected pediatric cancer and the reduced lag time. No other factors that could explain this result have been identified.

P-0406

DEALING WITH DATA SAFETY AND SECURITY IN TRANSLATIONAL AND PERSONALIZED MEDICINE

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Purpose/Objective: Translational and personalized medicine relies on heterogeneous data from patients. Their usage is constrained by legal and ethical regulations due to the sensitive nature of personal medical data. Here we describe a legal and ethical framework to facilitate the usage of data in translational and personalized medicine within Europe.
Materials and Methods: Within p-medicine (a European funded project; FP7-ICT-2009.5.3, GA: 270089; www.p-medicine.eu) a legal and ethical framework is elaborated to allow the secure and safe sharing of medical data in research, clinical trials and decision making. This framework takes in particular into account the European Data Protection Directive 95/46/EC and the Clinical Trials Directive 2001/20/EC.
Results: As translational research is not possible without genetic data and as genetic data cannot be anonymized stricto sensu the legal and ethical framework of p-medicine is based on three pillars. These are de-facto anonymity, informed consent and national research exemptions in Europe. To achieve de-facto anonymity legally binding contracts between data providers and data users are signed that regulate the usage of the data within p-medicine. In addition personal data are pseudonymized via an independent trusted third party. The necessary informed consent given by patients, as a second pillar, is regarded as a fall back if problems encounter with contracts or pseudonymization. Existing (but different) national research exemptions tune this framework. It will be discussed whether the upcoming European Data Protection Regulation will necessitate changes in the legal concept as well as other privacy frameworks developed in similar European projects will be reviewed.
Conclusions: The p-medicine project shows that the safe and secure usage of personal data within research can be achieved by establishing an ethical and legal framework. Such a necessary and easy to use framework will foster translational and personalized medicine.

P-0407

FANCONI ANEMIA AND CHILDHOOD SOLID CANCERS: A NATIONAL RETROSPECTIVE STUDY.

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Purpose/Objective: Children with Fanconi anemia (FA) mostly develop hematologic disorder and myeloid leukemias; solid cancers, mainly oral carcinomas, may occur in early adulthood. However, few cases of early onset solid cancers are reported in children with severe FA.
Materials and Methods: We have conducted a national retrospective series of solid tumors occurring in FA patients during childhood. For each patients, the malformative syndrome, tumour type, treatment and outcome was analysed. Whenever available, fresh-frozen tumours were analysed by array-CGH.
Results: We identified 7 patients and 1 fetus (two siblings) with FA and solid tumour within a 20 years period. The mean age at diagnosis was 13 months. For two patients, the diagnosis of Fanconi anemia was ignored until the cancer occurred. All patients had failure to thrive, dysmorphic features and abnormal pigmentation. 7/8 of these cases showed *BRCA2* mutations; four patients had more than one malignancy, and solid tumour types included 4 nephroblastomas, 2 embryonal rhabdomyosarcomas, 2 neuroblastomas and 2 brain tumours. The fetus died *in utero*. Two children died of complications of the chemotherapy, two died of the cancer and one died of a secondary leukemia. Only one *BRCA2* patient survived, after a tailored chemotherapy. The genomic pattern of the tumours showed a higher number of breakpoints than usually observed in the similar pediatric tumours. Finally, 1/8 patient had a *FANCA* mutation; he developed a low-grade glioma and survived.
Conclusions: Solid tumours in FA are extremely rare during childhood and mainly associated with *BRCA2* mutations. The proper genetic diagnosis is mandatory early on in order to tailor the treatment. Adpated doses may allow some patients to survive.

P-0408

ROLE OF "PHYSICIAN EXTENDERS" IN A PEDIATRIC ONCOLOGY PROGRAM IN A DEVELOPING COUNTRY

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Purpose/Objective: Many countries, especially in resource-constraint settings, are experiencing a shortage of pediatric oncologists. Mexico is an example, with only 135 certified pediatric oncologists for a population of 120 million inhabitants (ratio: 1 oncologist/ million), whereas the ratio in the US is 4 oncologists/million.

In 2008, Rady Children's Hospital in partnership with St. Jude Children's Research Hospital and Hospital General-Tijuana, the largest hospital in northwestern Mexico, initiated a twining project to improve pediatric cancer care.

We postulated that the role of a general pediatrician dedicated to the oncology service, trained lead nurses, and the establishment of a multi-disciplinary team could be a synergistic gap-filling measure to overcome this shortage.
Materials and Methods: We design a 5-year plan to provide salary supplementation for key staff, intensive education, and training for the medical staff. Core content included cancer diagnosis, chemotherapy complications, supportive care, infection control, and individual training regarding critical care management, including central line placement.

Six lead nurses and 8 pediatricians were appointed as "physician-extenders" and duties were carried out under preceptorship of trained pediatric oncologist.
Results: After 4.5 years, the pediatricians and the nurses have received over 300 hours ad 900 hours of education, respectively. Duties included management of disease and treatment-related complications, supervision of pediatric residents and general nurses, and collaborative work with a multi-disciplinary team that includes psychologists, social workers, pharmacists, and others. The patient:provider ratio improved from 1 oncologist and 1 nurse per 20 new patients/year to 10 physicians and 28 nurses per 60 new patients per year.
Conclusions: We implemented an effective sustained education program for general pediatricians and lead nurses that enabled them to succeed in their clinical duties. This

''physician-extender'' model in combination with a dedicated multi-disciplinary team has resulted in a 3-fold increase in the population served and has relieved the shortage of pediatric oncologist.

P-0409

THE RELATIONSHIP BETWEEN MEDICAL PROFESSIONALS AND IN-HOSPITAL CHILDHOOD CANCER PARENT SUPPORT GROUPS

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Purpose/Objective: Introduction: In Japan, In-hospital childhood cancer support groups for parents with children suffering from childhood cancer are a common occurrence. They have been implemented by parents of afflicted children, and fulfill a practical purpose, serving as a means of information exchange between the parents, and also function as a means of therapy. Cooperation and understanding between these parent groups and medical professionals is a constant aspiration.
Purpose: This study demonstrates the role of medical professionals when working with parent support groups.
Materials and Methods: Method: This study surveyed via questionnaire, 224 members from 15 different in-hospital childhood cancer parent support groups, and interviewed 20 medical professionals of five varying occupations, from four hospitals. Combining the results of both, the interaction of medical professionals and parent support groups is explored.
Results: Result: These groups had grievances about the ''lack of a designated organizer,'' ''difficulty securing members,'' ''lack of understanding from medical staff,'' ''lack of funding,'' and a ''lack of an allocated space for activity.'' Concerns on the part of Medical professionals regarding these groups were about the ''communication of false information,'' an overall ''lack of group organization,'' and ''pressures on the hospitals.''
Conclusions: Conclusion: The cooperation between Japanese cancer parent support groups and medical professionals is in valuable, therefore, it is important for medical professionals to adapt to better accommodate the needs of these groups.

P-0410

RACIAL/ETHNIC DIVERSITY IN PEDIATRIC ONCOLOGY CLINICAL TRIAL ENROLLMENT AT RADY CHILDREN'S HOSPITAL SAN DIEGO (RCHSD)

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Purpose/Objective: In the United States, more than 12,000 children ages 0-21 are diagnosed with cancer each year. Over the past few decades, survival rates in pediatric oncology have improved dramatically, as a result of the successful enrollment of approximately 70% of the cases in clinical trials. Little work has been done to assess cancer disparities in the pediatric population.

The purpose of this study was to assess rates of trial participation by age, sex, cancer type, and Hispanic ethnicity at RCHSD.
Materials and Methods: Data from newly diagnosed cases in 2009 and 2010 at RCHSD were collected and classified by race/ethnicity, age, sex, and cancer type (solid or liquid). Rates of enrollment among different sub-groups were obtained and compared.
Results: There were 237 cases included in the analysis. When analyzing by race/ethnicity, only comparisons between Hispanics and Non-Hispanic whites (NHWs) were assessed. The overall clinical trial accrual was 52%. Our analysis revealed significant underrepresentation among Hispanics when compared to NHWs in treatment protocols (67% vs. 91%) [$p = 0.01$] and in the cancer registry protocol (28% vs. 44%) [$p = 0.032$]. Males were overall underrepresented compared to females (46% vs. 63%) [$p = 0.009$] and patients ages 15-21 (39%) compared to patients ages 0-4 (65%), 5-9 (49%), and 10-14 (48%) [$p = 0.026$]. Enrollment into solid malignancy protocols for all subgroups was significantly underrepresented when compared to liquid malignancy (46% vs. 60%) [$p = 0.039$].
Conclusions: Participation in clinical trials at RCHSD is low overall. Significant underrepresentation was observed for Hispanics, solid tumor diagnoses, adolescents and males. Our results warrant replication in larger populations and in those with larger representation of additional racial/ethnic groups. Assessment of barriers encountered by Hispanics are underway. Targeted interventions will be implemented to address these disparities and to ensure the ethical practice of pediatric oncology, including equal clinical trial enrollment for Hispanics, who constitute the largest ethnic population served by RCHSD.

P-0411

CURRENT REFUSAL/DROPOUT RATES IN PAEDIATRIC ONCOLOGY-INSTITUTIONAL EXPERIENCE

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Purpose/Objective: Refusal of Treatment(RT) and Dropout (DO) are major challenges in developing countries. We analyzed the reasons for RT and DO in our cohort of patients.
Materials and Methods: We have analyzed all the cases less than 14 years registered at our center from Jan to Dec 2012. RT - not initiate treatment. DO - not complete planned treatment. We have analyzed the factors contributing RT/DO like distance from the treatment centre, gender, religion, self-paying/ Insurance, socioeconomic status, education of at least one parent (10th class) and length of treatment. The patient related factors like affordability, belief in alternative healthcare system, loss of job, poor prognosis of disease and other illness were analyzed.
Results: There were 117 children registered during the study period. Males to females ratio was 1.73:1. Most common diagnosis was ALL 44/117 (29.9%), Lymphoma 15/ 117 (12.8%), Wilms Tumor 12/117(10.2%), CML 10/117(8.5%), Brain Tumor 10/117 (8.5%) and others. Hundred patients (85%) initiated treatment under state/employer funded cashless facility (Arogyasri, ESI, GIPAP, State Departments). Eleven (9.4%) patients refused treatment. Sixteen (13.6%) patients dropped out. On interviewing the parents the most common factor were poor prognosis at diagnosis 9/27(33%), financial constraints 7/27(25.9%), alternative health care systems 3/27 (11.1%), loss of job 2/27(7.4%), Chicken pox and tubercuosis 3/27 (11.1%). None of the others factors were statistically significant. (Table 1).

TABLE 1.

Factors	Taking Treatment (n = 90)	Refusal/Dropout (n = 27)	P value
Distance from treatment center > 200	54	21	0.119
Male	59	15	0.369
Hindus (Gender)	72	21	0.790
No Cashless Treatment	13	7	0.345
Poor Socio Economic status	60	21	0.345
At least one parent is educated (10 class)	30	6	0.345
Prolonged treatment	34	9	0.827

Conclusions: In our center, nearly 25% patients refuse or drop out of treatment. Most common cause of the refusal/dropout are poor prognosis at diagnosis and financial constraints.

P-0412

A MULTIDISCIPLINARY DIAGNOSTIC ALGORITHM FOR PEDIATRIC ABDOMINAL MASS IN A RESOURCE-LIMITED SETTING

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Purpose/Objective: The diagnosis of a pediatric abdominal mass is complicated by its requirement for significant multidisciplinary coordination. Pediatric surgery, oncology, pathology and radiology practitioners must all work together to evaluate and stage patients. In low and middle-income countries, diagnosis is often delayed due to systemic limitations and the cost of diagnostics. In response to the lack of standardized guidelines for resource-limited settings, we created a decision support tool for the diagnosis of pediatric abdominal mass in a tertiary care facility in Davao City, Philippines.
Materials and Methods: Initial data gathered included pricing of laboratory and radiology modalities and the time currently required for each test to be performed at the Southern Philippines Medical Center (SPMC). We utilized process mapping of patient charts and interviews with the consulting services discussed above to identify current practice and target areas for system improvement. The above data was reconciled in a final process guided by local and international expert opinion.
Results: We created an algorithm in the form of a decision-tree intended for use by pediatric and surgical residents and nurses. It is organized into two phases, each with an expected time frame to completion. The first phase focuses on identifying the origin of the mass (liver, renal, adrenal, or indeterminate), obtaining basic laboratory and radiographic information and ensuring early notification of all necessary services. A comprehensive site-specific differential diagnosis is also included. The second phase is designed to confirm preoperative diagnosis and guide surgical biopsy and/or resection planning.
Conclusions: Abdominal tumors in low and middle-income countries represent a diagnostic challenge given the costs and multiple disciplines involved. We expect our algorithm will standardize the initial management and help ensure timely, cost-efficient assessment. Further research will evaluate whether the algorithm is followed and its impact on reducing diagnostic delay as part of an ongoing quality improvement program.

P-0413

RHEUMATOLOGIC PRESENTATION OF HEMATOLOGICAL MALIGNANCIES

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Purpose/Objective: Leukemia and lymphoma may present with rheumatological symptoms. These may lead to misuse of steroids, further masking the diagnosis of malignancy. We evaluated all hematological malignancies with such presentation.
Materials and Methods: We retrospectively reviewed 520 consecutive cases of pediatric hematological malignancies (2005-2012). All patients with bone and joint pain, arthritis, backache and inability to walk at initial presentation were included in this series.
Results: Among 520 patients, 76 (14.6%) had rheumatological symptoms: 70/334 (21.0%) children with acute lymphoblastic leukemia (ALL), 4/37 (10.8%) Hodgkin lymphoma (HL), 2/70 (2.9%) acute myeloid leukemia (including 1 mixed lineage leukemia), and 0/49 non-Hodgkin lymphoma. Median age was 7.5 years (2-17 years). Eleven patients presented with backache, 6 had inability to walk. Forty-one (53.9%) patients had arthralgia, of which 6 had migrating polyarthralgia. Arthritis was seen in 30 (39.5%) patients, with polyarticular involvement in 21. Fever was present in 59 (77.6%) children. Bleeding tendency ($n = 9$) and weight loss ($n = 5$) were rare symptoms. Hepatosplenomegaly was seen in 29 and lymphadenopathy in 7. Fifteen (19.7%) children were initially diagnosed as rheumatological disease, mostly Juvenile Idiopathic Arthritis. Forty-four (57.9%) patients had abnormal blood counts at presentation, although many patients had normal counts at the onset of symptoms, with a progressive deterioration over the next few months. Eleven patients had abnormal bone imaging with multiple bone uptake or diffuse vertebral uptake. Two patients with arthritis had normal bone scan. Ten patients were pretreated with steroids, including 2 with methotrexate and sulfasalazine. Delay between symptom onset and final diagnosis ranged from 1 week to 7 months. All patients had resolution of symptoms within a month of starting therapy.
Conclusions: Rheumatological symptoms are important presenting complaints in ALL and advanced-stage HL, often delaying diagnosis. Repeated blood count monitoring with peripheral smear are required. Bone marrow examination is advisable prior to starting steroids in such cases.

P-0414

DIFFERENTIALLY EXPRESSED MICRORNAS IN PEDIATRIC CANCER STEM CELLS AND THE PATHWAYS THEY REGULATE

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Purpose/Objective: microRNAs (miRNAs) have emerged to be an important class of non-coding RNA that is functionally involved in the control of many biological processes. Deregulation of miRNA is often associated with many cancers. Recent evidence suggests that most cancers, including pediatric, have their own stem cells, referred to as 'cancer stem cells' (CSCs). We proposed that a common signature of aberrantly expressed miRNAs (CSC-associated differentially expressed miRNAs (DEmiRs)) in the CSCs pool might explain the disrupted signaling pathways in the CSCs.
Materials and Methods: Using the neurosphere and ALDEFLUOR® surrogate assays as read-out strategies for enriching a stem-like cancer cell (CSC) population, we had uncovered specific DEmiRs that were dysregulated in this population. We profiled six pediatric cell lines, Hep293TT, HepG2, MG-63, Daoy, SH-SY5Y, and RD-ES using a high throughput qRT-PCR approach to survey global miRNA expression in their CSC fraction. We then applied a novel miRNA-pathway association algorithm to elucidate the characteristics of the CSC. We studied the potential effects of some of the DEmiRs in CSCs by gene silencing.
Results: A group of 26 DEmiRs (23 up-regulated and 3 downregulated) were found, including *hsa-miR-21-5p*, *hsa-miR-148a-5p*, *hsa-miR-181a-5p*, *hsa-miR-323-3p*, and *hsa-miR-487b-3p*, as highly expressed, and *hsa-miR-19a-5p* and *hsa-miR-25-5p*, as down-regulated DEmiRs. Our novel miRNA-pathway association algorithm identified 865 potential CSC associated DEmiR targets. These targets were subjected to KEGG, Biocarta and Gene Ontology pathway and biological processes analysis. Four annotated pathways were enriched: cell cycle, cell proliferation, p53 and TGF-beta/BMP. De-regulation in these four main signaling pathways has extensively been demonstrated in CSC. Knocking down *hsa-miR-21-5p*, *hsa-miR-181c-5p* and *hsa-miR-135b-5p* using antisense oligonucleotides and small interfering RNA in cell lines lead to the depletion of the CSC fraction and impairment of sphere formation.
Conclusions: Our findings presented in this study suggest additional targets for prognostic and therapeutic intervention in pediatric cancers.

P-0415

PEDIATRIC ONCOLOGY NETWORKED DATABASE IMPLEMENTATION IN JORDAN: THE KING HUSSEIN CANCER CENTER EXPERIENCE

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Purpose/Objective: The Pediatric Oncology Department at KHCC receives >300 new patients yearly, but little is known about their outcomes and toxicities, so a data management system and database were needed. The Pediatric Oncology Networked Database (POND, www.POND4Kids.org) was developed in 2004 by the SJCRH International Outreach Program, and is available at no cost to serve the global pediatric oncology research community.
Materials and Methods: In June 2006, POND was adopted by our department through the collaboration with the international outreach program. The KHCC site was created and a site administrator was identified. A SJCRH volunteer provided onsite training at KHCC. A committee was established and a coordinator was recruited whose job is to supervise data entry process, assess data quality, perform audits to ensure entry of all new cases and capturing of severe toxicities and detects missing or wrong information entered. Data entry is undertaken by the clinical nurse coordinators prospectively. An office equipped with 7 computers and high speed internet access was provided. Quality measures were put in place to ensure consistent and accurate data entry, in addition to several tools devised: an operational manual, data dictionary, new user, data request and toxicity collection forms, toxicity grading cards, POND brochure and video.
Results: Between July 2006-June 2012, 1524 new patients were entered into POND. Starting 2007 yearly audits were conducted to identify cases with incomplete or incorrect data. Post audit, all missing and incorrect data were completed. The percentage of incomplete or missing data decreased $<1\%$. No new cases were missed since 2009. Three hundred and seven episodes of $\geq$grade 3 toxicities were captured since December, 2008. In total, 51 reports were released from POND for quality, administrative and publication purposes.
Conclusions: POND is an easy to use web technology. Implementing POND in young institutions is feasible; it allows secure clinical research data storage, auditing and flexible sharing with other institutions.

P-0416

ASSESSMENT OF PEDIATRICS NECK MASSES BY DIFFUSION MR IMAGING

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Purpose/Objective: Neck masses in children are commonly of inflammatory, infective or congenital origin. Malignant lesions are only about 5% of masses arising in the head and neck region in this age group. Malignant head and neck tumors warrant awareness of their occurrence and imaging appearances that important for any radiologist to distinguish malignant tumors from benign lesions. Our objective was to determine whether DWI and calculated apparent diffusion coefficient (ADC) value correlates with pathologic diagnosis of pediatric neck tumors and therefore allows more accurate tumor characterization.
Materials and Methods: 55 pediatric hospital patients with recently presented with neck tumors who underwent preoperative conventional MRI and diffusion weighted images (DWI) were included in this study. All neck tumors analyzed were either solid-mass lesions or had a solid component suitable for region-of-interest analysis. The average ADC obtained from the solid component of each tumor was compared with the histological diagnosis either benign or malignant.
Results: We found a signi?cant negative correlation between average ADC and neck tumor histopathologic diagnosis ($P < 0.001$, $r = *0.43$): The mean ADC values were $1.45 \pm 0.52 \times 10^{*3}$ mm^2/ sec (mean $\pm$ SD) for the benign lesions and $1\ .00 \pm 0.38 \times 10^{*3}$ mm^2/ sec for the malignant tumors. With sensitivity: 92.5%, specificity: 86.66% and accuracy: 90.9%.
Conclusions: Diffusion MRI study is a significant, accurate, fast, non invasive and non enhanced technique that can be used for characterization of malignant lesions of the head and neck region and to differentiate it from benign lesions relying on signal of the lesion on DWI, ADC map and ACD value.

P-0417

IDENTIFICATION OF NOVEL AND INTERACTING PHARMACOGENETIC VARIANTS THAT DETERMINE DIFFERENTIAL SIROLIMUS CLEARANCE IN CHILDREN WITH TUMORS

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Purpose/Objective: The mTOR inhibitor, sirolimus, is widely used in tissue transplantation, and more recently in cancer therapy. CYP3A5*3 polymorphisms have been shown to influence sirolimus clearance, but effects of other drug metabolism enzyme and transporter (DMET) gene polymorphisms have not been investigated. We hypothesized that additional variants, alone or in combination, would better predict sirolimus clearance.
Materials and Methods: Sirolimus pharmacokinetics were determined in a phase II study of 42 children with tumors. Patients were genotyped for 1,931 known variants using the DMET GeneChip. Statistical analyses first calculated correlation coefficients for all SNPs to allometric clearance ($[(CL/Wt)x70]^{0.75}$) followed by multiple regression to determine relative effect sizes and interactions.
Results: Three polymorphic DMET genes significantly and independently influenced sirolimus clearance, including the multidrug resistance-associated protein *ABCC5* ($p = < 0.0001$), nucleoside transporter *SLC28A2* ($p = 0.0012$), and UDP-Glucuronosyltransferase protein *UGT2B7* ($p = < 0.0001$). *SLC28A2* and *UGT2B7* had the strongest effect size, with the log of allometric clearance increasing by 0.303 and decreasing by 0.233, respectively, with each polymorphic allele copy. The multiple regression analysis also identified 8 interacting polymorphic DMET genes influencing clearance. *SLC28A2* interacted with the aldehyde dehydrogenase *ALDH3A1* ($p = 0.0003$), organic cation transporter *SLC22A1* ($p = 0.0005$), and glutathione-S-transferase *GSTM3* ($p = 0.0002$). SLC22A1 interacted with *ALDH3A1* ($p = 0.0002$), UDP-Glucuronosyltransferase *UGT2B7* ($p = 0.001$), and the copper transporter *ATP7A* ($p = 0.0008$). GSTM3 interacted with ATP7A ($p = 0.038$) and ALDH3A1 ($p = 0.0003$). The model had an overall F-value of 13.29, a p-value of < 0.0001, and an R-square of 0.83.
Conclusions: Our novel genotype based regression model was able to significantly improve the prediction of patient dosing, preventing at least 25% of patients from being over or under dosed compared to contemporary practices. Future studies in larger populations are needed to confirm this model and possibly improve sirolimus' safe and effective use. This work also establishes a novel approach that could be used for identifying pharmacogenetic guided dosing of other drugs and chemotherapy.

P-0418

RISK FACTORS FOR ACUTE GRAFT VERSUS HOST DISEASE IN PEDIATRIC PATIENTS IN A DEVELOPING COUNTRY. MEXICO

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Purpose/Objective: Identify the major risk factors that influence the development of aGVHD in patients receiving allogeneic hematopoietic stem cell transplantation (allo-HSCT) at the National Institute of Pediatric«s Hematopoietic Stem Cell Transplantation unit. A 10 years review.
Materials and Methods: We performed univariate analysis in order to determine the frequency of aGVHD for each risk factor, by knowing bivariate associations between variables and estimating relative risk in the associations studied. Chi square was employed and Fisher test for determination of statiscal significance. The variables in the bivariate analysis were significant were entered into multivariate analysis (logistic regression) to determine the contribution of each of the factors for the appearance of disease. We considered significant value $p \leq 0.05$
Results: During this study, the Institute has conducted allo-HSCT to 115 patients, with different illnesses, wich are grouped as follows: hematologic malignancies 69 cases (60%), primary immunodeficiencies 27 cases (23.4%), benign hematological diseases 12 cases (10.4%), hereditary metabolic diseases 6 cases (5.2%) Others 1 case (0.86%).
Of the 115 patients, only 27 of them developed aGVHD with the results obtained by univariate and multivariate analysis we found that the factors increase the risk to develop aGVHD are: A) source.- peripheral blood (OR 4.11 $p < 000.1$), B) infections 3 months before transplantation (OR 4.5 $p < 0.03$) C) CMV infection in the recipient (OR 4.6 $p < 0.03$), D)peripheral blood greater than bone marrow (OR 3.16 $p < 0.001$), and E)cell dose $> 8.3 \times 106$/kg (OR 4.6 $p < 0.03$).
Conclusions: The 23.4% of patients developed aGVHD, which is a low value that may be secondary to that 50% of transplants are a source of cord blood cells which have a lower risk of developing aGVHD, however it is important note that the presence in our series of infections factor receptor are important for the development of the disease.

POSTER SESSION: POSTER SESSION - HYSTIOCYTOSIS

P-0419

DIAGNOSIS OF A SIMULTANEOUS OCCURRENCE OF NIEMANN PICK TYPE B DISEASE AND LANGERHAN'S CELL HISTIOCYTOSIS IN A 12 MONTH OLD CHILD: A FORTUITOUS ASSOCIATION?

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Purpose/Objective: We report the case of one-year-old- girl with Niemann Pick type B disease, who also developed Langerhan's cell histiocytosis (HL).
Materials and Methods: Niemann Pick disease type B is a lysosomal storage disorder, which is autosomal recessively inherited, linked to the mutation of the acid lysosomal sphingomyelin phosphodiesterase-1 gene (SMPD1). This mutation leads to the accumulation of sphyngomyelin in monocytes and histiocytes with progressive spleen and liver enlargement and delayed progressive lung failure. HL is a rare disease of unknown origin. Hepatosplenomegaly is frequent in HL but it can involve other tissues (skin, bone marrow, boneÉ). Recently, a link to BRAF mutation was described in HL which could be helpful for diagnosis assessment.
Results: We describe here a 1 year old child who presented association of thrombopenia, anemia, skin lesions, major spleen and liver enlargement, diarrhea, and fever. Histological analysis confirmed a HL disease with the BRAF mutations in skin lesions. NP was checked for since there was an atypical presentation with large hepatosplenomegaly. The patient is homozygous for the R608 deletion. She was treated with a high risk HL protocol (2Cda and cytarabine) and showed slow improvement on hematological and gut symptoms but persistence of liver and spleen enlargement.
Conclusions: This is the first reported case of the simultaneous occurrence of these 2 rare diseases both involving histiocytes (HL and Nieman Pick type B disease). We think that we should look for the Niemann Pick mutation in cases of HL occurring in children of a young age with spleen and liver enlargement as it can explain the severity of the disease and the persistence of a liver and spleen enlargement after treatment. As splenectomy can worsen Nieman Pick type B disease, it should be avoided in these cases

P-0420

CASE REPORT:RESPONSE TO BRAF V600E INHIBITOR VEMURAFENIB AND ADOPTIVE IMMUNOTHERAPY IN A PATIENT WITH MULTISYSTEMIC AND REFRACTORY LANGERHANS CELL HISTIOCYTOSIS

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Purpose/Objective: langerhans cell histiocytosis(LCH) is a complex disease of unknown etiology characterized by disorder proliferation and accumulation of dendritic cells. Patients with multisystemic LCH always suffer an aggressive disease course and a high moltality, while current therapies have little effects. Althogh LCH is not considered a neoplasm disease, BRAF etc. cancer-ralated gene mutations were recurrently observed, the efficacy of mutated BRAF inhibitor Vemurafenib in LCH is unknown.
Materials and Methods: We described a two-years-old boy with LCH admitted to the hospital because of a 1-month gradually enlarging left temporal mass, blood-tinged ear discharge, mild jaundice and diabetes insipidus. A MRI scan showed a soft-tissue mass in the left temporal, bone destruction of left temporal, lateral orbital wall and mandible, with bilateral temporal meninges involvement. An abdominal CT scan showed multiple hepatic nodules and splenomegaly. After receiving front-line and rescue combined chemotherapies, the disease was controlled for a short time and became refractory, the boy presented with deepening jaundice, ascites, hypoalbuminemia, bilateral legs edema, hepatomegaly and splenomegaly. He was diagnosed with biliary cirrhosis. Because BRAF V600E mutation was found, he was admitted to the targeted drug Vemurafenib.
Results: It had a dramatic efficacy: hepatic masses, ascites and bilateral legs edema disapeared and urine output reduced, but cholestatic liver enzymes were still not declined. After 5 months of oral Vemurafenib therapy, he was simultaneously treated with adoptive immunotherapy weekly, after 4 cycles, serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin significantly droped but MRI showed the left temporal mass was still stable.
Conclusions: This is the first known data-based case report of multisystemic and refractory LCH treated with combined Braf inhibitor Vemurafenib and adoptive immunotherapy and had a good response.

P-0421

OUTCOME OF COMBINATION CHEMOTHERAPY OF 2-CHLORODEOXYADENOSINE AND CYTOSINE ARABINOSIDE FOR REFRACTORY OR REACTIVATED LANGERHANS CELL HISTIOCYTOSIS

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Purpose/Objective: 2-chlorodeoxyadenosine (2-CdA) can be used in combination with cytosine arabinoside (Ara-C) in various dosing schedules for refractory or reactivated Langerhans cell histiocytosis (LCH). The aim of study was to assess the efficacy and tolerability of combination chemotherapy of 2-CdA and Ara-C in a single institute.

Materials and Methods: We retrospectively reviewed medical records of 11 patients who were treated with 2-CdA and Ara-C for reactivated or refractory LCH at Asan Medical Center.
Results: At initial diagnosis, 4 had multisystem disease with risk organ (RO) involvement, 5 multisystem disease without RO involvement, and 2 multifocal bone disease. At initiation of 2-CdA and Ara-C therapy, 2 had refractory disease in RO, 3 refractory disease in low-risk organ, and 6 reactivation in low-risk organ after vinblastine/prednisone-based chemotherapy. Chemotherapy was comprised of 2-CdA, 5 mg/m^2/day for 5 days and Ara-C, 200 mg/m^2/day for 3 days in 7 (group A), and 2-CdA, 9 mg/m^2/day for 5 days and Ara-C, 1 g/m^2/day for 5 days in 4 (group B). In group A, 5 were treated with 4 to 6 courses of chemotherapy followed by maintenance chemotherapy, 1 stopped chemotherapy due to complication, and 1 is on chemotherapy. In group B, 2 stopped chemotherapy due to poor tolerance and 2 completed 3 courses of chemotherapy followed by maintenance chemotherapy. Of 9 evaluable patients, all showed good response (complete resolution in 5, regression in 4). Infectious complications included bacterial sepsis ($n = 1$) and pulmonary aspergillosis ($n = 1$) in group A, and pulmonary tuberculosis ($n = 1$) in group B.
Conclusions: Combination chemotherapy of 2-CdA (5 mg/m^2/day for 5 days) and low-dose Ara-C was effective and tolerable in refractory or reactivated LCH, while higher dose 2-CdA combined with high-dose Ara-C was limited by poor tolerability and risk of infection. Further investigation is warranted to determine optimal dose and combination of 2-CdA and Ara-C.

P-0422

MUTATIONS OF PRF1 GENE IN CHINESE PATIENTS WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AND MALIGNANT LYMPHOMAS

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Purpose/Objective: PRF1 gene was responsible for familial hemophagocytic lymphohistiocytosis type 2 (FHL2). However, perforin de?ciency, either alone or in combination with other mutations of genes involved in cell-mediated cytotoxicity pathways (ie, Fas-mediated killing pathway), could also present in patients with lymphoma. We investigated the presence of either biallelic or monoallelic mutations of the PRF1 gene in groups of hemophagocytic lymphohistiocytosis (HLH)/lymphoma patients among Chinese population.
Materials and Methods: Peripheral blood samples from 40 newly diagnosed HLH patients, 20 children with lymphomas, and 50 healthy volunteers were obtained. PRF1 gene analysis using genomic DNA sequencing, and perforin protein detection with flow cytometry were performed.
Results: Four HLH patients were identi?ed with heterozygous mutations in PRF1 gene (c.282C > A, c.385T > A, c.630C > T, c.757G > A, c.839A > G, c.1061A > T, c.1620A > G). Compound heterozygous mutation of c.757G > A and c.1061A > T were found in PRF1 gene of a 6-year-3-month-old female, c.839A > G and c.1061A > T were found in PRF1 gene of a 61 year old male, respectively. Two patients with lymphoma were identi?ed to have heterozygous mutations in PRF1 gene (c.282C > A, c.1620A > G). SNP(single nucleotide polymorphism)c.822C > T (rs885821), c.900C > T (rs885822) and 1225G > A in exon3 (rs1889490) were found in all three groups. Patients with specific mutations in PRF1 gene presented with a low level of perforin expression with NK cells in the acute phase of their disease, and the levels of perforin expression were not able to return to normal even when their conditions of HLH were controlled.
Conclusions: Perforin detection with flow cytometry can help to direct genetic analyses. Patients with HLH or lymphoma associated with perforin deficiency may conceivably due to a defective cytotoxic mechanism of uncontrolled proliferation and development of malignant lymphoid cells, which warrants further study.

P-0423

CLINICAL EPIDEMIOLOGY AND OUTCOME OF HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) IN CHILDREN – RESULTS OF A SYSTEMATIC REVIEW AND POOLED ANALYSIS OF 272 PATIENTS FROM INDIA

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Purpose/Objective: HLH is a rare life threatening disorder well described in Western literature. Intensive chemoimmunotherapy approach has improved the 5 year survival to 50%, with/without haematopoietic stem cell transplant (HSCT).The clinical epidemiology and outcomes in resource-limited countries are less well known.
Materials and Methods: A comprehensive search of Medline, Embase, Scopus and Web of science (from inception to April 2012) databases were undertaken. Hand searching of abstracts from SIOP (2000-2012), ASCO (2000-2012) and PEDICON (2007-2012) annual congress was done along with reference lists of selected articles. Children $\leq$ 16 years of age presenting with HLH in India were included. Individual data was pooled and authors were contacted if additional information was required.
Results: Of the 513 studies identified, 57 studies (42 single case reports) with 272 children (median age 5 years, 57% male) were included. Clinical manifestations were fever (94%), hepatomegaly (90%), splenomegaly (86%), lymphadenopathy (36%), neurological symptoms (32%), oedema (15%) and jaundice (11%). Laboratory findings were Hb $<$ 9 (83%), neutrophil $<$ 1 (37%), platelets $<$ 100 (80%), hypertriglyceridaemia (36%), hyperferritinaemia (92%), hypofibrinogenaemia (39%) and haemophagocytosis (89%). Molecular/genetic investigations were rarely done.

Infectious (36%), familial/genetic (13%) and rheumatological (10%) were the suspected aetiologies/triggers. No cause was identified in 28% of the children. Common infectious triggers were dengue haemorrhagic fever, ebstein barr virus, leishmaniasis, tuberculosis, malaria and salmonella typhi.

Management included supportive care and treatment of primary cause where appropriate. Majority of patients had steroids (67%)(alone (27%), with ciclosporin (4%), as per HLH-2004 protocol (36%)). 25% of patients had immunoglobulin and 0.7% patients had an HSCT. 60% children were alive at end of treatment, 24% died and 6% abandoned treatment. Duration of follow-up was poorly reported. Survival was significantly lower in those with familial/genetic HLH ($p = 0.0002$).
Conclusions: HLH in children in India is characterised by older age at diagnosis, predominance of infectious aetiology and (consequently) better outcomes than that reported in the Western literature.

P-0424

CURRENT OUTCOMES OF LANGERHANS CELL HYSTIOCYTOSIS (LCH) AMONG CHILDREN IN INDIA: A SYSTEMATIC REVIEW

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Purpose/Objective: LCH is a unique disease with variable manifestations and disease-course ranging from spontaneous regression, progression, and recurrences to death and irreversible long-term disabilities. The outcomes of children with LCH in India are not well described and this systematic review aims to address this.
Materials and Methods: A search of MEDLINE, Scopus, Web of Science and EMBASE (from 2000 to August 2012) databases was undertaken. Abstracts from SIOP (2000-2012), ASCO (2000-2012) and PEDICON (2007-2012) were also handsearched.
Results: Of the 267 unique studies identified, 15 single-centre studies (7 published and 8 abstracts) from 12 centres met the inclusion criteria. There were a total of 508 children with LCH (5-69 children/study) with median age at presentation from 1.5-12 years and strong male predominance was noted in almost all studies. Treatment was mainly in the form of chemotherapy with observation, surgery and or radiotherapy used mainly for single system disease. Although treatment protocols were heterogeneous, there was stratification by risk group and vinblastine & steroids were commonly used.

Accounting for variable follow-up, overall survival ranged from 62-100% (median 89%) and event free survival (EFS) from 37-82% (median 58%) with death, active disease (refractory/progressive/reactivated disease) and abandonment counted as events EFS for single system unifocal disease was 75-100% (median 100%), single system multifocal disease 0-100% (median 93%), multisystem low risk 0-100% (median 85%) and multisystem risk organ involvement 0-64% (median 22%). Diabetes insipidus was the most common long-term sequel.
Conclusions: Reported outcomes of LCH in children in India are good except in multisystem disease with risk-organ involvement. However the variability in the outcomes and follow-up as well as the problem of treatment abandonment needs to be underscored.

P-0425

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS HLH): ADVANCES IN IMMUNOLOGIC AND GENETIC DIAGNOSIS, AND DISEASE TREATMENTS

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Purpose/Objective: Hemophagocytic Lymphohistiocytosis, encompasses a group of life-threatening immunodeficiencies characterized by excessive systemic inflammation. Here we describe important diagnostic advances through the development of rapid screening tests for various genetic forms of HLH. Furthermore, a new initial HLH treatment, new approaches to reactivation of HLH and conditioning prior to hematopoietic cell transplantation (HCT) are being tested in multi-institutional trials in an effort to improve survival and long term outcomes.
Materials and Methods: Important diagnostic advances include the development of rapid screening tests for various genetic forms of HLH. New immunosuppressive/ cytotoxic and biologic induction therapies, as well as Reduced Intensity HCT preconditioning (RIC) are being evaluated.

Results: Using flow cytometry, HLH due to perforin deficiency, X-linked Lymphoproliferative disease (XLP1), and X-linked Inhibitor of Apoptosis (XLP2 or XIAP) can be predicted within a matter of hours. Also flow-based, CD107a expression quantitates the degranulation of NK cells reflecting the function of four interacting molecules which assist the transfer of toxic molecules into the target cells (Rab27a, MUNC13.4, STX11 and MUNC18.2). Furthermore, all the steps of the cytotoxicity process can be 'visualized' with the Pantoxilux assay. An HLH 'gene chip' capable of rapidly detecting any of the known HLH-related genetic disorders is being tested.

Two clinical trials have recently opened: the induction protocol HIT-HLH which combines ATG up front followed by etoposide and steroids is in progress in the U.S., and a trial of a humanized anti-gIFN (gamma interferon) drug for treatment of reactivating HLH is currently active in Europe. Finally, several studies involving Alemtuzumab-based reduced intensity conditioning (RIC) prior to HCT are showing superior survival rates in patients with HLH compared to historical MAC HCT.

Conclusions: Once rapidly fatal, HLH today is more often cured.

P-0426

CORRELATION BETWEEN AGGRESSIVE RADIOLOGICAL FINDINGS AND CLINICAL OUTCOME IN LANGERHANS CELL HISTIOCYTOSIS WITH BONE INVOLVEMENT

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Purpose/Objective: Langerhans cell histiocytosis (LCH) is a multisystem disorder characterized by proliferation and accumulation of dendritic cells. The skeleton is the most common site of involvement. We describe the magnetic resonance imaging (MRI) characteristics of bone lesions and correlate these findings with clinical outcome.

Materials and Methods: A retrospective chart review of clinical records from 60 patients with LCH bone involvement from 1999 to 2008 were reviewed for imaging and clinical information. MR imaging characteristics included periosteal reaction, presence of a transitional zone or soft tissue mass, and intensity of enhancement (mild vs. intense).

Results: Overall, 61 patients were included with 62% being male with an average age of 5.8 years. The majority of patients had unifocal bone involvement (66%), followed by multifocal bone involvement (18%), with the remainder having multisystem or CNS special site involvement. Patients were treated with a combination of surgery and curettage (49%), chemotherapy (33%), indomethacin (13%), and other modalities (5%). With a median duration of follow-up of 69 months (range 4-142 months), 50 (82%) patients had a favorable outcome at the end of therapy, defined as no progression or reactivation of disease. On MRI, the majority of patients had periosteal reaction (86%) and presence of a transitional zone (68%). An associated soft tissue mass was seen in 60% of patients with favorable outcome, but in 100% of patients ($n = 11$) with an unfavorable outcome. Predictors of favorable outcome include older age ($P = 0.04$) and intensity of lesional enhancement on MRI ($P = 0.05$). Late effects were seen in 4 patients with diabetes insipidus, 1 with growth failure, and 1 with obesity.

Conclusions: Patients with LCH bone involvement typically have periosteal reaction and presence of a transitional zone. Lesions that enhanced more intensely were associated with a favorable outcome, likely indicating their biological sensitivity to treatment.

POSTER SESSION: POSTER SESSION - NEW DRUGS/EXPERIMENTAL THERAPEUTICS

P-0427

THE PRE-B-CELL RECEPTOR PATHWAY AS THERAPEUTIC TARGET FOR TCF3-REARRANGED B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: *TCF3*-rearranged B-cell precursor (BCP) ALL displays high levels of cytoplasmic Igμ (CyIgμ) which is a known component of the pre-B-cell receptor(pre-BCR). We investigated whether this results into an activated pre-BCR pathway in *TCF3*-rearranged BCP-ALL that may serve as therapeutic target.

Materials and Methods: The rearrangement pattern of immunoglobulin heavy chain (*IGH*), and light chains (*IGK* and *IGL*) was analyzed by multiplex PCR in leukemic cell samples of 190 non-*TCF3*-rearranged and 22 *TCF3*-rearranged childhood BCP-ALL patients. Expression levels of pre-BCR pathway components (EBF1, ZAP70, SLP65, BTK, PI3K-p110δ and IRF4) were measured by reverse-phase protein assays. Cytotoxicity of Ibrutinib (a BTK inhibitor) was determined in six *TCF3*-rearranged and six non-*TCF3*-rearranged cases by methyl-thiazol-tetrazolium (MTT) assays. The effect of Ibrutinib on Erk expression levels was tested by western blot.

Results: 84.6% (11/13) of *TCF3*-rearranged cases was highly positive for CyIgμ-expression compared to 20.9% (68/325) of non-rearranged cases ($p < 0.001$). The Ig-rearrangement pattern of the majority (86.4%) of *TCF3*-rearranged cases was arrested at IGH level without further processing of IGK/IGL genes. In contrast, only 17.9% of non-*TCF3* rearranged cases was blocked at *IGH* level ($p < 0.001$). Expression levels of pre-BCR pathway proteins (ZAP70, SLP65, BTK, PI3Kd110, IRF4 and EBF1) were 1.2 to 5.2-fold higher in *TCF3*-rearranged compared to non-rearranged samples ($p < 0.05$). The concentration of Ibrutinib lethal to 50% of primary leukemic cells was 16.7μM for *TCF3*-rearranged cases and > 50μM for non-rearranged cases ($p < 0.001$). Ibrutinib effectively reduced the expression of Erk in the MHH-CALL3 (*TCF3*-rearranged) leukemic cell line whereas this level remained unaffected in the non-rearranged cell lines NALM6 and MHH-CALL4.

Conclusions: This study indicates that *TCF3*-rearranged BCP-ALL is characterized by an immature pre-BCR signature with a concommitant activated pre-BCR signaling pathway. Inhibition of this pathway selectively reduced the cell viability of *TCF3*-rearranged BCP-ALL. These findings warrant clinical application of pre-BCR inhibitors (such as Ibrutinib) in the treatment of *TCF3*-rearranged BCP-ALL.

P-0428

RUXOLITINIB, A JAK1/JAK2 INHIBITOR, INHIBITS CELL PROLIFERATION AND INDUCES APOPTOSIS IN HODGKIN LYMPHOMA (HL) AND PRIMARY MEDIASTINAL B-CELL LYMPHOMA (PMBL).

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Purpose/Objective: HL and PMBL share similar molecular features and pathogenesis. Frequent gains of chromosome 9p exhibit higher Janus Kinase 2 (JAK2) transcript levels with increased JAK2 activity (Bentz *et al*, Genes Chromosomes Cancer, 2001), suggesting aberrant activity of JAK2 and Signal Transducer and Activator of Transcription (STAT) pathways, which may in part play an important role in the pathogenesis of HL and PMBL. Ruxolitinib (Rux) is a potent and selective JAK1/JAK2 inhibitor, with activity against myeloproliferative neoplasms (MPNs) including those harboring the JAK2V617F mutation; Rux also inhibits JAK2/STAT5 signaling *in vitro* and in a murine model of MPN (Quintas-Cardama *et al*, Blood, 2010). We hypothesize that rux will significantly inhibit the JAK2/STAT pathway, decrease cell proliferation and induce apoptosis in HL and PMBL.

Materials and Methods: Cell proliferation and apoptosis analysis were assessed using MTS and Caspase-3/7 assay, respectively. Protein and mRNA levels were examined by immunoblotting and qRT-PCR and statistical significance was determined by Student t-test.

Results: Rux significantly decreased STAT3, STAT5 and STAT6 phosphorylation in HL and PMBL cells. The reduction in cell proliferation by 10uM rux are 19% in L-428 (p

Conclusions: 1) Rux effectively inhibited JAK2 enzymatic activity by the abrogation of downstream STAT3, -5 & -6 phosphorylation. 2) Rux showed strong anti-proliferative effects and apoptosis but likely could be due to off-target effects. This may be related to a negative-feedback loop involving hyperphosphorylation of JAK2 that promotes cell survival. 3) Rux may prove to be a potential targeted agent for managing HL and PMBL.

P-0429

SLEEPING BEAUTY SYSTEM-MEDIATED EXPRESSION OF CHIMERIC ANTIGEN RECEPTORS (CARS) IN CIK CELLS: A NOVEL TOOL TOWARDS THE CURE OF CHILDHOOD LEUKEMIA

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Purpose/Objective: Stable gene transfer of chimeric antigen receptors (CAR) is a powerful tool to redirect antigen specificity of effector T cells for adoptive immunotherapy of tumors. The development of efficient and safe nonviral vectors would rescue the safety and manufacture concerns that limit so far their clinical application. The *ex-vivo* use of the latest generation Sleeping Beauty (SB) Transposon-mediated gene transfer offers a valid alternative to viral vectors for human gene therapy.

Materials and Methods: Here we used nucleofection of SB system and an optimized clinical-grade stimulation protocol to generate and propagate cytokine-induced killer (CIK) cells genetically modified to express CD123-specific 3rd generation CAR to redirect antigen specificity towards the acute myelogenous leukemia (AML) $CD123^+$ blasts. Indeed, CD123 overexpression is well known to be a poor prognosis marker in AML.

Results: With this system, the average transfection at 24hours was 68.9% ($\pm$ 1.0, $n = 6$) and mean survival percentage was 34.8% ($\pm$ 5.6, $n = 5$). Electroporation with the optimized stimulation protocol did not affect the phenotype of CIK cells, preserved their na●ve and stem cell memory populations, and resulted in a fold increase of 15.7 $\pm$ 3.3 at the end of the

CIK culture at day 21. Transposed CIK cells displayed stable expression of Tr_scFvCD123.3rdCAR (39.4% ± 8.6), efficient lysis of AML target cells, and CAR-specific cytokine secretion. Finally, long-term expansion (fold increase 423.8 ± 301.4, n = 2 at day 40) upon stimulation with AML cells *in vitro* promoted efficient selection of CAR$^+$ CIK cells with potent cytotoxic activity towards AML target (92.9 ± 1, n = 2), suggesting long-term persistence of functional CIK cells *in vivo*.
Conclusions: Efficient transfection of CARs together with a feasible manufacturing practice (GMP) strategy to select and propagate CAR-expressing CIK cells will be instrumental in defining novel therapeutic approaches to target childhood acute myeloid leukemia.

P-0430

DEVELOPMENT OF A NOVEL CHIMERIC RECEPTOR SPECIFIC FOR THE CD123 ANTIGEN FOR THE TARGETING OF ACUTE MYELOID LEUKAEMIA (AML)

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Purpose/Objective: Current therapeutic regimens for AML are still associated with high rates of relapse. Immunotherapy with T-cells genetically modified to express chimeric antigen receptors (CARs) represents a valid cell therapy approach for haematological malignancies. In this study we developed a new CAR molecule specific for the IL-3Rα (CD123) target antigen, which is overexpressed on AML blasts, CD34$^+$ leukaemic progenitors, and leukaemic stem cells (LSCs) compared to normal haematopoietic stem/progenitor cells (HSPCs), and whose overexpression is associated with poor prognosis.
Materials and Methods: Cytokine-Induced Killer (CIK) cells were transduced with an SFG-retroviral vector encoding an anti-CD123.CAR. The efficacy and safety profiles of transduced cells were characterized *in vitro* by short and long-term cytotoxicity assays. Their potential reactivity against HSPCs was evaluated by colony-forming unit assay after 4-hours co-incubation.
Results: Anti-CD123.CAR$^+$CIK cells strongly killed CD123$^+$ THP-1 cell line (60% ± 5.4%, Effector:Target *E:T- *ratio* of 5:1, n = 3), as well as primary AML blasts (59% ± 5.4%, E:T *ratio* of 3:1, n = 4) in 4-hours citotoxicity assays. In long-term cytotoxicity assay we observed a leukaemic cell recovery for THP-1 of 3.5% ± 1.5% (n = 5) and for primary AML cells of 2.4% ± 1.4% (n = 3) when co-cultured with anti-CD123.CAR$^+$CIK cells, compared to an average survival of up to 80%, when co-cultured with unmanipulated (NT) CIK cells. Interestingly, secondary colonies experiments after co-culture of cord blood-derived HSPCs with anti-CD123.CAR$^+$CIK cells demonstrated that anti-CD123.CAR better preserved the normal haematopoietic reconstitution in contrast to a previously generated anti-CD33.CAR (total number of colonies of 146.8 ± 6.6, 66.4 ± 5.1, 117.6 ± 4.6, after co-culture with NT CIK cells, anti-CD33.CAR$^+$CIK cells, anti-CD123.CAR$^+$CIK cells respectively, n = 4). Furthermore, a limited killing of normal CD123$^+$monocytes and CD123-low expressing endothelial cells was measured.
Conclusions: Taken together, our results indicate that anti-CD123.CAR strongly enhances anti-leukaemic CIK functions towards AML, while sparing HSPCs and normal CD123-expressing tissues, paving the way for the development of novel immunotherapy approaches for the treatment of resistant forms of AML.

P-0431

SYNERGISTIC CYTOTOXICITY OF SEQUENTIAL ADMINISTRATION OF THE CHECKPOINT KINASE-1 INHIBITOR MK-8776 WITH CYTARABINE IN ACUTE MYELOID LEUKEMIA

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Purpose/Objective: To evaluate the cytotoxicity of the checkpoint kinase-1 (Chk1) inhibitor MK-8776 in combination with standard chemotherapy agents in acute myeloid leukemia (AML) cell lines
Materials and Methods: The AML cell line panel included HL-60, MV4-11, THP-1, NB-4, Kasumi-1, Kasumi-3, and Kasumi-4, of which all except MV4-11 and Kasumi-4 have p53 abnormalities. 5×10^4 cells per well were plated in 96-well plates and incubated for 72 hours in the presence of cytarabine, fludarabine, or doxorubicin at concentrations of 10nM, 100nM, 1μM, 10μM, 100μM; 1nM, 10nM, 100nM, 1μM, 10μM; and 0.1nM, 1nM, 10nM, 100nM, 1μM, respectively, either simultaneously with MK-8776, 24-hours prior to MK-8776 or 24-hours post MK-8776 at MK-8776 concentrations of 10nM, 100nM, 1μM, and 10μM. Cell viability was assessed by MTS methodology.
Results: MK-8776 demonstrated significant single agent activity in two cell lines, Kasumi-3 and MV4-11, with an IC_{50} of ∼100nM. MK-8776 demonstrated synergy with chemotherapy in killing AML cell lines in an administration sequence-dependent fashion. Synergistic cytotoxicity was observed when cytarabine was administered prior to MK-8776 in HL-60, THP-1, Kasumi-1, and Kasumi-4 cells. Notably, in select cases administration of MK-8776 prior to cytarabine was antagonistic. Combination studies with fludarabine and MK-8776 demonstrated modest effect that did not appear sequence-specific.
Conclusions: These results are consistent with a mechanism in which cytarabine causes replication fork arrest and checkpoint activation as the cell attempts to repair the DNA damage; this cell cycle arrest is overcome by MK-8776 administered after cytarabine and the cells undergo apoptotic cell death. MK-8776 showed either single agent activity or significant synergy at concentrations of 100nM to 1uM, which is readily achievable *in vivo* at doses used in adult phase 1 studies. These data support the development of a phase 1 clinical trial of sequentially timed MK-8776 in combination with high-dose cytarabine-based chemotherapy in children with relapsed or refractory AML.

P-0432

CLINICAL EFFECTS OF WILMS TUMOR PROTEIN (WT)1PEPTIDE VACCINATION IN PEDIATRIC PATIENTS WITH RHABDOMYOSARCOMA

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Purpose/Objective: WT1 (Wilms' tumor gene) has oncogenic activity, and the gene product, WT1 protein, is overexpressed in more than 90% of rhabdomyosarcoma (RMS). We have initiated WT1 peptide vaccination trial for pediatric RMS patients.
Materials and Methods: The primary objective of this study is to test the safety and effectiveness of WT1 peptide vaccine in 18 patients with RMS with alveolar histology (n = 12), and embryonal histology (n = 6). Seven patients were classified for high risk and the other 11 patients were intermediate risk according to IRSG classification. Three cases had progressive disease and 15 cases had minimal residual disease (MRD) including 4 patients with recurrent tumor. These RMS showed WT1 expression by immunohistochemistry. Patients were intracutaneously injected with HLA*A*2402 restricted modified WT1 peptide with Montanide ISA51 weekly with the dose adjusted according to the body weight. After injection of 12 times, clinical response was evaluated by RECIST and vaccination was continued if they showed no adverse effect and no tumor regrowth.
Results: All the patients completed 12-time injection. Among fifteen patients with MRD including 4 recurrence cases, 9 cases showed complete response and are still alive between 6.3∼66.1 months (median: 20.4 months). In three cases with progressive disease, only one patient showed complete remission with the duration of 83.3 months. Although the frequency of WT1-spesific CD8+ T cells is below 0.4% before vaccination, it is increased after 6 or 12 vaccinations. In three patients, WT1-specific CD8+ T cells have not been detected throughout the vaccination, and the patients' tumor recurred. There were no systemic adverse events in this clinical trial.
Conclusions: We reported the first 18 cases in WT1 peptide immunotherapy for pediatric rhabdomyosarcoma patients. This immunotherapy was well-tolerated, and elicited WT1-specific immune response in association with clinical response. Our results highlight the potential of WT1 vaccination for pediatric rhabdomyosarcoma.

P-0433

TUMOR IMMUNOTHERAPY TARGETING WT1 (WILMS' TUMOR GENE) PEPTIDE FOR PEDIATRIC RARE TUMORS.

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Purpose/Objective: Pediatric rare tumors are composed of various types of infrequent tumors. Because there are no pediatric treatment guidelines, the management of these tumors can be challenging. WT1 is overexpressed in many kinds of solid tumors, and it is undisputed that WT1 protein can be one of the most promising molecular targets for cancer immunotherapy in adult. The primary objective of this study is to test the safety and effectiveness of WT1 peptide vaccine for pediatric rare solid tumors.
Materials and Methods: 29 pediatric patients with rare tumors which show the expression of WT1 protein were enrolled. They included 8 Neuroblastoma, 3 hepatoblastoma, 5 high grade glioma, 2 pulmonary blastoma, 2 osteosarcoma and 9 other tumors. HLA-A*2402$^+$ patients were intracutaneously injected with HLA-A*2402-restricted modified WT1 peptide with Montanide ISA51 weekly with the dose adjusted according to the body weight. After 12 times of injection, vaccination is continued if they showed no adverse effect and no regrowth of tumor.
Results: Of 29 patients, 27 patients accomplished 12 times of vaccination. 14 of 19 patients with very good partial response or complete remission at the time of vaccination start achieved or maintained complete remission and are still alive. 3 patients had a relapse of disease and one patient died. Another patient had stable disease. Of 8 patients with

progressive disease at the time of vaccination start, all of them had progressive disease. The frequency of WT1-spesific T lymphocytes in peripheral blood is increased after 6 or 12-time vaccinations in almost all a considerable proportion of patients.
Conclusions: We reported the first 29 cases in WT1 peptide immunotherapy for pediatric patients with rare tumor. These results show that the WT1 peptide vaccination is effective for the patients with remission or very good partial response. Our results highlight the potential of WT1 vaccination for pediatric rare solid tumor.

P-0434

SENSITIZATION OF HUMAN OSTEOSARCOMA CELLS TO HSP90 INHIBITION BY TELOMERASE INHIBITION IN VITRO AND IN VIVO

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Purpose/Objective: Cure rates for osteosarcoma are only 60-70% for localized disease and 25-45% for metastatic disease. Telomerase is an attractive therapeutic target because it is relatively specific to cancer and is a critical factor for cancer cell immortality. This study evaluated the effect of the telomerase inhibitor imetelstat in pre-clinical models of osteosarcoma. Because the chaperone molecule HSP90 facilitates the folding and assembly of telomerase protein, the ability of the HSP90 inhibitor 17-DMAG to potentiate the effect of telomerase inhibition was assessed.
Materials and Methods: The effect of single or combined treatment with imetelstat and 17-DMAG on long-term growth was assessed in osteosarcoma cell lines (143B, HOS and MG63) and subcutaneous osteosarcoma xenografts derived from 143B cells.
Results: Treatment with imetelstat inhibited telomerase activity, induced telomere shortening, and inhibited cell growth in all three osteosarcoma cell lines. However, complete growth arrest or cell death was not observed with imetelstat as a single agent. Combined treatment with imetelstat and 17-DMAG depleted telomerase activity and accelerated telomere shortening compared to either agent alone. Sequential administration of imetelstat followed by 17-DMAG resulted in complete cell growth arrest in all cell lines. The sensitivity of osteosarcoma cells to 17-DMAG was inversely proportional to the duration of imetelstat pre-treatment, indicating that sensitization to HSP90 inhibition was dependent on telomere length rather than an off-target effect of imetelstat. Combined telomerase and HSP90 inhibition resulted in greater activation of the ATM-P53 DNA damage response pathway and enhanced apoptosis compared to treatment with either agent alone. In xenograft models, all three treatment groups significantly inhibited tumor growth compared with the placebo-treated control group, with the greatest effect seen in the combined treatment group (imetelstat, $p = 0.045$, 17-DMAG, $p = 0.034$; combined treatment, $p = 0.004$).
Conclusions: Dual inhibition of HSP90 and telomerase provides a promising treatment strategy for osteosarcoma and other pediatric cancers.

P-0435

NOVEL DRUG DEVELOPMENTAPPROACH TARGETING STAT3 FOR SARCOMA THERAPY USING MLSD AND DRUG REPOSITION

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Purpose/Objective: To find and develop novel small molecule which could inhibit STAT3 phosphorylation in pediatric sarcoma...
Materials and Methods: To accelerate STAT3 drug development, we used a novel drug discovery approach with multiple ligand simultaneous docking (MLSD), To test STAT3 phosphorylation and apoptosis by western blot, STAT3 nuclear localization by immunofluorescence.
Results: Using this new method, we identified the FDA-approved drug celecoxib (a COX-2 inhibitor) with a novel function to target STAT3 [Predictive STAT3 binding dissociation constant (Kd) = 8.6mM].In addition, a novel celecoxib analog (8A) was developed exhibiting stronger STAT3 binding (Predicted Kd = 0.12mM;71-fold stronger than celecoxib). Although 8A has stronger STAT3 binding, it has weaker COX-2 binding (521-fold weaker than celecoxib), suggesting its selectivity on STAT3 versus COX-2. Minimal COX-2 inhibition of 8A may reduce cardiovascular and gastrointestinal risks associated with COX-2 inhibitors. The ability of 8A to inhibit STAT3 was tested. 8A inhibited the P-STAT3 stimulated by IL-6 but not the induction of STAT1 phosphorylation by IFN-g. 8A also inhibited the induction of STAT3 nuclear localization by IL-6, which could prevent STAT3 functions as a transcription factor. 8A inhibited STAT3 phosphorylation and resulted in the induction apoptosis on sarcoma cells as evidenced by caspase-3 cleavage. Further, 8A was more potent than celecoxib to inhibit STAT3 phosphorylation and induce apoptosis in sarcoma cells, which confirmed the stronger STAT3 binding energy than celecoxib
Conclusions: In summary, our study is the first report using MLSD and drug repositioning to develop drug-like STAT3 inhibitors. This novel method has a potential to significantly speed up the STAT3 drug development for the therapy of childhood sarcoma and possibly other types of human cancer express constitutive STAT3 signaling.

P-0436

EWING SARCOMA DISSEMINATION AND THERAPEUTIC RESPONSE TO EXPERIMENTAL T CELL THERAPY IN MICE ASSESSED BY WHOLE BODY MAGNETIC RESONANCE IMAGING

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Purpose/Objective: Novel treatment strategies in Ewing sarcoma include targeted cellular therapies. Preclinical *in vivo* models are needed that recapitulate the biology of multifocal disease and reflect the activity of novel therapies against systemic (micro)metastatic disease.
Materials and Methods: Here, we used whole- body magnetic resonance imaging (WB-MRI) to monitor the engraftment and dissemination of human Ewing sarcoma xenografts in mice and to address the therapeutic efficacy of adoptive T cell transfer.
Results: Among the first cohort of mice ($n = 18$) receiving intravenous injections of VH-64 cells, all developed disseminated tumors detectable by WB-MRI within 20 to 31 days (median of 27 days). All mice had lung tumors, and 16 mice had additional manifestations in bone, soft tissues, and/or kidney. The highest numbers of tumors were found in the lungs, with a median of 19.5 (range 1 to 60) per mouse. Sequential scans revealed *in vivo* growth of tumors at all sites. To assess the therapeutic efficacy of adoptive T cell transfer, cohorts of 9 mice each were intravenously injected with VH-64 Ewing sarcoma cells, followed by transfusions of human T cells redirected against the Ewing sarcoma associated antigen G_{D2} by chimeric receptor engineering, or analogous injections of non-transduced T cells. Animals receiving G_{D2}-targeted T cell therapy had lower numbers of pulmonary tumors than controls ($p < 0.0001$), and the median volume of soft tissue tumors at first detection was lower ($p = 0.019$), with a tumor growth delay over time. No overall survival advantage was found for mice receiving therapy using Kaplan-Meier analysis.
Conclusions: We conclude that MR imaging reliably visualizes disseminated Ewing sarcoma growth in mice. G_{D2}-retargeted T cells can not completely prevent disseminated tumor growth in this systemic disease model, but are active to delay and reduce pulmonary disease manifestations in this highly aggressive disease model. Future strategies aim to further increase efficacy of cellular therapy against Ewing sarcoma.

P-0437

ABRAXANE IS AN ACTIVE AGENT IN PEDIATRIC SOLID TUMOR XENOGRAFT MODELS

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Purpose/Objective: ABRAXANE, a novel, solvent free, protein-stabilized formulation of paclitaxel, was developed to reduce the toxicity of solvent-based paclitaxel and improve drug efficacy. In this pre-clinical study, we investigated the anti-tumor effect of ABRAXANE on pediatric solid tumor models.
Materials and Methods: A panel of seven neuroblastoma (NB) and three rhabdomyosarcoma (RMS) cell lines were exposed to increased concentrations of ABRAXANE in vitro. Cell viability was evaluated with Alamar Blue assay. Anti-tumor effect of ABRAXANE was further assessed *in vivo* with xenograft models. Animal survival was also evaluated in metastatic NB models. Xenograft sections were analyzed by immunohistochemistry for cleaved caspase-3 and phospho-histone H3. In addition, plasma and intratumoral paclitaxel concentrations were measure by liquid chromatography*mass spectrometry. Ratio of intratumoral and plasma concentration was compared between ABRAXANE and paclitaxel treatment groups.
Results: ABRAXANE displayed cytotoxicity against the majority of pediatric solid tumor cell lines tested in a dose-dependent manner. In vivo, ABRAXANE demonstrated antitumor activity in both NB (SK-N-BE(2) and CHLA-20) and RMS (RH4) xenograft models. In the SK-N-BE(2) metastatic model, ABRAXANE treatment significantly extended animal survival compared to control ($p < 0.01$). It was demonstrated that ABRAXANE treatment induced tumor cell cycle arrest and apoptosis in vivo. In the RH4 model, increased local *relapse*-free *intervals* was observed with ABRAXANE treatment (54 days) comparing to paclitaxel (34 days). Local relapsed tumors following paclitaxel treatment proved to be paclitaxel-resistant and remained responsive to ABRAXANE. Mechanistically, *elevated* intratumor and correspondingly lower plasma paclitaxel levels were observed with

ABRAXANE compared to paclitaxel, resulting in higher tumor/plasma paclitaxel drug ratio for ABRAXANE.
Conclusions: ABRAXANE demonstrated significant antitumor activity against pediatric solid tumors both *in vitro* and *in vivo*. T*herapeutic improvement* of ABRAXANE may be related to enhanced drug intratumor delivery. Results of this preclinical study support further testing of ABRAXANE in clinical studies with a pediatric solid tumor patient population.

P-0438

INHIBITION OF CARBONIC ANHYDRASES (CA) 9 AND 12 BY INDISULAM SHOWS SIGNIFICANT ANTIPROLIFERATIVE EFFECTS ON PEDIATRIC AND ADULT GLIOBLASTOMA CELL LINES

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Purpose/Objective: The glioblastoma (GB) is one of the most malignant human tumors and despite improvement in the conventional therapy its prognosis remains poor. An important factor for tumor progression is the acidification of the environment that is promoted by carbonic anhydrases (CAs) 9 and 12, directing to the acquisition of metastatic phenotype and chemoresistance to anticancer drugs. Indisulam is a novel anticancer drug with potent inhibition of CAs. The aim this study was to evaluate the expression and the effects of inhibition of the CA9 and CA12 by indisulam in proliferation, clonogenic capacity and apoptosis in 9 GB cell lines subjected to normoxia or hypoxia.
Materials and Methods: The MO59K, U87-MG, T98G, U251, U138-MG, LN319, U343-MG-a (adult) and KNS42, SF188 (pediatric) GB cell lines were cultured in conditions of hypoxia or normoxia. Functional studies of viability, cell proliferation, apoptosis, clonogenic capacity were performed in triplicate with Indisulan at different concentrations during 24, 48 and 72h. Gene expression of *CA9*, *CA12*, *VEGF* and *HIF1A* was assessed using qRT-PCR. Statistical analysis was made by one-way ANOVA and Bonferoni post-hoc
Results: The evaluation of gene expression under conditions of hypoxia compared to normoxia, showed a significant increase of the expression of the hypoxia-related genes *CA9*, *CA12*, *HIF1A* and *VEGF*. All experiments showed that the inhibition of CA9/12 with indisulam were dose- and time-dependent ($p < 0.05$) and caused a significant decrease on cell proliferation, viability, clonogenic capacity and increase of apoptosis.
Conclusions: Our results indicate increased gene expression on hypoxic condition and antiproliferative effect of indisulan. It suggests that indisulam may be an interesting candidate for the development antitumor therapies based on the inhibition of carbonic anhydrases.

P-0439

IODINE131- METAIODOBENZYLGUANIDINE THERAPY FOR NEUROBLASTOMA: A NURSING PERSPECTIVE

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Purpose/Objective: Despite substantive advances in pediatric oncology treatments, patients with high-risk neuroblastoma continue to have poor long-term survival. Intravenous I^{131}-meta-iodobenzylguanidine [MIBG] therapy provides high doses of radiation therapy directly to active neuroblastoma cells. Despite its promising role in neuroblastoma patient outcomes, due to necessary radiation safety precautions there are substantive nursing challenges involved with I^{131}-MIBG therapy.
Materials and Methods: Utilizing the experiences of the international MIBG therapy program at Cincinnati Children's Hospital Medical Center (CCHMC) in the United States from 2012 ($n = 27$), where a parent / familiar adult caregiver (FAC) of the patient is required to remain in the patient's room throughout their hospitalization, an analysis was performed to determine both FAC and bedside staff nurse deep dose equivalent radiation exposure. Utilizing staff expertise, the barriers and facilitators to providing safe and effective care for patients undergoing high-dose I^{131}-MIBG therapy were extracted.
Results: Analysis demonstrated a mean FAC deep dose equivalent radiation exposure of 73.5mRem / treatment (maximum 199mRem / treatment) post MIBG therapy. The maximum annual radiation exposure of a bedside nurse was 93mRem; for nurses with $> = 5$mRem exposure ($n = 44$), the mean exposure was 23.2mRem / year. Barriers and facilitators to providing safe nursing care included FAC availability, compliance and experience; patient age and compliance; language; patient and FAC preparedness; mechanizing urine disposal; MIBG room design; functionality of radiation safety measures; and staff nurse education.
Conclusions: As Low as Reasonably Achievable (ALARA) is the radiation safety principle utilized to minimize radiation exposure. Maintaining ALARA requires minimizing the time spent with, and maximizing the distance from, radioactive sources or materials, including patients recently treated with MIBG therapy. When working with the young neuroblastoma patient, realizing ALARA is a challenging, multi-disciplinary effort. However, as demonstrated at CCHMC, it is feasible to maintain acceptable radiation level exposures to both nursing staff and FACs post MIBG therapy while providing safe, effective patient care.

P-0440

ACETYL-L-CARNITINE HAS PROTECTIVE EFFECTS AGAINST EXPERIMENTAL DOXORUBICIN CARDIOTOXICITY

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Purpose/Objective: Anthracyclines have cardiotoxic side effects limit their usage. Acetyl-L-carnitine (ALCAR) prevents toxic deposition of free fatty acids and AcylCoA in cells and also acetyl-CoA provides to mitochondria for energy production. ALCAR has also neuroprotective and anti-apoptotic effects. The aim of this study was whether ALCAR has any impact on doxorubicin cardiotoxicity evaluated by ultrastructural and echocardiography measurements.
Materials and Methods: Wistar albino male rats were divided to four groups as control, doxorubicin, ALCAR, ALCAR + doxorubicin. Structural changes were evaluated by electron microscopy, H&E, Masson trichrome, TUNEL and Caspas-3 immunohistochemical applications. Cardiac functions were examined by echocardiography and ejection fractions were measured.
Results: Histopathologically, electron microscopically and apoptotic examinations showed that ALCAR was prevented doxorubicin induced cardiac injury at structural level. Echocardiography and ejection fractions measurements also indicated that pre-application of ALCAR was prevented doxorubicin induced cardiac injury at functional level.
Conclusions: Our study represented that pre-application of ALCAR seems to be able to prevent the cardiac injury that doxorubicin causes in both functional and structural ways, and to be able to reduce side effects of doxorubicin or to clear them all away. Acetyl-L-carnitine should be examined have any protective effect against doxorubicin cardiotoxicity in *in-vivo* experimental tumor models without impairing the efficacy of doxorubicin. Acetyl-L-carnitine has protective/preventive effects against doxorubicin cardiotoxicity.

P-0441

EFFICACY AND SAFETY OF HIGH DOSE TOPOTECAN IN RELAPSED OR REFRACTORY PEDIATRIC SOLID TUMORS

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Purpose/Objective: Although the prognosis for pediatric malignancies has been improving, relapsed or refractory cases remain difficult to treat, and their prognosis is poor. Intensive chemotherapy is required in such cases, however, the intensity may have to be reduced or the regimen may have to be changed altogether as a result of severe toxicity. Topotecan (TPT) has been reported to show significant anti-cancer activity and modest toxicity. Our experience with regard to activity and toxicity led us to increase the dosage of TPT to 12.5 mg/m^2/dose. We report here the efficacy and safety of chemotherapy including high-dose TPT for relapsed or refractory pediatric malignancies at a single institute.
Materials and Methods: Thirty-three patients (19 male, 14 female) with relapsed or refractory cases were treated with a regimen including high-dose TPT (2.5 mg/m^2/day, for 5 days). Underlying pathologies were: neuroblastoma, $n = 10$; rhabdomyosarcoma, $n = 8$; Ewing sarcoma, $n = 4$; germ cell tumor, $n = 3$; medulloblastoma, $n = 2$; retinoblastoma; $n = 2$, Wilms' tumor, $n = 2$; hepatoblastoma, $n = 1$; clear cell sarcoma of kidney, $n = 1$. The investigation period was from January 2005 until August 2012.
Results: Patients were evaluated by diagnostic imaging and other means after one course of chemotherapy. Major (complete/partial) response was observed in 16 of 33 cases (48%), stable disease in 11 (33%), and progressive disease in 6 (18%). This means that 27 cases (82%) could be treated safely without progression. The major complication $\geq$ grade 4 (NCI-CTCAE criteria) was hematological toxicity. Nine patients (27%) had fever due to drug allergy that was treatable. One secondary malignancy was identified although a direct association with drug could not be ascertained.
Conclusions: High-dose TPT combined chemotherapy could be effective for relapsed or refractory pediatric solid tumors. The toxicity profile was acceptable. Although more

evidence is necessary, our initial data indicated that TPT might be a promising therapeutic strategy for relapsed or refractory pediatric malignancies.

P-0442

A NOVEL SYNTHETIC COMPOUND BISMUTH ZINC CITRATE COULD POTENTIALLY REDUCE CISPLATIN INDUCED TOXICITY WITHOUT COMPROMISING THE ANTICANCER EFFECT

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Purpose/Objective: Background: Neuroblastoma had poor outcome with current therapeutic approaches. In recent years, some obligate and facultative anaerobic bacteria were reported to target the hypoxic solid tumor core. We constructed an 'obligate' anaerobic *Salmonella* strain YB1 and tested it on neuroblastoma.
Materials and Methods: Methods: The *in-vitro* cytotoxicity of YB-1 and wild type salmonella (SL7207) on neuroblastoma (SK-NLP/luciferase) cells were assessed by Annexin V assay (ratio of 500:1) under anaerobic or aerobic conditions. Toll like Receptor 4 and 5 (TLR4 and TLR5) were assessed by Q-PCR. Orthotopic neuroblastoma mouse model was adopted and 3 groups of mice (n = 6) were treated with bacteria (5×10^7 CFU/mouse): 1) YB1; 2) SL7207; or 3) PBS control via tail vein injections. Tumor growth was assessed by Xenogen-IVIS-100. Survival and body weight were recorded every 2 days. To observe side-effects, YB1 and SL7207 were also injected to 6 SCID mice. Organs were harvested and faeces + urine were collected and the bacteria in different organs were determined.
Results: Results: *In vitro*, YB1 induced apoptosis in up to 31.4% of the treated cells under anaerobic condition, three times more than that in aerobic condition (10.9%). The expression of both TLR4 and TLR5 in cancer cells were significantly increased ($p < 0.05$, p^1,

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Purpose/Objective: Next generation sequencing (NSG) technology provides detailed molecular characterization of tumors, and identification of genomic alterations in cancer related genes. Our aim is to demonstrate the application of genomic profiling of pediatric cancers, and to identify specific genetic alterations that may provide insight into cancer pathogenesis and prognosis, and potentially guide choices for novel molecularly-targeted therapies.
Materials and Methods: The entire coding sequence of more than 200 cancer-related genes was generated by a NGS assay from the tumor samples of 30 patients from Cincinnati Children's Hospital Medical Center with relapsed or very high risk leukemia, lymphoma, or solid tumors. Specimens analyzed included paraffin embedded tissue sections or prepared DNA extracted from tumor cells.
Results: Genomic alterations in tumor related genes were identified in 20 of the 30 tumor samples analyzed, including 8/12 leukemia/lymphomas, 3/3 neuroblastomas, 6/9 sarcomas, 1/2 renal tumors, 1/2 hepatoblastomas, and in 1 chordoma. One additional gastrointestinal stromal tumor harbored no mutation. In total, 45 genomic alterations were identified in 30 genes. Of these, 25 such alterations are considered 'actionable' in that they have been associated with specific pathways or molecular targets for which FDA approved drugs or clinical trial agents have known or suspected efficacy. Additional alterations identified suggested resistance to particular agents (i.e. crizotinib resistance in a neuroblastoma with ALK F1174L). The most common alterations identified across histologies were TP53 mutations in 8 samples, and loss of CDKN2A in 5 samples. Interestingly, of patients with actionable mutations, overlapping alterations were identified in only one patient with a positive ALK(2p23) break-apart probe and one patient with MLL gene rearrangement by standard clinical cytogenetic testing.
Conclusions: Focused exome sequencing of cancer related genes in pediatric tumors has the potential to broaden our understanding of tumor biology and guide therapy.

P-0448

HAPLOIDENTICAL HCT USING T-CELL DEPLETED GRAFTS: COMPARISON OF CD34 SELECTION AND CD3 ± 19 DEPLETION

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Purpose/Objective: To compare the efficacy of selection of CD34 cells with depletion of CD3 ± 19 cells as a T-cell depletion method in haploidentical stem cell transplantation (HHCT) in children and adolescents.
Materials and Methods: Thirty-three HHCTs were performed in 32 patients (SAA 20, MDS 2, AML 4, ALL 1, NBL 1, Graft failure 4) using CD34-selected (HHCT-CD34, n = 4) or CD3 ± 19-depleted (HHCT-CD3 ± 19, n = 29) grafts from haploidentical family donors between 2004 and 2012 at AMCCH. A total of 54 graft manipulations were performed with anti-CD34 (n = 18) or anti-CD3 ± CD19 (n = 36) microbeads (CliniMACS, Miltenyi Biotec). Donors included mother (n = 38), sibling (n = 11) and father (n = 5).
Results: As for 54 graft manipulations, mean recovery of CD34 + stem cells in $CD34^+$ selection and CD3 ± 19 depletion were 56.95% and 81.86%, respectively, and mean depletion of $CD3^+$ cells were 3.78 log and 2.97 log. Of a total of 33 HHCTs, 6 (18%) experienced graft failure(GF). Neutrophil engraftment of the remaining 27 HHCT was rapid with neutrophils > 500/μL at day 10.6 (range, 7-15) which was not different according to depletion methods. However, platelet engraft was faster in HHCT-CD3 ± 19 than HHCT-CD34 (median 19 vs 59 days, $P = 0.05$). Six patients who had GF proceeded to the second HHCT and all achieved engraft. Twelve (46%) of 26 evaluable patients developed grade II & III acute GVHD but there were no grade IV. Incidence of chronic GVHD was 46% (12 of 26) with 10 patients of limited type and 2 patients of extensive type. There was no GVHD related death. Among 32 patients, 26 patients (2 out of 4 HHCT-CD34 and 24 out of 28 HHCT-CD3 ± 19) are alive at a median of 25.2 months (range, 1.0-98.9) after HHCT.
Conclusions: D3 ± 19 depletion is a highly effective method to remove T-cells with rapid engraftment and minimal risk of GVHD. HHCT using CD3 ± CD19 depletion is a promising approach in children and adolescents lacking a suitable donor.

POSTER SESSION: POSTER SESSION - EPIDEMIOLOGY

P-0449

EFFECTS OF PRENATAL EXPOSURE TO DIAGNOSTIC IRRADIATION ON DEVELOPMENT OF CHILDREN'S LEUKEMIA

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Purpose/Objective: The past studies have suggested some increase of childhood leukemia in children born to the mothers who had diagnostic irradiation during pregnancy. This study performed to confirm these previous results, by using a large volume of data accumulated in the Japan Children's Cancer Registry (JCCR).
Materials and Methods: The data of 32,156 cases registered to JCCR in 1969-2006 were used. We calculated rate of leukemia cases with irradiation during mother's pregnancy. We used childhood cancer other than leukemia as control and calculated odds ratio of leukemia to other cancer.
Results: The trends in the rate were about the same in the leukemia and other cancer cases. However, irradiation rates have been lowered in both groups, especially irradiation to the chest. The rate was significantly higher in the leukemia group in children as a whole and in children born in 1965-69, 70-74 and 75-79. Odds ratios were 1.37 (95%CI: 1.28-1.47), 1.50 (95%CI: 1.25-1.80), 1.27 (95%CI: 1.10-1.47) and 1.41 (95%CI: 1.18-1.68), respectively. The irradiation rate to the mother's chest in the 1st trimester and the 2nd trimester of pregnancy was significantly higher in the leukemia group in children born in 1965-69 and odds ratios were 1.79 (95%CI: 1.18-2.70) and 1.65 (95%CI: 1.20-2.28), respectively, and the irradiation rate to the mother's abdomen in 3rd trimester was significantly higher in the leukemia group in children born in 1965-69, 70-74, 75-79 and 80-84 and odds ratios were 1.82 (95%CI: 1.26-2.64), 1.91 (95%CI: 1.47-2.48), 1.62 (95%CI: 1.20-2.18) and 1.55 (95%CI: 1.11-2.17), respectively. Afterward, both the irradiation rate and leukemia risk decreased.
Conclusions: Our study confirmed the previous studies and we conclude that irradiation to mother during pregnancy could be one of risk factors for children to develop leukemia.

P-0450

LOW SOCIOECONOMIC STATUS IS ASSOCIATED WITH WORSE SURVIVAL IN CHILDREN WITH CANCER: A SYSTEMATIC REVIEW

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Purpose/Objective: Low socioeconomic status (SES) has often been associated with inferior survival among adults with cancer. By contrast, the equivalent pediatric literature is sparse and at first glance contradictory. We therefore conducted a systematic review of the literature in order to determine the impact of SES upon outcomes in children with cancer in low-, middle- and high-income countries (LMIC and HIC).
Materials and Methods: We searched 3 databases to identify pediatric oncology populations for which at least one of several pre-specified survival-related outcomes was reported by subgroups defined by a socioeconomic variable, including both ecologic and individual-level measures. All languages were included. Two reviewers independently selected articles and extracted data. LMIC and HIC results were synthesized separately.
Results: Of 7,737 publications, 527 in ten languages met criteria for full text review. A total of 36 studies met final inclusion criteria. Among LMIC children, all 16 associations between SES and outcome uniformly found that lower SES was associated with inferior survival,

regardless of the SES measure chosen. The majority of these associations were statistically significant. Of 52 associations between socioeconomic variables and outcome among HIC children, 38 (73.1%) found low SES to be associated with worse survival, 15 of which were statistically significant. Of the remaining 14 (26.9%) that found either no association or found high SES to be associated with worse survival, only one was statistically significant. Of the two HIC studies examining the effect of insurance, both found uninsured status to be statistically associated with inferior survival.
Conclusions: Socioeconomic gradients in which low SES was associated with inferior survival are ubiquitous in LMIC and common in HIC. Future studies should elucidate the mechanisms underlying these gradients, allowing the design of targeted interventions mediating the effect of SES on outcomes.

P-0451

SOCIO-ECONOMIC PATTERNING IN THE INCIDENCE AND SURVIVAL OF MALES AND YOUNG MEN DIAGNOSED WITH TESTICULAR CANCER IN NORTHERN ENGLAND

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Purpose/Objective: Previous research from developed countries has shown a marked increase in incidence of testicular cancer. This has also been demonstrated in northern England, along with improving five-year survival. The aetiology of testicular cancer remains unclear. It has been postulated that environmental factors might be involved. This is supported by a previous finding of space-time clustering of incidence. The aims of the present study were to determine if socio-economic factors may play a role in both aetiology and survival from testicular cancer.
Materials and Methods: We extracted all cases of testicular cancer diagnosed in males aged 0-24 years during the period 1968-2003 from the Northern Region Young Persons' Malignant Disease Registry. This is a population-based registry and includes all cases of cancer in children and young adults who were resident in northern England at time of diagnosis. Negative binomial regression was used to examine the relationship between incidence and both the Townsend socio-economic deprivation score (and component variables) and small-area population density. Cox regression was used to analyse the relationship between survival and both deprivation and population density.
Results: There were 292 cases of testicular cancer diagnosed during the study period (29 aged 0-14 years, 71 aged 15-19 years and 192 aged 20-24 years). Negative binomial regression showed that there was a statistically significant decreased risk associated with living in areas of higher household overcrowding (relative risk [RR] per 1% increase in household overcrowding = 0.87; 95% confidence interval [CI] 0.81-0.93, $P < 0.001$). Household overcrowding was also associated with survival (hazard ratio per 1% increase in household overcrowding = 1.30 (95% CI 1.17-1.45, $P < 0.001$)).
Conclusions: The study has shown that increased risk of testicular cancer is associated with some aspect of more affluent living (as measured by area-based level of household overcrowding). In contrast, greater deprivation confers worse survival prospects.

P-0452

SOCIO-ECONOMIC PATTERNING IN THE INCIDENCE AND SURVIVAL OF CHILDREN AND YOUNG PEOPLE DIAGNOSED WITH MALIGNANT MELANOMA IN NORTHERN ENGLAND

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Purpose/Objective: Previous studies have found marked increases in the incidence of malignant melanoma. The increase amongst teenagers and young adults in northern England was especially apparent amongst females. Five-year survival has also improved in our region. Increased risk of melanoma is associated with exposure to UV radiation. It is not clear if risk is modulated by behaviours that may be related to social environment. The aims of this study were to determine if socio-economic factors may play a role in both aetiology and survival from melanoma.
Materials and Methods: We extracted all cases of melanoma diagnosed in children and young people aged 0-24 years during 1968-1993 from the Northern Region Young Persons' Malignant Disease Registry. The registry is population-based and includes all cancer cases in children and young adults who were resident in northern England at time of diagnosis. Negative binomial regression was used to examine the relationship between incidence rates and the Townsend deprivation score (and component variables) and small-area population density. Cox regression was used to analyse the relationship between survival and both deprivation and population density.
Results: There were 233 cases of melanoma diagnosed during the study period (23 aged 0-14 years, 210 aged 15-24 years, 68 males, 165 females). There was a statistically significant decreased risk that was associated with living in areas of higher household overcrowding (relative risk [RR] per 1% increase in household overcrowding = 0.70; 95% confidence interval [CI] 0.63-0.77, $P < 0.001$) with rates higher in less deprived areas. Survival was better in less deprived areas (hazard ratio per 1% increase in household overcrowding was 1.22 (95% CI 1.08-1.38, $P = 0.002$)).
Conclusions: This study has shown that increased risk of melanoma is linked with greater affluence (as measured by area-based level of household overcrowding). In contrast, worse survival is associated with living in a more deprived area.

P-0453

SOCIOECONOMIC VARIATION IN INCIDENCE OF CENTRAL NERVOUS SYSTEM TUMOURS IN CHILDREN AND YOUNG ADULTS IN NORTHERN ENGLAND, 1985-2011.

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Purpose/Objective: Previous studies have reported inconsistent associations between central nervous system (CNS) tumours incidence and socio-economic status (SES). This study examined the variation in incidence of CNS tumours in children and young adults by community level socio-economic deprivation using population-based data from northern England.
Materials and Methods: Data on all cases of CNS tumours between 0 and 24 years of age, diagnosed between 1985-2011, were extracted from the Northern Region Young Persons' Malignant Disease Registry. Socio-economic status was assessed using community-based measures; cases were divided into five groups on the basis of the quintile of the distribution of deprivation score for the census ward of residence. Age-standardised incidence rates per million persons per year were calculated using the 2001 census population. Poisson regression models were used to investigate the association between incidence of CNS tumours and SES.
Results: There were 665 CNS cases; 455 between 0 - 14 years, 200 between 15 - 24. For children between 0-14 years of age, the incidence rate per million was 46.98 (95% CI 35.3 * 61.3) for cases in the least deprived quintile and 29.08 (95% CI 25.2 - 33.4) for the most deprived quintile. Those who were in the most deprived quintile had a 38% significantly lower incidence risk (IRR 0.62, 95% CI; 0.46-0.84, $P = 0.002$) compared to those in the least deprived quintile. For cases aged 15-24, the incidence rate per million was 34.70 (95% CI 22.0 * 52.1) for cases in the least deprived quintile and 16.60 (95% CI 13.1 - 20.7) for the most deprived quintile, cases diagnosed from the most deprived quintile had a significantly 41% lower risk (IRR 0.59, 95% CI; 0.44-0.81, $P = 0.001$) compared to those in the least deprived quintile.
Conclusions: We found decreased risk of CNS tumours in more deprived areas in our region. This contrasts with most other studies, which have not identified this disparity.

P-0454

SOCIOECONOMIC VARIATION IN SURVIVAL FROM CHILDHOOD LEUKAEMIA IN NORTHERN ENGLAND, 1968-2010.

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Purpose/Objective: Despite marked improvements in survival from childhood leukaemia, 20% still die within 5-years of diagnosis. The study aimed to evaluate the relationship between socio-economic status (SES), as assessed by paternal occupation at birth, and survival from childhood leukaemia, using population-based data.
Materials and Methods: Data on all cases of leukaemia in children aged 0 * 14 years, diagnosed between 1968*2010, were extracted from the Northern Region Young Persons' Malignant Disease Registry. Paternal occupational social class at the time of the child's birth was obtained and classified into 3 categories: class I/II (professional/managerial), class IIIN/M (skilled non-manual/skilled manual) and class IV/V (semiskilled/unskilled). Kaplan-Meier methods were used to calculate survival at 1, 5 and 10 years. Cox regression analysis was used to analyse the associations between SES and survival.
Results: There were 1007 leukaemia cases; 565 (56%) were males and 442 (44%) females, 823 (82%) were acute lymphoblastic leukaemia and 144 (14%) were acute non-lymphocytic leukaemia and the modal social class category was class IIIN/M. Survival at each time point was greatest in the most advantaged social class group, with wider disparities seen for 5 and 10 years survival compared to one year. For all leukaemia cases, compared to the most advantaged group (I/II), those in the middle group (IIIN/M) had a 70% increased risk of death ($P < 0.0001$), while those in the least advantaged group (IV/V) had 77% higher risk ($P = 0.001$). While the survival advantage of children in class I/II was apparent from the time of diagnosis, survival for children in groups IIIN/M and IV/V were comparable until 3-4 years post diagnosis, when they began to minimally diverge.
Conclusions: The existence of such socio-economic disparities in survival from childhood leukaemia cannot be attributed to accessibility to health care in the UK. Further research into the likely factors underlying these disparities is required.

P-0455

INSTITUTIONAL SURVEY OF PEDIATRIC CANCER SURVIVAL IN SOUTHERN VIETNAM

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Purpose/Objective: Poor childhood-cancer survival rates have been reported in low-income regions such as southern Vietnam. These reports utilized surveys based on face-to-face interviews that extrapolated incidence rates and survival data. We report registry data assembled and analyzed at a large cancer referral center in Ho Chi Minh City, Vietnam.
Materials and Methods: Between 2003-2012, demographics and clinical data were collected at Oncology Hospital in Ho Chi Minh City, Vietnam. Pediatric data were analyzed for incidence and survival statistics. Oncology Hospital is the largest of three pediatric oncology referral centers in southern Vietnam with more than 500 new cases annually functioning as the regional 'safety-net' for patient care.
Results: 4534 pediatric oncology cases were identified during the study period. Breakdown of cases by classification included: 1324 (29.2%) Acute Leukemia, 692 (15.3%) Lymphoma, 641 (14.1%) Neuroblastoma, 377 (8.3%) Retinoblastoma, 347 (7.7%) Soft Tissue Sarcomas, 299 (6.6%) Renal Tumors, 294 (6.5%) Germ Cell Tumors, 256 (5.7%) Brain Tumors, 181 (4%) Liver Tumors, and 123 (2.7%) Osteosarcoma.

Survival statistics were analyzed for certain disease groups. Acute Lymphoblastic Leukemia (ALL) analysis revealed 66.2% 5yr OS (Standard Risk 77.3%; High Risk 46.9%) and 43.1% 5yr DFS (SR 49.6%; HR 27.9%). Hodgkin Lymphoma analysis revealed 92% 5yr OS and 88.6% 5yr DFS. NHL survival rates noted at 41% OS. Rhabdomyosarcoma analysis revealed 50% 5yr OS with 46.3% DFS. Wilms Tumor analysis noted 78.67% 5yr OS with stage delineation (I, II 100%; III 58%; IV 40%). Hepatoblastoma analysis revealed 42.8% 2yr OS with stage delineation (I, II 62.5%; III, IV 33.3%) and Osteosarcoma analysis revealing 13.58% 5 yr OS.
Conclusions: Prior published reports of pediatric cancer incidence and survival in Vietnam relied heavily on inference and supposition. This single institutional study represents a more objective assessment of pediatric cancer in the region. Further more comprehensive and multi-institutional studies, however, are warranted.

P-0456

INCIDENCE AND SURVIVAL FOR EMBRYONAL CANCERS IN CHILDREN, SHANGHAI, 2002-2010

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Purpose/Objective: Embryonal cancers are mainly occur in children and no study has been focused on its burden in Shanghai. The aim of this study was to analyze the incidence and survival of the embryonal cancers among children aged 0-14 in Shanghai during 2002-2010.
Materials and Methods: All data were from the Shanghai Cancer Registry and Shanghai Childhood Cancer Survival study. Embryonal cancers were reclassified according to ICCC-3. Average annual incidence and survival analysis were performed in the study population.
Results: A total of 170 embryonal cancer cases were diagnosed from 2002 to 2010 in Shanghai and the ratio of male to female was 1:1. Most of cases (83.5%) occurred in the 0-4 year age group. The total average age-standardized incidence rate (ASR) for embryonal cancer was 20.2 per million. The percentage and ASR were 50.0% and 10.1 per million for neuroblastoma, 21.2% and 4.2 per million for nephroblastoma, 18.8% and 3.9 per million for retinoblastoma, 8.8% and 1.8 per million for hepatoblastoma, respectively. Only two cases of pancreatoblastoma were diagnosed. The incidence rate of embryonal cancer in 2007-2010 was similar with that of 2002-2006. Overall 5-year relative survival was 60.4% for all embryonal cancer cases diagnosed in 2002-2006 (males: 64.3%, females: 57.0%). Survival figures changed over 4 main subgroups. The 5-year relative survival was 56.0% for neuroblastoma, 70.8% for nephroblastoma, 84.8% for retinoblastoma, and 33.6% for hepatoblastoma, respectively. The relative survival for embryonal cancer was lower in Shanghai than in the USA. Some cautions should be noticed when interpreting results involving a small number of cases and those with wide 95% confidence intervals.
Conclusions: This is the first study to describe the embryonal cancer burden in children in Shanghai., which could provide a basis for etiology research and prognostic study. The findings also suggest an ongoing need for longer population-based surveillance.

P-0457

INCIDENCE OF CHILDHOOD CANCER IN ADEN CANCER REGISTRY, YEMEN (2007-2011)

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Purpose/Objective: In Yemen, data regarding childhood cancers are very scarce. This paper aims at describing childhood cancers registered in Aden Cancer Registry, the first and only population based cancer registry in Yemen which covers an area of around three million inhabitants.
Materials and Methods: All registered cancers for patients under 15 years in the period 2007-2011 were analyzed. Can Reg 4 for cancer registry was used in the analysis. Validation checks of each entered data was carried out to maximize data validity.
Results: Childhood cancers accounted for 11.6% of all registered cancers with more males (60%) compared to females (40%).The most leading cancers were leukemias, non Hodgkin's Lymphoma, Hodgkin!s disease, brain and nephroblastoma. Both sexes showed similarities in the first five ranking cancers but they differ in their relative frequencies.
Conclusions: Despite that childhood cancers accounted for almost the same frequency relative to the overall cancer incidence, differences in the leading cancer order for both sexes and for each sex were observed compared to the previous five years report (2002-2006). Furthermore, differences with the pattern of childhood cancers in the Gulf Cooperation Council States are also clear. Further in depth analysis is obviously needed

P-0458

CENTRAL VENOUS CATHETER-RELATED INFECTIONS AMONG PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS OF THE NATIONAL CANCER INSTITUTE, RIO DE JANEIRO, BRAZIL

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Purpose/Objective: Catheter venous infections and complications in pediatric oncology patients who received treatment at a Cancer Center * INCA - Brazil/ RJ were investigated in this study.
Materials and Methods: A retrospective study of 812 cases of central line access (CVC) done in our Institution from January 2009 to December 2010 demonstrated the presence of pediatric patients less than 16 years-old, in treatment and making use of central line silicone catheter. During this period all patients were followed at outpatients catheter.
Results: From 812 cases, 40.76% were inserted in children. Of 261 patients with (CVC), 32.18% were hematological patients and 67.81% were solid tumors patients;135 were male and 126 were female. The pathology and social economic conditions were relevant in selecting the type of CVC used. Port or Hickman catheters were inserted in 27.96% and 72.03% of patients, respectively. In the latter group 89.28% were hematological patients. The selection of the French or lumens was in accordance to the vascular anatomy. In this group, a number of 188 patients used Hickman in which 43.61% were double lumen while 73 patients used Port and 12.32% were hematological patients; 78.16% of catheters were effective. The cause of catether removed were: 31.03% ended treatment, 28.58% infection (10.34% fungal infection), 13.79% thrombosis, 8.62% others complications and 10.34% death. Thirty cases of bacterial infections were caused by *Staphylococcus* (53.3%), *Burkholderia* (10%), *Corynebacterium* (6.6%), *E. coli* (6.6%), *Pseudomonas* (6.6%), *Micrococcus* (6.6%), *Citrobacter* (3.3%) and *Bacillus* (3.3%).
Conclusions: Despite many strategies being employed to reduce catheter infection such as lock antibiotics, anticoagulation solutions, and catheter with antibiotics there has not been a sufficient reduction of complications. Bacterial infection and thrombosis were the main cause of catheter removal. We can be reduced with a combination of Group and protocol. Further studies remain necessary in order to control bacterial biofilm and thrombosis in this patients with CVC.

POSTER SESSION: POSTER SESSION - LATE EFFECTS

P-0459

REDUCTION IN BETA-CELL FUNCTION AND PANCREATIC VOLUME IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA TREATED WITH BONE MARROW TRANSPLANATION AND TOTAL BODY IRRADIATION

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Purpose/Objective: Adult survivors of childhood Acute Lymphoblastic Leukaemia(ALL) treated with Bone Marrow Transplantation(BMT) and total body irradiation(TBI) have

increased risk of impaired glucose tolerance(IGT) and diabetes mellitus(DM). Insulin resistance(IR) has been described in these patients, but effects of TBI on pancreatic growth and beta(b)-cell function have not been previously reported.
Materials and Methods: Two groups of childhood ALL survivors were studied: Group1) Treated with($n = 21$,11M) and Group2) without($n = 31$,13M) BMT/TBI. BMT/TBI survivors received 10-14.4Gy TBI at mean age 9.3(1.0-10.8)years. A control Group3) was selected of obese subjects($n = 30$,10M). All were age 16-26years and had assessments of: pancreatic volume(PV) by abdominal MRI; IR by insulin-composite-insulin-sensitivity-index(ISIcomp) from oral glucose tolerance tests(OGTT); and b-cell function by acute-insulin-response(AIR) from Arginine intravenous glucose tolerance tests(AIRarg). Data were logarithmically transformed if positively skewed and analysed by ANOVA with post-hoc Scheff*'s multiple comparison tests, multiple regression and Pearson's correlations at 5% significance. Results are reported as mean(SD) or geometric means(range).
Results: Abnormal OGTT were reported in Groups 1($DM = 2$,$IGT = 7$) and 3($IGT = 1$). ISIcomp was lower in Groups 1[1.7(0.35-44.7),$p < 0.001$] and 3[4.8(0.75-9.6),$p = 0.001$] compared with Group 2[2.2(0.76-7.5)]. b-cell function assessed in the context of IR was lower in Group 1[60.0(CI:43.8-76.7)] than in Groups 2[105.4(CI:79.8-138.4),$p = 0.003$] and 3[83.8(CI:69.7-100.9),$p = 0.034$]. Absolute PV was lower in Group 1[52.0(14.2)] than in Groups 2[72.8(23.5),$p = 0.003$] and 3[72.8(19.7),$p = 0.006$] and correlated with AIR($r = 0.3$,$p = 0.01$). As PV correlated positively with height($r = 0.45$,$p < 0.001$) and as Group1 were shorter($p < 0.001$) than Groups 2 or 3[height SDS:-1.4(1.5);0.2(0.9) and 0.5(1.0) respectively], PV was corrected for height(cm^3/m^2) but remained less in Group 1[19.9(5.5)] than groups 2[24.9(8.0),$p = 0.048$] or 3[25.6(6.6),$p = 0.03$]. PV did not differ between Groups 2 and 3($p = 1.0$) and did not correlate with age at ALL diagnosis($p = 0.9$), time from treatment($p = 0.3$), age at BMT($p = 0.7$), time from BMT($p = 0.3$) or TBI dose($p = 0.8$).
Conclusions: Reduction in pancreatic size, and loss of b-cell compensation contribute, with increased IR, to the mechanism of abnormal glucose homeostasis in survivors of BMT/TBI in childhood.

P-0460

EVALUATION OF OTOTOXICITY IN CHILDREN WITH CANCER WHO RECEIVED CISPLATIN AND/OR CARBOPLATIN DURING TREATMENT

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Purpose/Objective: To evaluate hearing impairment in children with cancer who received platinum compounds.
Materials and Methods: Among 784 children, there were 221 (28%) patients who received platinum-containing chemotherapy. Medical records were analyzed for patient characteristics, details of treatment, co-administration of ototoxic drugs, head-neck radiotherapy (HNRT). Audiological assessments included pure tone audiometry, transient oto-acoustic emissions, auditory brainstem response testing.
Results: There were 97 eligible patients. The median age at treatment was 6.3 years, M:F ratio was 0.99. Patients divided into three groups; cisplatin-only group-1 (n:57), cisplatin&carboplatin group-2 (n:21), carboplatin-only group-3 (n:19). Ototoxicity incidence was 33% (n:19) in group-1, 43% (n:9) in group-2, and %5 (n:1) in group-3. According to the Brock's grading system 16 (55%) had grade-1, eight (27.6%) had grade-2, three (10.3%) had grade-3, and two patients (6.9%) had grade-4 ototoxicity. Majority (83%) of patients having ototoxicity was older than 5years of age during treatment. Seventy-seven percent (10/13) of patients with Brock's grade 2-4 ototoxicity were female, 60% of them were pubertal/ postpubertal females. Ototoxicity was significantly higher in patients who received both cisplatinum and HNRT (p:0.003), and in patients who received cisplatinum and aminoglycosides (p:0.001).
Conclusions: Children older than 5 years-old and adolescents were more susceptible to platinum ototoxicity in this study. Children who received cisplatin + HNRT have greater risk for ototoxicity. Co-administration of aminoglycosides was another risk factor. Colloboration of pediatric oncology and audiology departments is mandatory for early detection of ototoxicity in order to avoid further insult, managing the treatment, and improving quality of life.

P-0461

OVARIAN FUNCTION IS ASSOCIATED WITH OBESITY IN VERY LONG-TERM FEMALE SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: Obesity and gonadal dysfunction are known major side effects of treatment in adult childhood cancer survivors. In the general population, obesity has a negative influence on female fertility. The aim of the study was to evaluate whether obesity and serum insulin are associated with decreased ovarian reserve markers in childhood cancer survivors.
Materials and Methods: We performed a retrospective single-center cohort study in 191 adult female survivors of childhood cancer. Median age at follow-up was 27.1 years (range 17.7-50.0) and median follow-up time was 18.8 years (2.3-48.8). Outcome measures were serum levels of anti-MŸllerian hormone (AMH) and total follicle count (FC) and if measured during early follicular phase or during amenorrhoea antral follicle count (AFC). Potential risk factors were body mass index (BMI), body composition measures, determined by dual energy X-ray absorptiometry (total fat percentage, lean body mass and visceral fat percentage) and fasting insulin. Multiple linear regression analysis, adjusted for potential confounders, was used to evaluate the associations between potential risk factors and serum AMH and FC.
Results: Lower serum AMH was found in obese subjects (§ (%) -49, $P = 0.007$), and in subjects with fasting insulin in the highest tertile (§(%) -43, $P = 0.039$). Total fat percentage tends to be associated with serum AMH (§(%) -2.1, $P = 0.06$). Survivors in the highest tertile of insulin had significant lower FC than survivors in the lowest tertile (§ -6.3, $P = 0.013$). BMI and other measures of body composition were not associated with FC. Correlation between serum AMH and antral follicle count (AFC) was $\rho = 0.32$ ($P = 0.08$).
Conclusions: Obesity and insulin resistance are associated with gonadal damage, as reflected by decreased AMH and reduced FC in adult survivors of childhood cancer. In contrast to its highly predictive value for AFC in the healthy female population, serum AMH does not seem to correlate as well with AFC in childhood cancer survivors.

P-0462

CISPLATIN-INDUCED HEARING LOSS: THE NEED FOR A LONG-TERM EVALUATION SYSTEM

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Purpose/Objective: Although cisplatin-induced hearing loss is established as an important side effect in cisplatin-treated children, information concerning the problem is scarce, especially in Japanese pediatric patients. The objective of this study was to describe the frequency, severity, and clinical course of hearing loss in Japanese pediatric patients undergoing cisplatin-based multimodal therapy.
Materials and Methods: Data of 57 Japanese children who received cisplatin-based therapy between 1983 and 2013 and underwent audiologic evaluations were analyzed using the Brock criteria and Chang criteria to determine the onset, time to progression, and severity of hearing loss.
Results: Thirty-seven (65%) patients developed hearing loss.Eleven (58%) of 19 patients who received a cumulative cisplatin dose of $< 360\,mg/m^2$ developed hearing loss at a minimum $200\,mg/m^2$ dose. Median time of the onset of hearing loss since the last cisplatin dose was 71 days (range: -110*3446) and over 2 years in 6 (16%) patients. Hearing loss developed in 13 out of 17 older patients ($\geq$4 years) and in 24 out of 40 younger patients (< 4 years). It was more severe in the younger group than the older group. Children treated with cisplatin, carboplatin, and head radiation showed the highest rate of hearing loss (88%). Hearing aids were required by 4 patients; 6 patients developed progressive hearing loss; and 4 exhibited persistent hearing failure at low frequencies (125*500 Hz).
Conclusions: Risk factors for acquired hearing loss and its severity may be associated with a combination of factors, such as cisplatin and carboplatin therapy, head radiation, age at diagnosis, and genetic background. In addition, some patients developed progressive hearing loss at lower frequencies. All pediatric patients treated with cisplatin should have their hearing evaluated regularly, irrespective of the cumulative cisplatin dose. A prospective study is required to confirm these risks and establish an evaluation system.

P-0463

THE SALUB REGISTRY: SURVIVORSHIP PASSPORT AND NATIONWIDE REGISTRATION OF LATE-EFFECTS AFTER CHILDHOOD CANCER IN SWEDEN

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Purpose/Objective: To set up a national registry for late-effects after childhood cancer treatment and create a patient-friendly summary with recommendations for future follow-up.
Materials and Methods: The Swedish working group for long-term follow-up after childhood cancer (SALUB) has developed an extension of the on-line based Swedish Childhood Cancer Registry. The SALUB-registry contains detailed treatment information on cumulative doses of traditional chemotherapy, other anti cancer drugs, radiotherapy doses

towards targets and risk organs, surgery, central catheters and severe complications during treatment. The treatment data is separated into primary and relapse treatment with calculation of cumulative doses from all treatments. The health status at transition to adult care is reported in detail and relevant parts are transferred to the summary for the patient, the so called survivorship passport. The passport contains recommendations on future follow-up and contact information to the physician responsible for the transition. The passport function is primarily based on free text, in order to personalize the information for the patient. The registry also contains an event reporting form, aimed to be used in our late-effect clinics.
Results: The SALUB-registry was launched in October 2012 and in the first two months more than 100 patients were registered. The treatment data may be entered by a research nurse, but the health status and follow-up plan is signed by the physician responsible for transition.
Conclusions: The SALUB-registry forms a basis for future research on long-term side effects of cancer treatment during childhood. It provides detailed health status information at the age of 18 and a survivorship passport for the patient. With the further development of late-effect clinics the registry can be used for prospective registration of late-effects during adult life, as well as retrospective studies of the approximately 7,000 former childhood cancer patients in Sweden now 18 years of age or older.

P-0464

FINAL HEIGHT AND INSULIN-LIKE GROWTH FACTOR-I IN ADULT SURVIVORS OF WILMS TUMOUR

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Purpose/Objective: One-sided nephrectomy, as part of standard treatment for patients with Wilms tumour, is followed by increased levels of insulin-like growth factor-I (IGF-I), associated with linear growth during childhood. The aim of this study was to evaluate final height and IGF-I levels in nephrectomized Wilms tumour survivors as compared to healthy Dutch references and other survivors.
Materials and Methods: In this retrospective cross-sectional study, data of 575 adult long-term survivors were analysed. Median follow-up time was 17.8 years (range 5.0-48.8). IGF-I and height were compared with Dutch references by calculating standard deviation scores (SDS). Analysis of (co)variance was performed to evaluate differences between the following four subgroups: nephrectomized Wilms tumour survivors treated with or without abdominal irradiation ($n = 41$ and $n = 36$); survivors of other cancer types treated with or without irradiation involving the cranium, abdomen, spine or total body ($n = 149$ and $n = 349$).
Results: Although genetic mutations were found in 2 survivors (one *WT1* mutation and one hypomethylation of *LIT1*), no clinical overgrowth was diagnosed. Except for non-irradiated nephrectomized Wilms survivors (height SDS -0.24, $p = 0.155$, IGF-I SDS -0.05, $p = 0.817$), height SDS and IGF-I levels were significantly lower than Dutch references in all subgroups (non-irradiated survivors of other cancer types: height: SDS -0.47, $p < 0.001$; IGF-I SDS -0.28, $p < 0.001$; Wilms treated with abdominal irradiation: height: SDS -0.87, $p < 0.001$; IGF-I SDS -0.51, $p = 0.011$; others treated with irradiation: height: SDS -1.45, $p < 0.001$; IGF-I SDS -1.36, $p < 0.001$). After adjustment for age at diagnosis, former treatment with corticosteroids and renal insufficiency, height SDS in nephrectomized non-irradiated Wilms survivors was significantly higher than in non-irradiated survivors of other cancer types (SDS -0.09 versus -0.49, $p = 0.044$).
Conclusions: Adult survivors of Wilms tumour showed better attainment of final height and relatively higher IGF-I levels, than survivors of other cancer types who had significantly shorter stature and lower IGF-I levels than Dutch references.

P-0465

BRAF ALTERATIONS PREDICT LONG-TERM OUTCOME IN SURVIVORS OF PAEDIATRIC LOW GRADE GLIOMA.

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Purpose/Objective: Paediatric Low Grade Gliomas (PLGG) are the most frequent paediatric CNS malignancy marked by excellent 5 year overall survival (80-90%). Existing data is focused on short-term outcomes due to lack of follow up in adulthood. Several groups have recently reported of genetic alterations involving MAPK pathway (BRAF-KIAA1549 fusion and V600E mutation) in PLGG. However the role of these alterations in long term outcome is unclear.
Materials and Methods: We performed a population based study of all patients treated for PLGG in Southern Ontario since 1985. Comprehensive demographic, clinical, treatment and pathological data was collected from all patients. Long term outcome was gathered from the Pediatric Oncology Group of Ontario (POGO), Ontario Cancer Registry (OCR) and Institute for Clinical Evaluative Sciences (ICES) databases. BRAF-fusion was determined by fluorescent in situ hybridization (FISH) and V600E mutation by sequencing of all relevant tumors.
Results: 872 PLGG patients were identified. Overall survival (OS) was $93.9 +/- 1\%$ at 5 years and $83.6 +/- 2\%$ at 15 years for the whole cohort. Out of 56 (6.4%) deceased patients, only 13 (24%) died after age 18, and only 7 patients died during long term (> 10 years) follow up. Preliminary analysis on a subset of patients with molecular data ($n = 175$) revealed that OS for patients with BRAF-fusion positive tumors was $89.9 +/- 4.5\%$ at 10 and 15 years post diagnosis, while survival for BRAF-fusion negative ones continued to drop to $63.7 +/- 8.02\%$ by 15 years ($p = 0.0048$). Moreover, of the deceased patients with BRAF-fused tumors only 25% died of tumor progression.
Conclusions: Long term outcome for children with PLGG is excellent. BRAF-fusion is a positive predictor of long term survival. These observations suggest that BRAF-fused PLGG should be managed conservatively. Further molecular investigations of the entire cohort and the role of BRAF V600E mutation in long term outcome are ongoing.

P-0466

LONG-TERM SEQUELAE IN SURVIVORS OF CHILDHOOD LEUKEMIA WITH DOWN SYNDROME: A MATCHED COHORT STUDY FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Purpose/Objective: Children with Down Syndrome (DS) are at increased risk of acute leukemia and of acute therapy-related toxicities compared to children without DS. Whether they are at a heightened risk for late effects is unknown. This study describes the prevalence, severity and cumulative incidence of late chronic conditions in DS survivors of childhood leukemia compared to survivors without DS.
Materials and Methods: In a matched cohort study, 52 DS cases with childhood leukemia and a comparison group of 213 non-DS survivors (matched by leukemia, age at diagnosis, race, gender and treatment factors) from 4,830 five-year survivors in the Childhood Cancer Survivor Study cohort. Hazard Ratios (HR) and 95% Confidence Intervals were evaluated in Cox Regression models to determine relative risk of chronic health conditions as classified using the NCI Common Terminology Criteria for Adverse Events.
Results: The percent of subjects experiencing at least one chronic condition (Grade 1 - 5) more than 5 years after diagnosis of leukemia was similar in the DS population of survivors when compared to the non-DS group (DS 21.2%; non-DS 28.6%, HR = 0.9[0.5-1.8]). Severe chronic conditions (Grade 3 - 5) developing at least 5 years after diagnosis were more common in DS survivors of leukemia (DS 19.2%; non-DS 10.3%, HR = 2.1[1.0-4.4]). The cumulative incidence of a severe chronic health condition was 44% for DS survivors and 24% for non-DS survivors at 35 years post diagnosis; however, cataracts, hearing loss and endocrine effects, particularly hypothyroidism, accounted for much of the observed difference.
Conclusions: The incidence of late onset chronic conditions is similar in DS survivors when compared to non-DS survivors of leukemia. While DS survivors are at higher risk of developing serious chronic conditions, this likely reflects the natural history of DS. Regardless, practitioners should be aware of the increased risks of certain chronic conditions.

P-0467

ENDOCRINE COMPLICATIONS AND PARAMETERS OF THE METABOLIC SYNDROME IN SURVIVORS OF PEDIATRIC SOLID TUMORS

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Purpose/Objective: To evaluate the endocrine outcomes and components of the metabolic syndrome in survivors of childhood malignant solid tumors and to identify risk factors for their occurrence.

Materials and Methods: We conducted a medical records review of 139 survivors of pediatric non-brain solid tumors (study group) and 140 survivors of pediatric hematological malignancies (control group). Patients were evaluated with medical history, physical examination, and laboratory tests.

The frequency and types of endocrine dysfunction and parameters of the metabolic syndrome were measured and compared between the study group and the control group.
Results: The mean duration of follow-up in both groups was 9.5 ± 4.8 years (range 1.5-29.5 years). Forty-four patients (31.7%) in the study group had at least one endocrine abnormality, compared with 33 (23.6%) in the control group. The most common types of endocrine conditions in the study group were hypogonadism (11.5%), hypothyroidism (9.4%), short stature (9.4%), growth hormone deficiency (8.6%), and components of the metabolic syndrome (9.4%), without a significant difference compared with the control group.

Height-SDS was significantly lower in the study group compared with the control group ($p = 0.039$) with a tendency of decrease in the height-SDS during the follow-up in both groups, but more significantly in the study group ($p = 0.007$). BMI-SDS was significantly lower in the study group compared with the control group ($p = 0.016$), with a tendency of increase in the BMI-SDS during the follow-up in both groups without a significant difference between them.

In a logistic regression model, treatment with cranial radiation, local radiation and bone marrow transplantation were associated with significantly higher hazard of an endocrine complication.
Conclusions: The observation that a high percentage of solid tumor survivors suffer from endocrine late effects indicates the need to optimize screening for endocrine disorders and early intervention in this group.

P-0468

THE LONG-TERM FOLLOW-UP CLINIC (LTFC) EVALUATING THE LATE EFFECT AFTER CANCER THERAPY (LE) AND THE LONG-TERM HEALTH PROBLEMS (LTHP) FOR SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: Fascinates improvements in cancer therapy have resulted in increased survival of children with cancer, with the 5-year survival rate approaching 80%, which resulted in a growing LE and LTHP: physical, cognitive and psychosocial. Like a part of Paediatric Oncology Departments is established a LTFC for survivors of childhood cancer in Region South Denmark, including pediatric oncologists, nurses, other pediatric and medical specialists, surgeons, gynecologists, primary care physicians, psychologists and social workers.
Materials and Methods: There were selected 241 survivors derived from the Children's Oncology Unit with the 5-year survival rate. They were evaluated with medical history, physical and laboratory examination, with the long term follow up guidelines (LTFUG).
Results: The oncological pathologies were divided in 5 groups: I ALL, 82 survivors (34%); II AML, 7 (3%); III Lymphoma, 39 (16%); IV central nervous system tumors; 44 (18,2%)and group V, other solid tumors, 69 (28,6%). Late effect were observed generally in 82 (32,8%) survivors in all of the groups: 25.6%, 43%, 30,8%, 45.5% and 34,8% respectively for group I,II,III, IV and V. Endocrine disorders (growth, weight, puberty, gonadal, bone, thyroid and adrenal disorders) were found in 52.4%, cognitive (difficult schoolwork, learning and memory difficulties, particularly during physical education classes, anxiety, depression,) in the 24.4% and skeletal in the 12%, survivors. Highest risk for LE include patients treated for CNS tumors and lymphoma.
Conclusions: Approximately one-third of survivors of childhood cancer experienced at least one LE. Timely and appropriate recognition of LE and LTHP can result in improved Quality of Life.

P-0469

THYROID FUNCTION AFTER TREATMENT OF HODGKIN'S LYMPHOMA IN CHILDHOOD

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Purpose/Objective: The study aimed at estimation of thyroid function up to 29 years after completing therapy for Hodgkin's Lymphoma (HL) in patients treated in childhood at single center with regard to applied chemotherapy (MVPP/B-DOPA), radiotherapy (RT), age at disease onset, gender and HL stage.
Materials and Methods: 193 patients (139 males, 54 females), aged 3.7 * 41.7 years (mean 21,2 years), 0.1 * 28,9 years (mean =9.8) from HL treatment cessation in first remission were evaluated. Serum TSH, fT3, fT4, thyroglobulin (Tg), thyroperoxidase antibodies (TPO-Ab), thyroglobulin antibodies (Tg-Ab) were assessed.
Results: Elevation of TSH, fT3, fT4, Tg, TPO-Ab, Tg-Ab levels was observed in 0.5%, 3.1%, 2.1%, 1.1%, 4.7%, 1.6% of patients, respectively. Decreased fT3 and fT4 concentrations were found in 19.7% and 13.5% of patients, respectively. Positive correlation was found between serum TSH levels and RT dose applied to mediastinal lymph nodes ($R_S = 0.4654$, $p < 0.01$), fT3 serum levels and number of MVPP, B-DOPA courses ($R_S = 0.2403$, $p < 0.01$; $R_S = 0.1963$, $p < 0.05$), RT dose applied to cervico-supraclavicular nodes ($R_S = 0.2884$, $p < 0.001$), period from therapy cessation ($R_S = 0.4479$, $p < 0.001$), fT4 levels and period from therapy cessation ($R_S = 0.2302$, $p < 0.005$), Tg concentration and RT dose on mediastinal lymph nodes ($R_S = 0.3959$, $p < 0.05$), period from therapy cessation ($R_S = 0.1624$, $p < 0.05$), TPO-Ab and period from therapy cessation ($R_S = 0.3189$, $p < 0.001$), Tg-Ab and period from therapy cessation ($R_S = 0.5121$, $p < 0.001$). Negative correlation was found between fT_3, fT_4 and age at the disease onset ($R_S = -0.893$, $p < 0.01$; $R_S = -0.2056$, $p < 0.01$), TPO-Ab and clinical stage ($R_S = -0.1702$, $p < 0.05$).
Conclusions: Frequency of fT3, fT4 serum abnormalities after HL treatment was not related to gender and disease stage and decreased in time after therapy cessation. Increase of fT3 serum levels is proportional to number of MVPP and B-DOPA cycles, and to RT dose applied to cervico-supraclavicular nodes. Frequency of fT3, fT4 serum abnormalities is inversely proportional to age at the onset of disease.

P-0470

THYROID MORPHOLOGY AFTER TREATMENT OF HODGKIN'S LYMPHOMA IN CHILDHOOD

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Purpose/Objective: The study aimed at assessment of thyroid gland morphology of patients in first remission after Hodgkin's Lymphoma (HL) therapy with relation of thyroid disorders to applied chemotherapy (MVPP/B-DOPA), radiotherapy (RT), age at disease onset, gender, HL stage.
Materials and Methods: A total of 160 patients, aged 3.7 * 41.7 years (mean * 21.2 years), were assessed 0.1 * 28.9 years (mean - 9.8 years) after completing HL therapy in childhood at a single center.

Thyroid morphology was assessed by physical and ultrasound examination in all patients. Fine needle aspiration biopsy was performed in selected cases.
Results: Abnormal thyroid echogenicity was found in 65% of patients. Increased thyroid volume was observed in 12.1% of patients, while decreased volume in 52.9%. Thyroid nodular disease was diagnosed in 29.4% of patients. Mean period after completion HL treatment in patients with no nodular disease (7.8 years) was significantly shorter than in patients with single (13.8 years; $p < 0.005$) or multiple nodules (17.3 years, $p < 0.0001$). The number of patients with thyroid nodular disease increased significantly in time ($p < 0.001$). The risk for development of nodular disease was significantly increased after 11 years ($RR = 6.39$, $OR = 12.99$, $p < 0.0001$), after receiving >4 cycles of MVPP ($RR = 3.55$, $OR = 6.25$, $p < 0.001$); after RT to cervico-supraclavicular lymph nodes >26 Gy ($RR = 5.84$, $OR = 8.79$, $p < 0.001$); and correlated with serum concentration of thyroglobulin antibodies >6.5 IU/ml ($RR = 3.79$, $OR = 5.04$, $p < 0.05$). In five patients thyroid papillary carcinoma was diagnosed.
Conclusions: Most patients treated for HL in childhood experience decrease of thyroid gland volume, this particularly concerns children younger at initial diagnosis. Almost one-third of patients develop thyroid nodular disease * more frequent in females, proportional to MVPP cycles, RT of cervico-supraclavicular region and time from completing therapy.

P-0471

A SYSTEMATIC REVIEW OF NUTRITIONAL INTERVENTIONS FOR CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: Childhood cancer survivors (CCS) are at a higher risk of developing chronic conditions such as, obesity, cardiovascular disease, hypercholesterolaemia and type II diabetes. It may be possible to reduce or lessen the incidence of these chronic conditions with focused prevention strategies. The purpose of this systematic review is to assess the literature in regards to nutritional interventions developed for all childhood cancer survivors, to facilitate the production of best-evidence management guidelines.
Materials and Methods: Using the methodology of the COCHRANE Collaboration, a systematic review was undertaken of five electronic databases; The Cochrane Central Library of Controlled Trials (CENTRAL), MEDLINE/PubMed, EMBASE/OVID, CINAHL and PsycINFO. Nutrition/diet studies that involved childhood cancer survivors who were diagnosed with any type of cancer during childhood were eligible.
Results: Only three studies met the inclusion criteria, meaning that a meta-analysis of treatment efficacy was not possible. Two studies focused on interventions in adolescent CCS. The results suggested that interventions with a focus on both nutritional education and behaviour change were the most effective in improving nutritional intake. One study suggested a difference in outcomes between males and females, when post-hoc analysis was

completed. Nutrition interventions appeared less effective in younger CCS, though future studies including a behavioural change component are needed.
Conclusions: Interventions that combined dietary education with behaviour change appeared most effective in improving CCS nutritional intake. There remains a gap in the literature regarding nutritional interventions in younger CCS. When designing future studies, gender-specific interventions may also need to be considered.

P-0472

PREDICTION OF IMPAIRED BONE MINERAL DENSITY IN LONG-TERM ADULT SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: Osteoporosis is a complication of childhood cancer treatment, but it is unknown how many and which adult childhood cancer survivors (CCS), are at risk. We examined bone mineral density (BMD), assessed possible determinants and developed a risk model to identify adult CCS with a risk for osteoporosis.
Materials and Methods: The single-center cohort study included 410 adult CCSs (median age at diagnosis: 6.6 years (range: 0-17 years), median follow-up time:15.2 years (range 5-39 years). Total body BMD (BMDTB) and BMD of the lumbar spine (BMDLS) were measured with dual X ray absorptiometry (DXA). In a subsample of 188 survivors, a sequential DXA scan was performed (median time after first DXA: 3.2 years). The model was developed using multiple regression analysis.
Results: Survivors had a lower BMDTB (median standardised difference score (SDS): -0.60; $p < 0.001$) and BMDLS (SDS:-0.40; $p < 0.001$) as compared to healthy peers. In the subsample, BMDTB and BMDLS significantly increased between the first and second DXA (mean SDS: BMDTB = 0.08; $p = 0.003$; BMDLS: 0.06; $p = 0.03$). Use of glucocorticoids (GC) during treatment (st. $\beta = -0.22$), and lower BMI at follow-up (st. $\beta = 0.53$) were determinants of low BMDTB, whereas lower BMI (st. $\beta = 0.22$) and use of cyclophosphamide (st. $\beta = -0.18$) were associated with impaired BMDLS. A risk model for low BMDTB included ALL, AML, a brain tumor or sarcoma at primary disease, age higher than 30 years, BMI at follow-up below 20 kg/m2, and previous craniospinal or total body irradiation (adjusted $R2 = 0.25$). A risk model for BMDLS included higher age, low BMI and use of cyclophosphamide (adjusted $R2 = 0.10$).
Conclusions: Long-term childhood cancer survivors have a lower BMDTB and BMDLS as compared to healthy peers, but improvement in BMD may still occur. We developed a prediction model for BMDTB that can assist clinicians to select adult CCS for surveillance by DXA in order to identify subjects at risk to develop osteoporosis.

P-0473

PSYCHOSOCIAL OUTCOMES IN LONG TERM SURVIVORS OF CHILDHOOD CANCER IN HONG KONG

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Purpose/Objective: To evaluate the psychosocial outcomes in long-term survivors of childhood cancer in Hong Kong.
Materials and Methods: Childhood cancer survivors who had completed anti-cancer treatment in five paediatric oncology centers in Hong Kong for at least 5 years were recruited. They were individually interviewed by social worker from Hong Kong Children's Cancer Foundation (CCF).
Results: Total of 733 childhood cancer survivors were recruited from 2007 to 2012 (male = 441; female = 292; age range: 5-39). There were 107 (14.6%) survivors identified of psychosocial problems. They were survivors of leukaemia = 45, lymphoma = 9, solid tumour = 30, brain tumour: 21, born tumour = 2. The psychosocial problems included study failure = 35(5%); employment difficulty = 20(3%); emotional problem = 12(1.6%); interpersonal social skill problem = 9(1.2%); family relation problem = 4(0.5%); others = 27(3.6%).

Specific services were further provided to these survivors by the CCF family service centre. Survivors were referred to study tuition class = 43(5.9%); vocation training or employment assisting program = 77(10.5%) and clinical psychologist counseling = 7(1%).
Conclusions: This study showed a significant percentage of childhood cancer survivors in Hong Kong suffered from psychosocial problems. Study and employment failure were the most common problems. Specific supportive service should be provided to the long term survivors.

P-0474

PHARMACOGENOMICS LINK RS11615 OF ERCC1 TO CISPLATIN-INDUCED OTOTOXICITY

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Purpose/Objective: Despite improved supportive care, ototoxicity still limits the use of cisplatin in children with cancer. ERCC1 is required for the repair of DNA lesions formed by electrophilic compounds like cisplatin, and polymorphisms in this gene have been associated with response as well as toxicity to platinum based chemotherapy.
Materials and Methods: To investigate whether the polymorphisms rs11615 and rs3212986 in *ERCC1* affect the individual risk of ototoxicity by cisplatin, we analysed the allele frequencies of rs11615 and rs3212986 in paediatric cancer patients treated with cisplatin. To control for non-genetic risk factors, only children older than five years, who had no pretherapeutic hearing loss, no cranial irradiation, and had no renal insufficiency were included in this study. A total of 54 patients fulfilled the inclusion criteria. Because children with an early onset of cisplatin-induced hearing loss are suggested to be less tolerant to the ototoxic side effects of cisplatin, the genetic analysis focused on a subgroup of patients with an early and high grade hearing impairment (group EH, 15 patients) in comparison to 27 patients who experienced no ototoxicity by cisplatin (group N).
Results: We observed a higher frequency of the C-allele of rs11615 among patients with early and high grade hearing impairment (group N: 0.35; group EH: 0.67; $p = 0.065$, Fisher Exact Test). In contrast, allele frequencies of rs3212986 were unchanged between both groups (group N: 0.29; group EH: 0.27; $p = 1.00$, Fisher Exact Test).
Conclusions: The results, though being explorative, indicate an association of functional DNA repair mechanisms and susceptibility to cisplatin-induced ototoxicity. The marked difference in the frequency of the *ERCC1* rs11615 C-allele between patients with an early and high grade hearing impairment in comparison with control patients without hearing loss encourages more differentiated pharmacogenomic analyses of nucleotide excision repair pathway genes in larger patient cohorts.

P-0475

IS BREAST CANCER SCREENING IN CHILDHOOD CANCER SURVIVORS JUSTIFIED?

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Purpose/Objective: Female patients receiving radiotherapy to a field involving the breast tissue (chest radiation) during treatment for childhood, adolescent and young adult cancers are at an increased risk of developing breast cancer (BC) in later life. In an attempt to detect these cancers at an early stage screening guidelines have been published in several countries around the world. However, the published recommendations vary between countries. This literature review looks at the underlying evidence for five of the published guidelines and also the recommendations made by the International Harmonisation Group.
Materials and Methods: Guidelines from the UK, Scotland, USA, Sweden and the Netherlands were compared. The evidence behind the guidelines was carefully evaluated and further systematic literature searches were performed to provide additional evidence to answer formulated questions.
Results: The guidelines vary in both the defined screening population and also in the choice of screening methods. Only in Scotland is no screening recommended due to the lack of studies undertaken specifically in survivors of childhood. Screening guidelines are based upon studies in other high-risk populations, eg. carriers of the BRCA genes. Extrapolating data from these studies is justified by the similar BC incidence rates in this group compared to women treated with radiotherapy. A higher risk of BC was associated with radiation treatment received under the age of 30 years and with a radiation dose > 20 Gy. The cumulative risk of BC is significantly increased 8 years after radiation or at age 25 years, whichever comes first.
Conclusions: The increased risk of BC after chest radiation in childhood, adolescence and young adulthood is well established, but evidence regarding screening programmes in this specific population is lacking. Screening in other high-risk populations has been proven to be successful, thereby indicating a role for screening in these patients.

P-0476

LATE EFFECTS IN TEENAGE AND YOUNG ADULT CANCER PATIENTS - ARE THEY RECOGNISED IN EVERYDAY PRACTICE?

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Purpose/Objective: Many teenage and young adult (TYA) cancer patients receive treatments similar to their paediatric counterparts, but the late effects of treatment have rarely been studied. In order to better understand the spectrum of late complications, patterns of follow up and healthcare professional awareness of late effects in this population, we undertook a case notes review of a consecutive series of TYA patients diagnosed with a solid tumour malignancy .
Materials and Methods: Our cohort consisted of patients aged 16-24 years diagnosed with a solid tumour malignancy at a single institution between 2003-2009.
Results: Sixty-eight patients were identified with a mean age at diagnosis of 21 years. Median follow up was 5 years. Diagnoses included testicular cancer (n = 28) Hodgkin Lymphoma (n = 15) and CNS tumours (n = 5). Twenty-three patients underwent surgical resection alone, whilst 45 received chemotherapy or radiotherapy or both, of whom 10 were still in follow-up at less than 5 years since last treatment. One patient had self-referred to a specialist late effects clinic.

Seventeen (25%) patients had adverse health outcomes documented during follow-up including; hearing impairment, secondary malignancies and hypothyroidism. Three had been referred for breast cancer screening. Thirteen had received anthracyclines; one had undergone an echocardiogram post-treatment. Four of fifteen patients who had received platinum-based chemotherapy reported hearing loss and tinnitus; no patient had undergone routine surveillance audiograms. There was no documentation of follow-up counselling respecting fertility.
Conclusions: Although follow up for this group of patients is relatively short, a number have documented late effects but signicantly less than reported in childhood cancer survivors. Follow up was focussed on detection of disease recurrence and patients were routinely discharged after 5 years follow-up. There was evidence of healthcare professional awareness of the risk of radiation related second malignancy, but little evidence of a systematic approach to screening for chemotherapy related late effects.

P-0477

CISPLATIN-INDUCED OTOTOXICITY IN CHILDREN AND YOUNG ADULTS TREATED IN SINGAPORE

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Purpose/Objective: Cisplatin-induced ototoxicity is an irreversible, progressive, high frequency sensori-neural hearing loss. Prevalence and risk factors for hearing loss are not well defined in the Asian population. We investigated the frequency of cisplatin-induced ototoxicity in children and young adults treated in 2 main pediatric cancer centers in Singapore and its relationship to demographic and clinical factors.
Materials and Methods: The data for this preliminary analysis were derived from the large database of an on-going case control study looking into clinical and genetic risk factors for ototoxicity.

We included all patients who received cisplatin and had baseline hearing tests done. Patients, who underwent cranial surgery or radiation, had pre-existing neurological or hearing problems were excluded. Audiologic testing was performed at study entry: pure tone audiometry (age > 5 years), play audiometry (3 * 5 years) or otoacoustic emissions (below 3 years). Significant cisplatin-induced ototoxicity was defined as grade 2-4 hearing impairment using CTCAE version-4.0 scale. Patients with grade 1 or normal hearing tests served as controls. Univariate analysis was performed on cumulative cisplatin dose, age at diagnosis, sex, and aminoglycoside use, hypomagnesemia requiring supplementation, tumor type and ethnicity.
Results: To date 33 patients have been enrolled. Mean age at diagnosis of the malignancy was 13 years (0.8-24.8). Male:Female ratio was 2.3. Majority were Chinese (75%) and Malay (12%). The diagnoses were osteosarcoma (57%), germ cell tumour (18%), neuroblastoma (15%) and hepatoblastoma (9%). Thirty-one have completed treatment. Mean cumulative Cisplatin dose was 503mg/m^2 (120 * 760 mg/m^2). Twenty four children (72%) had significant hearing loss (grade 2 = 36%, grade 3 = 36%). Univariate analysis showed only aminoglycoside use was associated with hearing loss (p = 0.04).
Conclusions: A high incidence of significant cisplatin-induced hearing loss among Singapore children and young adults is seen. The prevalence is higher if they received aminoglycosides.

P-0478

REDUCED CARDIOPULMONARY FITNESS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVORS

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Purpose/Objective: One in 600 adult individuals in USA is a survivor of childhood cancers. A number of chemotherapeutic agents are associated with long-term cardiopulmonary toxicities. Low cardiopulmonary fitness is a strong predictor of all-cause mortality, cardiovascular disease and functional limitations. The purpose of this study was to evaluate cardiopulmonary fitness in Chinese paediatric acute lymphoblastic leukemia (ALL) survivors and to identify high risk group for early behavioral modification.
Materials and Methods: Childhood ALL survivors were recruited. Cardiopulmonary fitness expressed as peak oxygen consumption (peak VO_2) was measured. Exercise response of ALL survivors was compared to a group of age, gender and BMI matched healthy controls. Maximal effort was defined as a respiratory exchange ratio (RER) > 1.10 with clear signs of exhaustion
Results: Fifty-one survivors (27 males, 24 females) with a mean age of 18.3 ± 4.5 years were included in the analysis. Peak VO_2 was significantly reduced in survivors compared with controls (35.2 ± 9.8 vs 39.9 ± 11.9 mL × Kg^{-1} × min^{-1} respectively, $p < 0.05$). Survivors also had significantly lower peak heart rate (HR) (186 ± 9 vs 192 ± 11 bpm, $p < 0.05$) and greater heart rate reserve (HRR) (5.3 ± 9.8 vs −0.9 ± 11.5 bpm, $p < 0.05$) than controls. Sixty-seven percent of survivors (15 males, 19 females) failed to achieve a peak HR greater than 95% of predicted maximal HR, compared to 41% in the control group ($p < 0.05$). The mean duration from assessment and termination of treatment for survivors with suboptimal peak HR (n = 34) vs those who could achieved optimal peak HR (n = 17) was 8.9 ± 3.5 and 12.2 ± 4.7 years respectively ($p < 0.05$). ALL risk stratifications in these 2 groups were similar.
Conclusions: Significant proportion of ALL long-term survivors had reduced cardiopulmonary fitness which was a negative risk factor or subsequent cardiovascular risk. Early behavioral modifications are probably justified in this group of patients.

P-0479

CARDIAC MUSCLE FUNCTION IN SURVIVORS OF CHILDHOOD ACUTE MYELOID LEUKEMIA TREATED WITH CHEMOTHERAPY ONLY: A NOPHO-AML STUDY

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Purpose/Objective: To evaluate cardiac muscle function in patients treated according to the NOPHO-AML -84, -88, or -93 protocols, and alive by June 30, 2007 without relapse or transplantation.
Materials and Methods: Ninety-eight out of 138 eligible patients were examined with standardized centrally reviewed echocardiogram and combined assessment of the systolic and diastolic function (Tei-index) was performed. Results were compared with 30 age and sex-matched controls.
Results: Mean age at diagnose was 5 (range 0-15) y and at study 17 (5-36) y, and the follow-up time was 12 (4-25) y. All patients had received doxorubicin (mean cumulative dose 148(+/− 39) mg/m^2) and the majority (N = 88) had received combinations of doxorubicin and mitoxantrone (mean cumulative dose 37(+/− 14) mg/m^2). The mean total anthracycline dose was calculated (doxorubicin + (5 x mitoxantrone)) to 317(+/− 67) mg/m^2). Ten patients and one control had fractional shortening (FS) < 28%, and 13 patients had left ventricular ejection fraction (LVEF) < 55%. There was a significant difference in FS between patients 32.6 (+/− 4.0) % and controls 35.2 (+/− 3.4) % (p = 0.002) and also in LVEF (59.5 (+/− 6.8) % vs. 64.2 (+/− 4.4) %), (p = 0.001). The Tei-index was higher in patients 0.32 (+/− 0.081) than controls 0.26 (+/− 0.074) (p < 0.001). Cumulative dose of doxorubicin was significantly related to lower FS (p = 0.037) and LVEF (p = 0.016). Longer follow-up time was associated with lower FS (p = 0.034). Higher Tei-index was related to young age at diagnosis (p = 0.04) and longer follow-up (p = 0.031), but not to the calculated cumulative dose of anthracyclines or dose of mitoxantrone.

Conclusions: In this study of Nordic AML patients treated with chemotherapy only, there was a significant reduction in left ventricular function compared with healthy controls, although most patients had cardiac function within normal limits. Higher doses and longer follow-up were associated with decreased cardiac function.

P-0480

PHYSICAL ACTIVITY THROUGH HOME-BASED EXERCISE-GAMING AFTER CHILDHOOD BRAIN TUMOUR TREATMENT- A FEASABILITY STUDY

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Purpose/Objective: Childhood brain tumour therapy carries a substantial risk of impaired intellectual development in the survivors. Voluntary physical activity appears to have a positive effect on executive function in humans and on neurogenesis in animal models. We hypothesized that exercise gaming could be used to achieve regular, enjoyable, physical exercise.
Materials and Methods: Children 7-17 years who completed treatment, including radiotherapy, for a malignant brain tumour 1-5 years earlier were randomized to an exercise group or a wait-list group. After 10 weeks the groups shifted in a cross-over fashion. A motion-controlled video console (Nintendo Wii) was used for home-based physical exercise during the exercise period, for a minimum of 30 min per day, at least 5 days a week, for 10 weeks. The children had weekly contact with a coach using internet based video-conferencing technology, to improve compliance, assess the past week«s gaming, and stimulate continuous exercise-gaming. Every second week patients wore a multisensory activity monitor, SenseWearPro_2 Armband, calculating energy expenditure and intensity of activities as Metabolic Equivalent of Task (METs). All children were tested with cognitive tests, motor and process skills before and after each period.
Results: 13 children, mean age 12.5 years, completed the program. 8/13 reached the target of 10 weeks exercise-gaming, 4/13 completed 9 weeks and 1/13 7 weeks (mean 9.5 weeks). Reasons for non-compliance were mainly intercurrent illness or travel and only rarely lack of motivation. The participants rated 49% of the gaming weeks as 'OK/good', 35% as 'fun' and 1.5% as 'boring'. Mean energy expenditure was 1.9 METs at baseline, 1.99 during gaming weeks and 3.0 during gaming sessions.
Conclusions: Exercise gaming can be used as a home based intervention in childhood brain tumour survivors accomplishing a moderate physical exercise, although not increasing their overall physical activity. Coaching probably improves compliance.

P-0481

A NOVEL SERUM BIOMARKER, KERBS VON LUNGREN 6 AG (KL-6) AS AN EARLY PREDICTOR OF BRONCHIOLITIS OBLITERANS SYNDROME IN CHILDREN FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION (ALLO-SCT).

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Purpose/Objective: Bronchiolitis obliterans syndrome (BOS) is common and potentially devastating noninfectious pulmonary complication post allo-SCT with significant mortality in children. Early detection is key for successful stabilization with immunosuppressant therapy prior to occurrence of end stage lung disease. Pulmonary function tests (PFTs) are the mainstay for diagnosis, however, significant lung damage occurs prior to PFT's changes and children may be uncooperative or unable to perform PFTs. Some lung specific serum biomarkers may aid BOS detection earlier than PFTs changes
Materials and Methods: We recruited 39 children receiving allo-SCT in a prospective study and 6 healthy controls at SickKids, Toronto. We measured PFTs and collected blood samples at 8 time points; Pre SCT, 1, 3, 6, 9, 12, 18 and 24-months post SCT. We quantified the levels of specific lung proteins in patients' serum samples, surfactant proteins (SP-A, SP-D), Clara cell secretory protein (CCSP) and KL-6 by ELISA testing. End point was the development of BOS using the new NIH criteria or lung biopsy. Data was analyzed by Non-parametric 2-tailed Mann-Whitney U test without assuming Gaussian distribution.
Results: Six patients developed BOS during the study period at a median time of 192 days (range 94-282). KL-6 in healthy controls is undetectable. However, patients who had high levels of KL-6 at Pre-HSCT time point developed BOS (median, interquartile range; 32.56, 9.66-89.34 U/ml) compared to live non-BOS patients (5.81, 2.07-12.63 U/ml; $p < 0.0357$). KL-6 levels at 1-month post SCT also were high in BOS patients (52.53, 20.21-121.3 U/ml) compared to live non-BOS patients (11.36, 5.73-35.99 U/ml; $p < 0.046$). SP-A, SP-D and CCSP levels were related to infections at different time points in BOS and non-BOS patients.
Conclusions: KL-6 as a serum biomarker identifies patients receiving allo-SCT who are at risk for BOS development early. This helps to intensify screening for these patients with early intervention to avoid end stage lung disease

P-0482

SUBSEQUENT MALIGNANT NEOPLASMS AMONG A POPULATION-BASED COHORT OF PEDIATRIC CANCER PATIENTS IN ONTARIO, CANADA

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Purpose/Objective: To describe the risk for the development of subsequent malignant neoplasms (SMN) among a population of childhood cancer patients in the Canadian province of Ontario.
Materials and Methods: The population was identified from the Pediatric Oncology Group of Ontario Networked Information System (POGONIS). The cohort comprised all children aged 0 to 14 years treated for a cancer at any provincial pediatric hospital between January 1985 and December 2008. SMN (excluding non-melanoma skin cancer and meningiomas) and vital status were determined by linkage to the Ontario Cancer Registry (OCR). The cohort was followed until June 2011.
Results: 8,415 children were treated for cancer over the 24 year study period. Median follow-up after diagnosis was 11.2 years (range: 0.0-26.4 years). 2.4% of patients (205/8415) developed 218 SMN (standardized incidence ratio: 9.6) at a median of 7.5 years (range: 0.0-24.9 years) from diagnosis. Among 6,268 5-year survivors (median follow-up: 14.8 years, range: 5.1-26.4 years), 119 developed SMN. Subjects with an original diagnosis of soft tissue sarcoma, bone tumor or central nervous system tumor were at highest risk for developing a SMN over the follow-up period (3.5%, 2.6% and 2.4% respectively). The most common SMNs were central nervous system tumors (22.9%), leukemia (21.1%), thyroid cancer (15.6%) lymphoma (10.6%) and soft tissue sarcomas (8.7%). Subjects who developed SMNs were older at the time of their initial diagnosis compared to those that did not develop a SMN (6.3 versus 5.8 years, $p < 0.001$). Childhood cancer survivors who developed a SMN were nearly twice as likely to die as those that did not (31.7% versus 16.7%, $p < 0.001$).
Conclusions: In this cohort, 2.4% developed a SMN. Among 5-year survivors, 1.9% subsequently developed a SMN. This is consistent with estimates from Childhood Cancer Survivor Study (with cumulative incidence at 15 years approximating 1.9%).

P-0483

SUBSEQUENT MALIGNANT NEOPLASMS (SMN) IN CHILDHOOD CANCER PATIENTS TREATED WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT).

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Purpose/Objective: Data regarding SMN in pediatric patients after a malignancy treated with HSCT are sparse. We aimed to describe the development of SMN among a population-based cohort of childhood cancer patients whose primary therapy included HSCT.
Materials and Methods: The population was identified from the Pediatric Oncology Group of Ontario Networked Information System (POGONIS), a provincial registry of children aged 0 to 18 years at the time of diagnosis of a first and any subsequent malignancy at an Ontario pediatric hospital. The cohort was diagnosed between January 1985 and December 2009. SMNs in the adult period were identified by linkage to the Ontario Cancer Registry. SMN development in patients treated with HSCT was compared to patients treated without HSCT over the same period.
Results: Of 9,168 children diagnosed with a malignancy, 895 (9.8%) underwent HSCT (51% autologous, 49% allogeneic). Median follow-up after primary malignant diagnosis was 6.0 years in the HSCT group and 11.5 years in the non-HSCT group (range in both groups: 0-27.6 years). In the HSCT group, 26 patients (2.9%) were diagnosed with a SMN at a median of 66 months after HSCT (range: 2-236 months). This did not differ from the proportion who developed SMN among the non-HSCT group (2.0%, $p = 0.07$). Although patients who underwent an allogeneic HSCT comprised 49% of the HSCT group, they accounted for 73.1% of the SMNs (19/26, $p = 0.02$). The most frequently observed SMN after HSCT were thyroid cancers (23.1%), leukemia (19.2%), lymphoma (15.4%) and central nervous system tumours (11.5%).
Conclusions: Childhood cancer patients treated with HSCT were no more likely to develop a SMN than patients treated without HSCT. Allogeneic HSCT carried the highest risk for SMN among HSCT patients.

P-0484

NEW APPROACH TO SPECIFIC SYMPTOMS OF BRAIN DAMAGE DUE TO TUMOR. MORE THAN LOCALIZATION OF THE LESION

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Purpose/Objective: The purpose of the study was to describe cognitive deficits and affective problems of brain tumor survivors. Symptoms typical for various tumor types and its localizations were identified. Specific symptoms strongly associated with particular region of the brain and other not so obvious were evaluated. This project is dedicated to clarify the nature of these symptoms.
Materials and Methods: Psychological repeated testing and long-term observation was performed in 350 childhood brain tumor survivors (various types and localizations of tumor) to determine psychological and social late effects of disease and treatment. Age at psychological diagnosis ranged from 6 to 26 years. Full psychological outcome included assessment of psychophysical, cognitive and affective problems. The patients were examined using battery of neuropsychological methods and psychological interview. Analysis of medical history was also performed.
Results: In the series of patients with hemispheric tumors we observed serious problems with: shearing attention, following activities of others, switching topic of activity, respecting rules and strong predisposition to the perseveration. This specific behavioral phenotype disturbed learning process (despite normal IQ)) and their social life. Patients with posterior fossa tumors were distinctly slow in cognitive activities and every day routines, had loss of previous interests, were socially motiveless (hipobulic, anhedonic) and had low level of expressed emotions. This specific functioning causes exclusion from the peer group. Hypochondrial focus on body was typical for patients with midline brain tumors, as well as emotional overreaction to common life situations. This resulted in difficulties in interpersonal relations.
Conclusions: The results of our study suggest that multiple factors (beside tumor localization) are responsible for neuropsychological symptomatology of childhood brain tumors and play a role in patients psychosocial functioning. Draft recommendations for diagnosis of specific brain tumors symptoms will be presented and discussed.

P-0485

FREQUENCY AND PREDICTORS OF SURVIVOR CLINIC NON-ATTENDANCE IN A POPULATION-BASED SAMPLE OF CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: Little is known regarding why childhood cancer survivors rarely receive recommended long-term follow up care and surveillance at survivorship clinics. We quantified clinic non-attendance and identified associated demographic and disease predictors.
Materials and Methods: A population-based tumor registry of patients diagnosed with cancer at Yale from southern Connecticut identified all eligible patients diagnosed from 3/1/2000-3/1/2008, $\leq$18 years at diagnosis, alive as of 3/30/2004 (one year after the start of HEROS, Yale's regional survivor clinic) and off cancer treatment at least one year. Patient records, supplemented by phone calls, were reviewed to determine vital status, and whether patients attended any survivor clinic.
Results: 498 eligible childhood cancer survivors had a median age of 9.0 years (+/− 5.7 years SD) at cancer diagnosis, were 56.2% male with the following diagnoses: 28.1% leukemias, 18.7% CNS tumors, 16.1% lymphomas, and 27.5% with other solid tumors. Overall, 407 (81.9%) had not attended a survivor clinic. Particularly, 20.6% status post-radiation therapy, 90.3% of CNS tumor patients, and 60% with a history of chemotherapy never attended survivor clinic. In a multivariate analysis, not visiting their primary oncologist within 2 years (OR = 1.88, 95%CI: 1.13-3.13), and not having received radiotherapy or chemotherapy (OR = 5.55, 95%CI: 2.22-13.84) significantly predicted survivor clinic non-attendance. Gender, age, diagnosis, health insurance, history of recent primary care doctor visit, and income were not significant predictors of survivorship clinic attendance.
Conclusions: About 80% of childhood cancer survivors in our population-based sample had not attended survivor clinic. Particularly worrisome was the substantial percentage of non-attendance among survivors with CNS tumors given the high risk for late effects. Our results suggest that remaining in follow-up with the primary oncologist is an important predictor of survivor clinic attendance. Survivors with no radiation or chemotherapy history have lower risk for late effects, which may be why they are less likely to attend survivor clinic.

P-0486

VALIDATION OF THE SIOP BOSTON OTOTOXICITY SCALE- AN INTERNATIONAL SCALE FOR THE EVALUATION OF PLATINUM-INDUCED OTOTOXICITY IN CHILDREN.

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Purpose/Objective: Permanent hearing loss is frequently a significant late effect in children treated for childhood cancer with platinum chemotherapy. Further research and trials into otoprotection are required. There is a need for an internationally accepted hearing score to detect ototoxicity in children treated for childhood cancer to facilitate such trials. The SIOP Boston otoxicity scale was developed by expert multidisciplinary consensus at SIOP Boston and published for this purpose. Here we aim to validate this scale.
Materials and Methods: 103 children who had received cisplatin and /or carboplatin were identified from a database of 194 children treated with chemotherapy for cancer between 1999 and 2011 at Great Ormond Street Hospital (GOSH). The study received approval from the GOSH Research and Development Department. All children had pure tone audiograms (PTAs) available for analysis which were graded according to the Brock, Chang and SIOP Boston scales by our audiologist. In order to validate the PTAs, a subset of 48 were graded by 2 external audiologists and the gradings compared.
Results: Of the 103 children, 38% were female and they had a median age of 5.55 years (0.43-11.85) at diagnosis. 61% of children had a Brock score $\geq$1, 64% had a Chang score $\geq$1a and 67% had a SIOP Boston score $\geq$ 1. The external validation showed a 97% agreement for Brock, 96% agreement for SIOP and 93% agreement for Chang between 3 assessors.
Conclusions: This validation study shows that the SIOP ototoxicity scale can be consistently applied by independant assessors from Europe and North America. We would encourage oncologists and audiologists to adopt the Boston scale for use in international clinical trials. It has been particularly designed to detect, monitor and compare hearing loss across clinical trials. It should not be used as a guide for individual treatment decisions.

POSTER SESSION: POSTER SESSION - SUPPORTIVE CARE/PALLIATIVE CARE

P-0487

ANXIETY OF PEDIATRIC AND ADOLESCENT PATIENTS UNDERGOING CHEMOTHERAPY: LOW VERSUS HIGH ORAL MUCOSITIS BURDEN

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Purpose/Objective: To compare the levels of anxiety reported by pediatric and adolescent patients with low and high mucositis burden.
Materials and Methods: A total of 140 patients (mean age, 11.8 $\pm$ 3.3 years; 63%, males) diagnosed with hematological malignancy (56%) and solid tumor (44%) completed the Mouth and Throat Soreness Oral Mucositis Daily Questionnaire (MTS OMDQ) with assistance from their parents, daily from day 1 of chemotherapy until day 14. In addition, patients completed the short form of the State Anxiety Scale for Children (SAI-C) on days 1, 7 and 14. The area under curve (AUC) representing mucositis severity across 14 days was calculated, and the hierarchical cluster analysis was used to categorize the patients into groups with distinct levels of mucositis based on the mean AUC scores (low versus high mucositis burden).
Results: The mean AUC MTS OMDQ score across 14 days was 0.59 $\pm$ 0.69 (range, 0 to 2.19; 95% CI, 0.48 to 0.71). The mean AUC of limitations on swallowing, eating, drinking and talking ranged from 0.29 to 0.51. Hierarchical cluster analysis generated two clusters: a low-mucositis burden group (n = 91; 65%) and a high-mucositis group (n = 49; 35%). The mean AUC scores for all mucositis-related symptoms were significantly higher in the high-mucositis burden group (mean 0.77 to 1.26) compared with the low-mucositis burden group (mean 0.02 to 0.1) ($p < 0.001$). The effect sizes of the differences were 0.49*0.86. The mean score for AUC SAI-C was significantly higher in the high-mucositis burden group (mean 19.1 $\pm$ 3.77, 95% CI 18.02 * 20.19) compared with the low-mucositis burden group (mean 14.97 $\pm$ 2.41, 95% CI 14.47 * 15.47). The effect size of the difference was 0.55, indicating moderate effect size. In addition, significant moderate correlation was noted between mean AUC MTS OMDQ and SAI-C scores (r = 0.62, $p < 0.01$).
Conclusions: These findings suggest that prevention and management of mucositis may impact anxiety during chemotherapy.

P-0488

IMPACT OF CONVENTIONIAL CHEMOTHERAPY ON HUMORAL IMMUNITY AGAINST MEASLES, MUMPS, RUBELLA AND VARICELLA-ZOSTER IN CHILDREN TREATED FOR CANCER

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Purpose/Objective: Intensive chemotherapy in children with cancer results in long-term impairment of humoral immunity. Whereas most studies to date focus on children with acute lymphoblastic leukemia (ALL), little data are published on patients suffering from Hodgkin disease (HD) or from solid tumors. We therefore analyzed the loss of protective immunity (defined as protective immunity at the time of diagnosis and lack of immunity after therapy) against vaccine-preventable diseases in children treated for various malignancies.
Materials and Methods: Children < 18 years at diagnosis and treated between 2001 and 2008 for various malignancies in our center were included in the study. Antibody levels against measles, mumps, rubella and varicella-zoster-virus (VZV) were routinely assessed at the time of diagnosis and until 12 months after cessation of treatment.
Results: The study population consisted of 193 children (103 male); 80 patients suffered from ALL, 15 from acute myeloid leukemia (AML), 76 from various solid tumors and 22 from HD. Loss of protective immunity for measles, mumps, rubella and VZV was observed in 30%, 45%, 30% and 26% of the children with ALL, respectively. In contrast, less than 10% of children treated for AML, solid tumors and HD lost their preexisting protective immunity against any of the diseases (exception: loss of protection against mumps in 29% of children with solid tumors). Notably, 14% and 9% children with ALL lacking immunity at diagnosis against rubella and VZV, respectively, had protective antibody levels post-chemotherapy. In contrast, seroconversion against these diseases was rarely seen in all other patient groups.
Conclusions: Loss of protective immunity against measles, mumps, rubella, and VZV occurs more often in children with ALL than in children with AML, solid tumors and HD. The data suggest that loss of protection does not depend on chemotherapy intensity alone, but also on other factors such as the class of chemotherapeutic drugs administered.

P-0489

PALLIATIVE CARE SERVICE IN CHINESE CHILDHOOD CANCER PATIENTS: THE EXPERIENCE OF A TERTIARY PAEDIATRIC ONCOLOGY CENTRE IN HONG KONG

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Purpose/Objective: Paediatric palliative care has gained attention over the past decades. Due to cultural difference, Western models may not be fully adopted in the Chinese setting. Data from Chinese experience is needed.
Materials and Methods: We performed a 10-year retrospective review from 2000 to 2009 in a tertiary paediatric oncology unit to describe the palliative care referral pattern, clinical characteristics of referred cases and palliative services provided for Chinese paediatric oncology patients.
Results: 117 children were referred to palliative care. The commonest diagnoses were CNS tumour (32.5%), leukaemia (25.6%) and neuroblastoma (9.4%). The median time of referral after diagnosis for these three conditions was 257 days (interquartile range (IQR): 40, 770); 748 days (IQR: 557, 1361) and 751 days (IQR: 394, 1137) respectively. Ninety-one percent of children were referred after stopping curative treatment. The 5-year referral rates of patients who died of lymphoma, neuroblastoma and rhabdomyosarcoma increased from 50%, 75% and 80% in 2000-2004 to 100% in 2005-2009. 65% of oncology patients who died from 2000-2009 were referred. The median number of hospital admission after referral was 2 (IQR: 1, 5), with a median duration of 27 days of hospital stay (IQR: 10, 60). The most common reasons for admission were palliative chemotherapy (16.1%), pain control (12.1%) and platelet transfusion (11.2%). The most common reasons for walk-in clinic visit were bleeding tendency, pain and anaemic symptoms (29.5%, 21.5%, 14.3%). For the death episode, the median duration of hospital stay was 15 days (IQR: 2, 46). Majority of children ($n = 111$, 94.9%) died in hospital. Only 4 (3.4%) died at home. Of those 111 patients who died in hospital, 5 (4.5%) died in ICU.
Conclusions: With the understanding of common symptoms experienced by terminal childhood cancer patients, we may develop a 'Chinese model' of palliative care to help avoid unnecessary hospital admissions and clinic visits.

P-0490

SUCCESSFUL TREATMENT OF DIFFUSE ALVEOLAR HEMORRHAGE WITH ACTIVATED RECOMBINANT FACTOR VII IN CHILDREN WITH CANCER

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Purpose/Objective: Diffuse alveolar hemorrhage (DAH) is a life threatening pulmonary complication of patients with hematologic malignancies. It is associated with a high mortality rate; however, current treatment options using steroids, transfusions, immunosuppressants, mechanical ventilation, and ECMO are very limited and mostly unsuccessful, as well as accompanying multiple complications. Intrapulmonary administration of activated recombinant factor VII (rFVIIa) via bronchoscopy has been reported in the adults, but there is scarce data on the use in children. We review our institutional experience with intrapulmonary rFVIIa for the treatment of DAH in children with hematologic malignancies.
Materials and Methods: During 2011-2012, five children with acute, bronchoscopically confirmed DAH were included. Median age of the patients was 11 years, and diagnoses of the patients were acute myeloid leukemia (2 patients), myelodysplastic syndrome (1 patient), hemophagocytic lymphohistiocytosis (1 patient) and T-cell lymphoblastic lymphoma (1 patient). The patients were treated with intrapulmonary administration of 50 μg/kg rFVIIa in 50mL of normal saline by bronchoalveolar lavage (BAL) with 10mL in each of the bronchi, concurrently with methylprednisolone, fresh frozen plasma and maintenance of platelet count $> 50{,}000/mm^3$.
Results: Complete and sustained hemostasis after a single dose of rFVIIa was observed in 4 patients. For one patient, sustained hemostasis was achieved by a repeated rFVIIa administration after 24 hours. No toxicity or adverse events were observed with rFVIIa treatment. The oxygen capacity (PaO2/FiO2 ratio) increased significantly, and rapid clinical and radiological improvements were observed in all patients. Except one patient with MDS following umbilical cord blood transplantation died with subsequent acute respiratory distress syndrome with respiratory syncytial virus infection, all patients showed rapid improvement, were weaned off the ventilator successfully and alive.
Conclusions: Our experience indicates that intrapulmonary administration of rFVIIa is an effective and safe treatment option for DAH in children with hematologic malignancy; although further clinical studies are needed.

P-0491

SEROPREVALENCE OF HEPATITIS B, HEPATITIS C, AND HIV IN CHILDREN WITH CANCER AT DIAGNOSIS AND FOLLOWING THERAPY IN TURKEY: CURRENT SITUATION

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Purpose/Objective: Children with cancer receiving intensive chemotherapy require multiple transfusions and are at increased risk for blood transmittable diseases such as HBV, HCV, and HIV. The aim of this study was to investigate the seroprevalence of HBV, HCV, and HIV in children with cancer and to compare with findings in our previous studies with cancer conducted before the national free HBV vaccination in Turkey and before the HCV screening program in blood banks was established
Materials and Methods: Between 2002-2012, HBsAg, anti-HBs, anti-HCV, anti-HIV results were collected retrospectively at diagnosis and at end of therapy from records of 100 children (51 female, 49 male) with cancer. Patients were born after 1998, when the national free hepatitis B vaccination program for children had started.
Results: HBsAg, anti-HBs, anti-HCV and anti-HIV seropositivities were 0%, 58%, 0%, 0% at diagnosis and 0%, 42%, 0%, 0% at end of therapy, respectively. Seropositivity of HBsAg was 0% at diagnosis and at end of treatment was lower than 10% found during 1994-95 and also lower than 40% during 1986-89. HCV was 0% in contrast to 14% during 1994-95. HIV seropositivity was 0% in children with cancer in this and previous studies. Although anti-HBS seropositivity was below than expected (58%) in vaccinated children, none that were reported to be vaccinated found to be seronegative at diagnosis developed HBV infection. Seventeen with had anti-HBs seropositivity at diagnosis were found to be seronegative at the end of treatment as expected after intensive chemotherapy, none of these developed HBV infection.
Conclusions: These results suggest the importance of national vaccination programs for hepatitis B for infants. The nil seroprevalence of HBV, HCV and HIV signifies the importance of high technology viral serological screening for HBV, HCV and HIV used in blood banks. Hygienic measures used in pediatric hematology-oncology wards is also very important.

P-0492

TIMING THE BREAKING POINT: A DIFFICULT ETHICAL PROBLEM IN CHILDHOOD CANCER CARE

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Purpose/Objective: The treatment for paediatric cancer is physically, socially and psychologically demanding, and often gives rise to ethical problems about treatment and care. The purpose of this presentation is to describe a difficult ethical problem frequently experienced in childhood cancer care.
Materials and Methods: Health care professionals from three paediatric units, which all treat children with cancer, at a major hospital in Sweden answered a study-specific questionnaire. Qualitative content analysis was used to analyse answers to open-ended questions.
Results: Different perspectives affected which treatment was considered to be ethically right, especially when the treatment was of uncertain benefit for the patient. Writing about the breaking point, health care professionals described an invisible point in time when the transition from curative to palliative treatment occurred. They expressed that opinions diverged between physicians, nurses and parents about when the breaking point occurred and the breaking point was a major concern for all professional groups and often led to conflicts in the team. Physicians had to make the decisions regarding limitations of life-sustaining

treatment and the changed aim of the treatment. Uncertainty aroused about when to make this decision to achieve the best possible care for the patient. Nurses wished for the breaking point to appear earlier in the care process in relation to the perceived suffering of the children. Parents were sometimes perceived to be blinded by the fear of losing their child and by grief, resulting in them wanting to continue with life-sustaining treatment as long as possible.
Conclusions: Even though all health care professionals and parents were focusing on what they thought was the best for the child, they ended up having different perspectives of when the breaking point occurred. There could be various reasons for the differences including professional and cultural as well as personal values or preferences.

P-0493

VARICELLA VACCINATION IN PEDIATRIC ONCOLOGY PATIENTS WITHOUT INTERRUPTION OF CHEMOTHERAPY

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Purpose/Objective: The morbidity and mortality from primary varicella-zoster virus (VZV) infection is increased in immunocompromised children. Vaccination of VZV-seronegative cancer patients with live attenuated varicella vaccine has proven to be safe and effective. All vaccination programs performed in this group of patients required the interruption of chemotherapy. This is the first cohort of pediatric oncology patients who received the varicella zoster vaccine in an early phase of their treatment without interrupting chemotherapy. The pilot study was reported to the SIOP 2006, now we report the full cohort.
Materials and Methods: Newly diagnosed pediatric oncology patients,seronegative for VZV were included in this study. Patients had circulating lymphocyte counts of $>700/mm^3$, no bulky disease and were not septic at the time of vaccination. Before and after vaccination no steroids were given for at least one week, the vaccination did not lead to interruption of chemotherapy but was given in a phase when no steroids were needed
Results: Thirty-one patients with hematological malignancies (n = 24) or solid tumors (n = 7) were vaccinated with VZV vaccine. Seroconversion occurred in 14 of the 31 patients (45%) after one vaccination and in 70% after 2 vaccinations. Seven patients (22.5%) developed a mild rash of which 4 patients also had fever. 5 were treated with antivirals and recovered completely without interrupting chemotherapy. In 26 patients VZV-specific $CD4^+$ T cells were analyzed and found positive in 20 patients (=77%). After a second vaccination all patients showed VZV specific $CD4^+$ T cells. Adaptive immunity was induced despite incomplete seroconversion. Mild wild-type chickenpox (Vazquez score, <7) developed in 5 patients (16%) during follow-up without the need of hospital admission.
Conclusions: This study demonstrates that it is feasible to administer VZV-vaccine in an early stage of chemo-therapy in paediatric oncology patients without interruption of chemotherapy, and that vaccination protects against severe clinical varicella infection.

P-0494

REPORT ON CURRENT ACTIVITIES OF THE INTERNATIONL PEDIATRIC ONCOLOGY NUTRITION GROUP (IPONG)

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Purpose/Objective: The International Pediatric Oncology Nutrition Group (IPONG) and the International Committee on Nutrition & Health for Children with Cancer were established in 2011 at the 43rd SIOP meeting in New Zealand. The committee identified three priority domains: establish international administrative support for health care providers in pediatric oncology nutrition; develop international, modifiable nutritional guidelines for pediatric oncology; and establish international research collaborations in pediatric oncology nutrition.
Materials and Methods: Currently the group consists of 77 members from 26 countries and 6 continents. Members of the Committee meet monthly on Cure4Kids. Different working groups have been established, pairing members from Low Income Countries (LIC) and High Income Countries (HIC). Nutritional education sessions have been established as part of the Asociaci—n De Hemato-Oncolog'a Pedi‡trica De Centro Am*rica (AHOPCA) meetings and a conference following the SIOP meeting.
Results: Projects currently in progress are: International survey on nutritional practices at hospitals caring for children with cancer; development of modifiable algorithms addressing nutritional guidelines in pediatric oncology; a proposal for an educational nutrition study in LIC using local resources; and a range of nutritional intervention studies in LIC. Another study on which the group is collaborating is food safety education for illiterate populations. Future plans for IPONG are to develop an online training course in pediatric oncology nutrition utilizing the Cure4Kids network, continue to support collaboration and research between LIC and HIC, and nutrition clinical guidelines modifications for LIC. The overarching goal of the group is to garner support for dietitians from LIC to attend educational conferences to help augment the local standards of practice.
Conclusions: Nutrition support is important during treatment, especially for those patients in LIC who are malnourished at diagnosis. Collaboration between nutritional healthcare professionals from LIC and HIC is feasible and the work of IPONG will advance the nutritional management of children with cancer.

P-0495

HOPE AND FAITH DURING THE PALLIATIVE PHASE IN RELATION TO LONG-TERM PSYCHOLOGICAL FUNCTIONING IN PARENTS WHO LOST A CHILD TO CANCER

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Purpose/Objective: One of the components of paediatric palliative care involves care for the child's and family's mind and spirit. The aims of this study were to investigate 1)the importance of faith and dimensions of hope for parents of a dying child 2)the impact of faith and hope for a cure on parents' long-term traumatic grief and depression, and 3)parents' sources of coping.
Materials and Methods: Eighty-nine parents of 57 children who died of cancer between 2000 and 2004 participated in a retrospective cross-sectional single centre study and completed a set of questionnaires measuring traumatic grief and depression, and exploring faith, hope, and sources of coping.
Results: Fourteen per cent ($N = 12$) of parents could be categorised as having traumatic grief and about one quarter of parents ($N = 22{,}25\%$) showed symptoms of clinical depression. For 19 parents (21%) faith was very important. The majority of parents had hope for: a meaningful time with their child ($N = 68{,}76\%$); a pain-free death ($N = 58{,}65\%$), and a cure ($N = 30{,}34\%$). Social relationships were main sources of coping (child (N = 70,79%), health care professionals (N = 46,52%) and family and friends (N = 34,51%)). Parents' faith was not associated with less long-term traumatic grief (OR = 0.86,$P = 0.49$) or depression (OR = 0.96,$P = 0.78$), and parents' hope for a cure was not related to more long-term traumatic grief (OR = 1.08,$P = 0.70$) or depression (OR = 1.13,$P = 0.42$).
Conclusions: Faith was important for a minority of parents, and was not associated with less traumatic grief and depression. The majority of parents had hope. Hope for a cure was not associated with more traumatic grief and depression.

P-0496

EARLY CORTICOSTEROID ADMINISTRATION BENEFITS PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS WITH HIGH INFLAMMATORY CYTOKINE LEVELS IN SEPTIC SHOCK

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Purpose/Objective: The roles of cytokines in pediatric hematology-oncology patients with septic shock have not been well illustrated and whether the use of corticosteroids or not remains controversial. The aim of this study was to investigate the roles of cytokines on children with septic shock and to evaluate the necessity of corticosteoids for those patients and the potential benefits..
Materials and Methods: 100 episodes of septic shock from 96 pediatric hematology-oncology patients were enrolled from 2006 through 2010 in our department. Blood samples were taken for quick measurement of 6 cytokines including interleukin (IL)-2, IL-4, IL-6, IL-10, tumor necrosis factor (TNF)-α and interferon (IFN)-γ by flow cytometry based bead array technology at the initial onset of septic shock. The relationship between the cytokine levels and disease severities was evaluated with pediatric index of mortality 2 (PIM2) and the multiple cytokine score (MSC). Corticosteroids were recommended to administer at the early phase of septic shock according to cytokine levels since 2008.
Results: The serum levels of IL-6 and IL-10 were significantly elevated in majority of patients, while TNF-α and IFN-γ were markedly increased in patients with high PIM2 score and non-survivors. The MCS, which integrated the four cytokine scores into the system, was related to hemodynamic disorder and mortality as well. The 28-day mortality of this cohort was $14.0 \pm 3.0\%$. Corticosteroid treatment reduced the mortality ($8.8 \pm 3.4\%$ in corticosteroid group vs. $25.0 \pm 7.7\%$ in non-corticosteroid group, $P = 0.032$) and the

shortened duration of vasopressor infusion in vasopressor dependent patients (median: 44 hours vs. 92 hours, $P = 0.035$). Patients with medium/high MCS were benefited from corticosteroid treatment. Corticosteroid administration showed a trend of increasing the superinfection rate (22.1% vs. 6.3%, $P = 0.084$) but it did not increase the superinfection-related mortality.
Conclusions: Inflammatory cytokines are early predictors of disease severity and fatal outcome in pediatric hematology-oncology patients with septic shock. Patients with highly elevated cytokine levels are benefited from early corticosteroid administration.

P-0497

INITIAL DEVELOPMENT OF THE SYMPTOM SCREENING IN PEDIATRIC TOOL (SSPEDI)

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Purpose/Objective: We previously conducted a systematic review of symptom assessment scales used in pediatric oncology. Our objective for this study was to identify a symptom assessment scale to adapt as a self-report symptom screening tool for use by children with cancer or to create one.
Materials and Methods: A consensus group of ten pediatric cancer clinicians and a patient advocate was convened. First, the group identified properties of an ideal self-report symptom screening tool for pediatric cancer patients. Next, the previously identified symptom assessment scales were evaluated against these properties. None of the assessment scales were considered adequate for symptom screening; consequently nominal group technique methodology was used to begin creation of a new tool by identifying the most important symptoms for inclusion.
Results: The focus group identified that an ideal symptom screening tool entailed minimal respondent burden and focused on the bother of subjective symptoms. Previously identified scales were not adequate because they lacked content validity, were too long or too difficult for young children to understand. Nominal group technique resulted in the generation of 44 items. Voting processes established the 15 most important items, which were selected to be included in the initial iteration of an instrument, Symptom Screening in Pediatrics Tool (SSPedi). The format of the initial questionnaire, recall period and response options were created through focus group methodology.
Conclusions: This study identified the lack of an existing self-report symptom screening tool for pediatric cancer patients. We determined the initial items and draft of a symptom screening tool. Future work will use patient and parent opinion to revise this draft with a focus on understandability, acceptability and content validity. A self-report pediatric symptom screening tool will facilitate more timely symptom-directed treatment, inprove quality of life and reduce morbidity in children with cancer.

P-0498

DETECTION OF ORAL HERPES SIMPLEX VIRUS 1 AND 2 IN CHILDREN ON CHEMOTHERAPY: A COMPARISON OF SEROLOGY, CONVENTIONAL PCR AND QUANTITATIVE REAL-TIME PCR

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Purpose/Objective: Data on prevalence of HSV in oral mucositis in children on treatment for cancer is limited, particularly from developing countries. A comparison of varied diagnostic tests is reported.
Materials and Methods: Children on treatment for cancer and oral mucositis were enrolled as cases. Healthy children were recruited as controls. Mucositis was graded by clinical and functional NCI oral toxicity scale. A swab from the oral lesion in cases and scape material in controls was obtained. PCR and real-time quantitative viral load assay using Taqman probes for HSV-1/2 was performed. Serum was utilized for ELISA-IgG/IgM for HSV-1/2 antibodies (NovaLisa-Dietzenbach-Germany). Study was funded by Indian Council of Medical Research.
Results: 32 cases (mean age: 6.3 $\pm$ 3.4 years) and 30 controls (mean age: 8.4 $\pm$ 3.2 years) were enrolled. Majority (69%) of cases had ALL. Clinical and functional grading of mucositis was grade 3/4 in 21 (65.6%) and 15 (46.9%) cases, respectively. All patients had febrile neutropenia, except two.

ELISA-IgM-HSV-1/2 was not positive in any case or control. ELISA-IgG-HSV-1/2 was positive in 11 (34%) cases and 9 (30%) controls ($p = 1.0$). Qualitative-PCR for HSV-1 detected the virus in 8 (25%) cases and none controls ($p = 0.009$). HSV-2 was not detected in either cases or controls by PCR. With real-time quantitative-PCR, HSV-1 was detected in 21 (66%) and HSV-2 in 22 (69%) cases. In controls, real-time quantitative-PCR detected HSV-1 in 3 (10%) and HSV-2 in none. In patients, the mean viral load of HSV-1 ($5500 \pm 15987 \times 10^4$ copies/nano-gram DNA) was more than HSV-2 ($4.03 \pm 8.5 \times 10^4$ copies/nano-gram DNA), though not significant ($p = 0.11$). There was no correlation of HSV-1/2 with grading of mucositis.
Conclusions: ELISA is unsuitable for diagnosis of HSV in oral mucosal lesions in children with cancer. Conventional and real-time PCR detected HSV-1 in 25% and 66% oral mucosal lesions, respectively. Real-time PCR detected copies of HSV-2 in 69% cases, all missed by conventional PCR.

P-0499

PREDICTORS FOR ADVERSE OUTCOMES IN CHILDREN WITH FEBRILE NEUTROPENIA

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Purpose/Objective: To identify predictors for adverse outcomes in children with febrile neutropenia (FN)
Materials and Methods: We retrospectively reviewed medical records of admitted patients with FN for a period of 1 year 6 months. Clinical and laboratory variables during the first 24 hours considered associated with adverse outcomes were recorded and analyzed. The adverse outcomes included bacteremia, persistent fever more than 5 days, requiring antibiotic more than 10 days, major organ failure, deep- seated infection, and mortality. The significant factors were identified and used for creating a predictor score formulation.
Results: A total of 169 FN episodes occurred in 69 children. The underlying diseases were acute lymphoblastic leukemia (39.6%), acute myeloid leukemia (25.4%), lymphoma (7.1%), and solid tumors (27.8%). The FN episodes were categorized into 5 groups: microbiological defined infection (MDI) with bacteremia 19 episodes (11.2%), MDI without bacteremia 22 episodes (13%), clinically diagnosed infection 77 episodes (45.6%), unexplained fever 48 episodes (28.4%), and non-infectious fever 3 episodes (1.8%). Gram negative bacteria was the cause of bacteremia in 16 episodes (84.2%). The adverse outcomes occurred in 59 episodes. The significantly independent risk factors for predicting adverse outcomes included absolute neutrophil count (ANC) $<$ 100/cu mm (OR 2.92; 95%CI, 1.3-6.58), peak temperature (T) $>$ 38°C (OR 1.85; 95%CI, 1.1-3.2), and platelets $<$ 50,000/cu mm (OR 3.23; 95%CI, 1.36-7.73). The predictive score formulation was 3(ANC $<$ 100) + 3(fever prior admission) + 3(platelets $<$ 50,000) + 2(peak T) + (time to antibiotic). The score $>$ 7 predicted the adverse outcomes with a sensitivity of 89.9% and specificity of 42.6%.
Conclusions: Three adverse parameters including ANC $<$ 500/ cu mm, peak T, and platelets $<$ 50,00 were identified in this cohort. A prospective validation study of the predictive score formulation is warrant.

P-0500

RISK FACTORS FOR SEVERE OUTCOME IN NEUTROPENIC ENTEROCOLITIS IN ONCOLOGY PATIENTS; A SYSTEMATIC REVIEW

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Purpose/Objective: Neutropenic enterocolitis (NEC) is a potential life threatening complication of the treatment of malignancies. NEC is characterized by a triad of symptoms: neutropenia, fever and abdominal pain and the aetiology is not well understood. The outcome can be very unpredictable with a reported mortality rate of more than 50%.

The aim of this systematic review was to evaluate the evidence of risk factors for severe outcome of NEC in oncology patients.
Materials and Methods: MEDLINE and EMBASE were searched. All studies describing risk factors for mortality or ICU admittance were included. Information about study characteristics, prevalence and risk factors were abstracted and the quality of the studies with prognostic factors was assessed.
Results: The search identified 1,613 studies. 16 studies reported on risk factors for outcome of NEC. The prevalence of NEC in oncology patients was 0.34% - 16%, the mortality rate varied between 2.1% - 66%. In total 16 risk factors were suggested, potentially useful in the risk assessment of NEC. All studies had severe methodological limitations and various definitions of NEC were used.

Only two studies used multi-variate analysis. Rizzatti found a 3-fold relative risk for deat for both the use of cytarabine and the presence of abdominal distention. A 6-fold relative risk

was found for high CRP and a relative risk of 11 for elevated Interleukin-8 by Van de Wetering. .
Conclusions: There is limited evidence to predict the course and outcome of NEC in oncology patients. Literature suggests a high mortality rate. More investigation is necessary to validate risk factors for severe outcome.

P-0501

RANDOMIZED DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL TO EVALUATE THE ROLE OF CYPROHEPTADINE HYDROCHLORIDE IN PROMOTING WEIGHT GAIN IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: Studies from India indicate that the prevalence of malnutrition in children with ALL range from 30-75%. Malnutrition adversely impacts the prognosis of children with cancer. There are no randomized trials that have investigated the role of cyproheptadine hydrochloride (CH) as an appetite stimulant in children with ALL.
Materials and Methods: The randomized, double-blinded, placebo-controlled study was conducted from January 2010 to June 2011. Children in the age group of 2-9 years, on maintenance chemotherapy for ALL, with a weight-for-age z-score $<$-1 SD were included. Patients were randomized to receive either CH (0.25 mg/kg/day) or placebo for 8 weeks. Anthropometric assessment was made at baseline, week 4, 8 and 12.
Results: 35 patients completed the study. The mean age of patients in CH ($n = 17$) and placebo ($n = 18$) groups was 74 ± 17 and 72 ± 16 months, respectively ($p = 0.73$). Nearly 50% patients in both the groups had moderate or severe malnutrition. Weight-for-age z-score at enrollment in CH and placebo groups was -2.15 ± 0.73 and -1.89 ± 0.78, respectively ($p = 0.32$).

The mean weight gain at the end of 12 weeks in the CH group was 1.5 kg (-0.66 to 3.5) ($p = 0.06$) and in placebo group was 1.1 kg (-2.1 to 3.7) ($p = 0.32$). The CH group had a significant increase in BMI ($p = 0.025$) and BMI z-score ($p = 0.026$) at 12 weeks but not weight-for-age z-score ($p = 0.25$), when compared to baseline. However the gains were not significant when compared in the two groups by Bonferroni post-hoc analysis. The comparison of the change in weight, change in weight for age z-score or change in BMI between the two groups was not significant at week 8 or 12. CH as well as placebo were well tolerated. Drowsiness was noted in 5 patients receiving placebo and in one patient receiving CH.
Conclusions: Cyproheptadine hydrochloride administered for 8 weeks failed as a weight promoting agent in malnourished children with ALL during maintenance phase of chemotherapy.

P-0502

AZOLE-BASED CHEMOPROPHYLAXIS OF INVASIVE FUNGAL INFECTIONS IN PEDIATRIC PATIENTS WITH ACUTE LEUKEMIA: AN INTERNAL AUDIT

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Purpose/Objective: Incidence rates of invasive fungal infections (IFI) of $>10\%$ and high case fatality rates justify systemic antifungal prophylaxis (SAP) in children with AML and recurrent acute leukemia (RAL).
Materials and Methods: Oral azole-based SAP has been implemented in 2006 as standard of care (SOP) in pts. with AML and RALs admitted to our department. Pts. ≥ 13 yrs receive posaconazole (200mg TID), and pts. ≤ 12 to 2 yrs voriconazole (200mg BID) starting upon completion of chemotherapy until hematopoietic recovery. Pts. with inability to take oral medication/ contraindications are placed on IV voriconazole, liposomal amphotericin B or micafungin as appropriate. Algorithms for neutropenic fever or signs and symptoms of infection include monitoring with blood cultures, HR-CT, serial serum galactomann, invasive diagnostics and preemptive therapy with change in class.
Results: From 2006-2010, 40 new pts. (median: 9 yrs; r, 0.8 * 17) with AML (31) or recurrent leukemia (9) were admitted. 36 received a total of 149 courses of chemotherapy (reasons for not receiving prophylaxis: Contraindications/early death ≤ 3 days, resp.). The target attainment of episodes with azole prophylaxis was 87.2% ($n = 130/149$). Preemptive therapy for pulmonary infiltrates was initiated in 5/36 (13.8%) patients or 6/130 (4.6%) episodes for a mean duration of 12 days (range, 3-22). No proven or probable IFIs occurred. Antifungal prophylaxis was tolerated without grade III/IV toxicities. In simultaneously admitted new pts. with ALL ($n = 101$) and pediatric lymphomas ($n = 29$) not receiving SAP per SOP, proven/probable IFIs occurred in 4 pts. with ALL (3.9%), and 5/130 pts. (3.8%) received preemptive therapy.
Conclusions: Azole-based SAP in pts. with AML/RALs was satisfactorily implemented, well tolerated and effective with no breakthrough infections and few and short courses of preemptive treatment. The low rate of IFIs in patients with ALL and lymphomas confirm the lack of indication for general SAP in these populations at our center.

P-0503

BLOODSTREAM INFECTIONS AT A EUROPEAN PEDIATRIC CANCER CENTER: TRENDS IN EPIDEMIOLOGY AND OUTCOME BETWEEN 2000 AND 2010

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Purpose/Objective: Little data exist on the current epidemiology of bloodstream infections (BSI) in pediatric patients with cancer and/or undergoing hematopoietic stem cell transplantation (HSCT).
Materials and Methods: In a single-center, retrospective study, we analyzed all BSI in children and adolescents with cancer and/or allogeneic HSCT during the past decade and compared the time periods 2000-2004 and 2006-2010. All pts. received MRSA-Screening and prophylaxis with twice weekly TMP/SMX and non-absorbable polyenes. Quinolone prophylaxis was restricted to allo-HSCT pts., and systemic antifungal prophylaxis to pts. with AML, recurrent leukemia, and post allo-HSCT. Blood cultures were obtained for evaluation of fever and/or signs of systemic infection and further processed using standard methods.
Results: 446 BSI were observed in 289 pts. (55% male; median 8 yrs; 59.2% hem. malignancies, 35.6% solid tumors, 5.6% other; 24.9% s/p allo-HSCT; 23.6% recurrent cancer; 96.7% with indwelling permanent catheter). There was a significant increase in BSI over time from 32 to 46.7 /1000 discharges and from 5.6 to 8.4 /1000 inpatient days, respectively ($p < 0.001$) with a predominance of *Gram*-positive organisms (75.8%; *Gram*-negative, 22.3%; *Candida* spp., 1.9%; no trends). Coagulase-neg. staphylococci were most frequent (41.5%), followed by *viridans* streptococci (8.1%), *Pseudomonas* spp., *E.coli* (6.7% each), and enterococci (3.8%). While MRSA and glycopeptide-resistant enterococci were not observed, ESBL producers and multiresistant *E.coli* and *P.aeruginosa* emerged in the second period (from 0% to 3.9, 1.4 and 1.4%, respectively ($p < 0.001$)). 31.5% of catheters were removed, and 5.5% of episodes resulted in ICU transfer. The 30-day overall mortality rate was 6% without trend over time.
Conclusions: This analysis documents a significant increase in the incidence of BSI and the emergence of resistant *Gram*-negative organisms in pediatric cancer/HSCT pts. receiving care at a large European treatment center.

P-0504

EVALUATING HOME-BASED PEDIATRIC PALLIATIVE CARE GLOBALLY: A SYSTEMATIC REVIEW

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Purpose/Objective: Home-based care (HBC) can extend access to essential pediatric palliative services and uniquely accommodate families' needs, particularly in low-income and middle-income countries (LMIC), where hospital-based services may be costly and beyond reach. We conducted a systematic review for outcomes of home-based palliative services worldwide and secondarily evaluated their programmatic components.
Materials and Methods: Two reviewers searched PubMed to identify publications (1980*present, no restrictions for language) reporting home-based palliative services for young people with life-limiting conditions. Studies that reported outcomes for at least 20 subjects under age 25 were selected for further analysis, including narrative synthesis of results and risk of bias assessment.
Results: Of 1746 records screened, 315 met criteria for full-text review. Eleven studies (five from LMIC) qualified for analysis. All provided in-home educational and psychosocial support, as well as varying clinical services and care coordination, including 24/7 telephone triage, infusion therapy, and advance care planning. Two programs (in Latvia and Costa Rica) reported countrywide provision of HBC. Nine studies assessed parental satisfaction; all reported high levels. Parents prioritized emotional support and education among HBC services, with unmet needs including education and resources for end-of-life and parent-led symptom management, and basic needs support. Six studies (260 total patients) used historic or concurrent controls that did not receive HBC, with three highlighting outcomes in addition to satisfaction. Of these, HBC was associated with improved family quality of life concurrent with an average patient expenditure reduction of 11%; improved parent satisfaction concurrent with increased home deaths (50 to 92%); and increased home deaths (18 to 69%) with similarly high satisfaction irrespective of place of death.

Conclusions: While quality studies of pediatric palliative HBC were scarce, many components valued by families, including family education and psychosocial support, can be promoted through policies supporting training of palliative care workers, even with limited material resources.

P-0505

BODY MASS INDEX AND SURVIVAL OF PAEDIATRIC PATIENTS UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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Purpose/Objective: To determine the prevalence of over- and under-weight in paediatric patients pre-haematopoietic stem cell transplant (HSCT) at The Children's Hospital at Westmead. To determine whether body mass index (BMI) has an impact on overall post transplant survival.
Materials and Methods: One hundred and thirty seven consecutive patients (91 male and 46 female, mean age 7.7 years, range 2-18 years) who had received an autologous (n = 49) or allogeneic (n = 88) HSCT between January 2003 to January 2010 were included in this audit of BMI and 3 year overall survival.

Of the 137 patients, 111 (81%) had a malignant condition with the remaining 26 (19%) participants having non-malignant conditions.

Patients were categorised into 3 weight groups; underweight, ideal weight and overweight using the International Obesity Taskforce (IOTF) criteria. Kaplan Meier Survival analysis was used to compare overall survival between (1) underweight and normal weight children and (2) normal weight and overweight children. Significance of differences was assessed using the Log Rank test.
Results: Of the 137 patients, 31 (23%) were overweight or obese pre-transplant, whereas 16 (12%) were classified as underweight pre- transplant.

The 3 year overall survival was not significantly different between the underweight versus ideal weight patients in both the malignant (58.6% vs 61.2% respectively, p = 0.755) and non-malignant groups (50% vs 74.5%, respectively, p = 0.0.549). Likewise, no significant difference in overall survival was found in the overweight versus ideal weight in patients with malignant (66.8% vs 61.2%, respectively, p = 0.627) or non-malignant conditions (85.7% vs 74.5%, respectively, p = 0.653).
Conclusions: A recent study suggested that patients' pre-HSCT BMI may influence outcome. When analysing our patient population in Sydney, we found that BMI before HSCT had no significant impact on overall post-transplant survival. One limitation of using BMI pre-transplant is that growth and nutritional changes between diagnosis and prior to transplant are not considered.

P-0506

ALTERNATIVE MEDICINE, A PROSPECTIVE STUDY ABOUT ITS USE IN MEXICO

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Purpose/Objective: Complementary & Alternative Medicine (CAM) is common practice in Mexico. We conducted a survey with the aim to acknowledge the clinical and epidemiological aspects that drive parents of children with cancer to benefit from these
Materials and Methods: 100 surveys were registered consecutively at the Oncology Service from the Instituto Nacional de Pediatria M*xico City. The same researcher in all cases did the survey.
Results: All patients interviewed were alive, 68% were receiving treatment, 15% had relapsed or were non responsive to treatment, 7% in a diagnostic stage, 6% in follow up, 3% in post-transplant stage and only one patient was being treated for a second neoplasm.Fifty-one percent of the patients referred having used alternative medicine, 10% being treated by non-medical professionals (healers, chiropractors, bioelectromagentism). The method most frequently used was naturotherapy. Thirty percent of the patients did not inform their doctor the concomitant use of alternative medicine because of fear or they assumed it was not important to inform.
Conclusions: This paper shows that more than half of the patients treated at the Oncology Service use alternative medicine, with the possibility of altering clinical course and prognosis, increase treatment complications, and make a big impact in the family economy

The use of alternative and complimentary medicine (ACM) in our country is frequent, so patient-oncologist communication has to improve both ways, keeping an open mind to listen and explain possible interactions or complications when using with chemotherapy

P-0507

IMPACT OF LUNG BIOPSY IN MANAGEMENT OF PERSISTENT PULMONARY INFILTRATES IN PEDIATRIC MALIGNANCIES

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Purpose/Objective: To evaluate the impact of lung biopsy in management of persistent pulmonary infiltrates in pediatric oncology patients.
Materials and Methods: A prospective study conducted from 2010 till 2012 to evaluate the impact of lung biopsy in management and outcome of persistent pulmonary infiltrates of patients with pediatric malignancies and post-transplant treated in Children Cancer Hospital, Egypt.
Results: There were thirty six (36) patients who underwent forty one (41) separate lung biopsies. Trans- bronchial biopsy was done in eighteen 18/41 (43,9%) cases, while open lung biopsy was done in fifteen 15/41 (36,6%) cases and computed tomography (CT) guided biopsy was done in eight 8/41 (19.5) cases. Out of forty one lung biopsies, Fungal infection was seen in nine biopsies 9/41 (21.9%), pulmonary tuberculosis was seen in four cases (9,7%), nonspecific inflammation (biopsy negative for atypical cells or specific microorganisms) seen in fifteen biopsies (36,5%), granulomatous lesion seen in two cases(4,8%) and organized pneumonia seen in three cases (7,3%). Noninfectious causes diagnosed in six cases 6/41(14,6%), included malignancy in four cases, diffuse alveolar hemorrhage in one case and graft versus host disease in one case. Out of forty one procedures, two cases (4,9%) had complications, No major complications seen in open lung biopsy group. Biopsy lead to change line of treatment in twenty three cases (56%). Diagnostic yield of open lung biopsy was better than trans bronchial and computed tomography (CT) guided biopsy.
Conclusions: Lung biopsy is safe and has an important impact in management of pediatric oncology patients with persistent pulmonary infiltrates.

P-0508

A SURVEY OF HEALTH BEHAVIOR OUTCOMES OF YOUNG ADULT CHILDHOOD CANCER SURVIVORS IN HONG KONG

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Purpose/Objective: There are inconclusive research evidence on the likelihood that childhood cancer survivors (CCS) will adopt health promotion behavior to prevent health hazards.

This study aimed at exploring the health behaviours and their predicting factors of young adult CCS who had received cancer treatment in the last two decades. These health data were compared between the survivors and their sibling controls.
Materials and Methods: A telephone survey was adopted. Nearest age (>16 year-old) siblings of CSS were invited to participate as a comparison group. A convenience sample of 614 survivors and 208 sibling controls were recruited from three regional hospitals in Hong Kong.

Participants were interviewed using the Baseline Questionnaire developed in the Childhood Cancer Survivor Study of University of Minnesota.
Results: The CCS were more likely to be unemployed, single and attained lower level of education and income than sibling controls. An unexpected outcome was no significant differences on smoking habits between the two groups. Significantly fewer survivors reported alcohol consumption than sibling controls (9% vs. 91%). The alcohol consumption of the CCS remained significantly lower after an adjustment for their socio-demographic factors. Univariate and multivariate linear regression models detected male, employment and higher educational level were important factors associated with alcohol consumption among CSS. Those CSS probably consumed alcohol for stress reduction. About 77% of the survivors did not have health insurance and those with lower educational level had higher difficulty in getting insurance coverage. In addition, significantly less CCS practiced cervical cancer screening and breast self-examination than sibling controls.
Conclusions: Lack of insurance coverage, smoking habit, and unsatisfactory health behaviour were found to be the important health risks of the CCS in Hong Kong. Access to appropriate screening and counselling of these survivors, especially for those at higher risk of poor health behaviors, are recommended to mitigate their health risks.

P-0509

INFECTION PROFILE IN PEDIATRIC PATIENTS UNDERGOING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: SINGLE CENTER EXPERIENCE OF 66 CASES

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Purpose/Objective: Infectious complications are frequent in most patients during autologous hematopoietic stem cell transplantation (ASCT). The objective of this study was to analyze infection profile in pediatric cancer patients who underwent ASCT at our center.
Materials and Methods: This is a retrospective review of clinical and infection profile in pediatric cancer patients who underwent ASCT between July 2007-December 2012 at our center.
Results: Sixty-six paediatric patients were included in the study with a median age of 11 years (range:1-18); male: female ratio of 51:15. Febrile neutropenia during neutropenic phase of ASCT was observed in 98% (n = 65/66) patients. Microbiologically documented infections (MDI) accounted for 18 (28%) of febrile episodes, clinically documented infections (CDI) for 19 (29%), and fever of unknown origin (FUO) for 41% cases. Mean time to defeverescence with antibiotic therapy was five days for FUO and seven days for documented infections (p = 0.15). The main source of infec-tion was grade 3 or 4 mucositis in 14 (21%) and bacteremia in 10 (15%). Infection was predominantly due to Gram-negative bacteria (n = 13/20, 65%). Fever responded to first-line antibiotic therapy in 11 (17%) patients. Median duration of hospitalisation was 17 days (range:12-49). Infections were fatal in 3 (4.5%) patients. None of the factors including sex, age, CD34 count, mucositis grade, diarrhoea, conditioning regimen, stem cell harvest source, length of neutropenia, underlying disease, pre-transplant disease status predicted risk of development of MDI, CDI, gram negative or gram positive organism, use of 2nd line antibiotics. Days of neutropenia did not correlate with conditioning regimen, underlying disease, pre-transplant disease status, type of infection and type of organism.
Conclusions: Majority (98%) of patients had infectious complication during ASCT, and gram negative infections were commonest (60%) in MDI. Toxic death was 4.5%. None of the baseline factors predicted risk of developing MDI, CDI or the type of organism.

P-0510

EVALUATION OF A LIMITED BLOOD SAMPLING MODEL FOR INTRAVENOUS BUSULFAN AREA UNDER THE CURVE CALCULATION IN CHILDREN UNDERGOING HEMATOLOGICAL STEM CELL TRANSPLANTATION

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Purpose/Objective: Busulfan (Bu) is a cornerstone of high-dose conditioning regimens for children undergoing stem cell transplant. Monitoring of Bu levels insures that treatment remains within the drug's therapeutic window. At our centers, plasma Bu level sampling has traditionally been performed 8 times during and after intravenous administration of the second of 16 doses of this drug to insure that the area- under-the-curve (AUC) falls within the desired range; this sampling regimen exposes patients to the risks associated with repeated handling of indwelling venous catheters, and significantly impacts the workload of the nursing staff. As an alternative, we have modeled a limited sampling model (LSM) for Bu AUC determination using only 4 plasma samples.
Materials and Methods: Plasma samples were obtained at 0, 30, 60, 120, 150, 240, 300 and 360 minutes after the start of a 2 hour intravenous Bu infusion in 71 children (aged 0.5-18 yrs and weighing 5-81 kg) receiving Bu dosed in accordance with a published body- weight adjusted nomogram. Most children received concurrent seizure prophylaxis with oral lorezapam. Bu levels were determined by gas chromatography at a single laboratory, and AUC was calculated by a non-compartmental model. AUC $>1400\,\mu M*min$ led to Bu dose reduction in 11 patients.
Results: To assess the reliability of the LSM, we retrospectively performed a simulation using only the Bu plasma concentration determinations that had been obtained at timepoints 0, 120, 240 and 360 to calculate a LSM AUC. Comparison of LSM AUC with 8 sample-based AUC determinations for each patient demonstrated a correlation coefficient of r = 0.97 between the two methods; correlations were equally robust regardless of patient age or weight.
Conclusions: We conclude that limited sampling of plasma Busulfan levels is an effective method for monitoring treatment in patients receiving this drug.

P-0511

VANCOMYCIN DOSAGE OPTIMIZATION IN PEDIATRIC PATIENTS WITH SOLID TUMOR DISEASE BY POPULATION PHARMACOKINETIC ANALYSIS.

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Purpose/Objective: International guidelines recommend the use as empirical treatment of vancomycine in febrile patient with neutropenia in suspected catheter related-infection. Determination of optimal dosage is essential because of the high risk of inadequate concentrations and bacterial resistance. Precedent studies have shown the difficulty to achieve vancomycin effective concentrations in cancer population. Consequently, the aim of this study was to determine the optimal dosages of vancomycin in pediatric population with solid tumor disease.
Materials and Methods: We retrospectively reviewed the use of vancomycin in pediatric patients treated for solid tumor disease with febrile neutropenia. Vancomycin was administrated by continuous infusion (30mg/kg/day) in association with third generation cephalosporin and amikacin. Dosages were adjusted according to therapeutic drug monitoring results. Blood cultures were performed before the first dose of antibiotic. Vancomycin pharmacokinetics population parameters were determined using the NONMEM software. Dosage simulations were performed according to the target concentration.
Results: Thirty five patients were included in this study. Forty-three percent of blood cultures were positive and 79% of observed pathogens were identified as *Staphylococci*. Vancomycin pharmacokinetics was best described by a one-compartment model. Population pharmacokinetic parameters were (Inter Individual Variability %): total apparent clearance $4{,}63x(WT/70)^{0.75}$L/h (7.3%), volume of distribution 34.7L (17.8%). In order to obtain target concentrations, simulations showed that vancomycin dosages should be adjusted to each child according to its body weight. For example; 65 mg/ kg was recommended for a patient of 5 kg and 35mg/kg for a patient of 60kg.
Conclusions: Pharmacokinetic parameters and variability of vancomycin in pediatric patients with solid tumor disease were estimated. Simulations have allowed to describe a new dosage schedule, adjusted to each child body weight. We suggest an increase of vancomycin dose according to the body weight, in order to obtain early effective concentrations and avoid the bacterial resistance. But due to pharmacokinetic variability, still requires therapeutic drug monitoring.

P-0512

IMPACT OF FINANCIAL SUPPORT ON TREATMENT MODALITIES, ABANDONMENT AND OUTCOMES IN CHILDREN WITH HODGKIN LYMPHOMA AND NON-LYMPHOBLASTIC NON HODGKIN LYMPHOMA AT A TERTIARY CARE CENTRE

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Purpose/Objective: Cure rates for pediatric hodgkin lymphoma (HL) and Non-lymphoblastic non-hodgkin lymphoma (NHL) remain among the highest in pediatric oncology. But limited availability of access to good supportive care and financial restraints brings down the survival rate in a developing country. The Pediatric Lymphoma project at our institute is supported by private funding and covers all the costs of treatment including investigations irrespective of the risk. We analyzed the impact of this funding on the abandonment, treatment modalities and outcome in pediatric HL and Non-lymphoblastic NHL in our unit.
Materials and Methods: Children diagnosed as HL and Non-lymphoblastic NHL were included in the study. Patient data on clinical, lab and treatment profile were recorded. A PET scan was done for staging and response assessment and therapy was tailored. Outcomes were recorded in terms of abandonment, completion of treatment, survival, death.
Results: A total of 24 were patients were included. 15 had HL and 40% of children were stratified as stage IV at diagnosis. Out of nine with NHL, eight were B cell non-lymphoblastic lymphoma, one was anaplastic T cell lymphoma. Three children with HL identified as slow early responders received IFRT and therapy was intensified for two with early poor response in NHL. Five (20%) children with lymphomas died either during therapy or following relapse. The overall survival rate of lymphomas in our study is 80%.
Conclusions: Treatment abandonment of children with lymphomas was nil in our unit due to good financial support. None of the children died due to non-availability or lack of good supportive care and treatment. This emphasizes the need to address survival rates in developing countries by increasing access to care and effective use of limited resources.
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P-0513

A STUDY ON PEADIATRIC PALLIATIVE CARE AWARENESS AMONG PEDIATRIC POST-GRADUATE STUDENTS OF SOUTH INDIA

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Purpose/Objective: Currently inIndia there isanincrease in growing population of terminally ill patients among the pediatric age group contributing to 15.8 percent. However, the palliative care needs of these pediatric patients are inadequately met because of lack of

knowledge and training programs.The objective of the study is to evaluate the palliative care awareness among pediatric post graduate students.
Materials and Methods: An observational cross sectional study was conducted using a 19-point questionnaire in the post graduate exam review course attended by post-graduates from various universities of south India. 188 post graduates attended our pediatric exam review course of which,150 postgraduates participated in this study
Results: 88% of them reported that they have never had any palliative care training throughout their curriculum. 86%were not aware of any palliative carecenters intheir area.60.7% were uncomfortable with the care of theterminally ill children.87.3%felt that a formal training in palliative care would help them.64.7%felt that they did not have sufficient knowledge to identify the signs of the terminally ill.77.3% were not comfortable in initiating a discussion about palliative care.71.3% felt that the family members of the terminally ill patient needed spiritual support.55.3% felt that the period of taking care of the terminally ill affected their personal life.79.3% felt that the health care providers involved in palliative care also needed emotional support.
Conclusions: The results of the study show that the post-graduates do not have adequate knowledge and training in palliative care and that there is an immediate need to include palliative care training as a part of their curriculum.

P-0514

THE FEASIBILITY OF HIGH DOSE METHOTREXATE THERAPY IN CHILDHOOD CANCER IN A DEVELOPING COUNTRY – EXPERIENCE FROM A TERTIARY CARE PEDIATRIC ONCOLOGY UNIT.

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Purpose/Objective: High-dose methotrexate (HDMTX) therapy followed by leucovorin rescue is an important component in the treatment of variety of childhood cancers. Administration of HDMTX requires a careful and vigilant monitoring. The limited availability of resources and financial restraints for supportive care often pose problems in a developing country. The aim of this study was to assess the toxicity profile and feasibility of high dose methotrexate infusion in a developing country.
Materials and Methods: A retrospective review of cases diagnosed as acute lymphoblastic leukemia (ALL) and Non hodgkins lymphoma (NHL)and who received high dose methotrexate were included. Patient details with respect to HDMTX infusion, toxicity, serum methotrexate levels, additional hospitalization, and delay in next cycle of chemotherapy were obtained. A dose of either 5 g/m^2 and 3 g/m^2 as a 24 hour infusion were used in ALL and 5 g/m^2 as a 3 hour infusion in NHL. Blood counts, serum creatinine, transaminase levels were checked in all patients before each cycle with hyperhydration, alkalinization and leucovorin rescue. Serum creatinine at 42 hours and methotrexate levels at 72 hours was done after starting methotrexate infusion. The toxicity was graded as per the Common Terminology Criteria for Adverse Events v 4.0.
Results: 23 patients were included of whom 10 of them had acute lymphoblastic leukemia, 3 had T lymphoblastic lymphoma, one with anaplastic large cell lymphoma and 9 of them had B-NHL. A total of 83 cycles of HDMTX were administered. The toxicities observed were mucositis in 20% (6/30) of children i.e. in 5.4% of cycles (6/110),neutropenia and thrombocytopenia of grade $\geq$2 in 5.4% of cycles (6/110).
Conclusions: High dose methotrexate can be used safely in developing countrieswith the necessary precautions for high risk children to improve the event free survival. Clinical monitoring for toxicity can be done along with a cost-effective usage of lab investigations in a resource poor setting.

P-0515

EXPERIENCE ON DEEP SEDATION ANESTHESIA GIVEN TO CHILDREN WITH MALIGNANCY FOR INVASIVE PROCEDURES AT THE PEDIATRIC WARD

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Purpose/Objective: Children with malignancy frequently require invasive procedures. One of the complications of these invasive procedures is pain. By using deep sedation general anesthesia, we can eliminate the pain during invasive procedures.
Materials and Methods: Between August 2012-January 2013, children with malignancy were given deep sedation in a room in the pediatric ward (in contrast to the operative room) by the anesthesiologist for bone marrow aspiration/biopsy (BMA/B) and/or lumbar puncture (LP) and intrathecal treatment (IT). The patients had premedication with midazolam 0.03 mg/kg and atropine 0.01 mg/kg and respirated with 5 lt/minute O_2. The O_2 saturation (SpO2), electrocardiography, heart rhytm and blood pressure were measured continuously during the procedure and propophol 1mg/kg with ketamine 1mg/kg were given for deep sedation. When the deep sedation level reached RAMSEY sedation scale 3 or 4, the procedures were done under stable vital findings at prone position. The patients were returned to supine position before waking them up.
Results: The patients had a median age of 8.3 $\pm$ 5 years. Twenty patients (neuroblastoma n = 7, hematologic malignity n = 11, rhabdomyosarcoma n = 1, Ewing sarcoma n = 1) had 33 BMA/B, and 8 patients had 14 LP and IT during the same procedure with BMA/B. No desaturation or hypoxia occured during procedures. The patients were sent to their rooms after the termination of the procedure and waited until their arousal under 5 lt/minute O_2. Parents, patients and physicians were interviewed before and after the procedure regarding pain and anxiety.
Conclusions: In children with cancer, invasive procedures might be done safely in the pediatric ward by the supervision of the anesthesiologist. Deep sedation anesthesia prevents pain of the patient. Performing the procedure in the pediatric ward instead of the operating room decreases the anxiety of the patient and family, thus of the health care team and saves time for the health care team.

P-0516

VOCAL CORD PALSY IN CHILDREN WITH CANCER: A 10 YEAR ANALYSIS OF UK PAEDIATRIC INTENSIVE CARE UNIT ADMISSIONS

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Purpose/Objective: Vocal cord palsy (VCP) is a rare but potentially life-threatening presentation in children with cancer. Most children with VCP present with hoarseness, stridor and respiratory compromise. There are limited studies regarding the requirement for respiratory support and outcome for children with cancer and VCP. This study reviews Paediatric Intensive Care Unit (PICU) admissions over a 10 year period for children with VCP and a primary diagnosis of cancer.
Materials and Methods: Anonymised data from the Paediatric Intensive Care Network (PICANet) database were obtained for children less than 16 years with a diagnosis of VCP admitted to collaborating PICUs across the UK from 2002-2012. These cases were retrospectively analysed according to demographics, diagnosis, respiratory support requirement and outcome. Information to ascertain the cause of VCP was not possible using PICANet data.
Results: 26 children were admitted to PICU with VCP and a primary diagnosis of cancer over the 10 year period (13 male, 13 female, median age 3.4 years). 8 children were less than 12 months old. There were 9 children with acute lymphoblastic leukaemia (34.6%), 10 with brain tumours (38.5%) and 7 with other malignancies (26.9%). 3 of the children with ALL also had Down Syndrome.

The mean length of PICU stay was 7.75 days (range 0.06-39.92 days). 21 children (80.8%) required respiratory support (17 with endotracheal ventilation, 8 with non-invasive ventilation and 5 with tracheostomy). The average duration of invasive ventilation was 7.18 days (range 1-38 days). All were alive on discharge from PICU.
Conclusions: Most children with VCP and underlying cancer required respiratory support with a proportion needing tracheostomy. VCP should be considered early in children with cancer presenting with signs of upper airway obstruction, especially in those receiving vinca-alkaloids, as this is potentially reversible. It is important to confirm the diagnosis with early laryngoscopy.

P-0517

ANTIEMETIC EFFICACY OF PALONOSETRON IN CHILDREN RECEIVING MODERATELY EMETOGENIC CHEMOTHERAPY: PRELIMINARY RESULTS

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Purpose/Objective: Chemotherapy-induced nausea and vomiting (CINV) is the most frequent and distressing side effect of cancer treatment both in adult and in pediatric populations. Palonosetron, a second generation 5-HT(3) receptor antagonist, with prolonged half life (> 40 hrs) compared with the preceding 5HT(3) RAs, has shown improved efficacy in the prevention of CINV. Only few studies investigating palonosetron in pediatric patients have been performed so far.

We report the preliminary results of a prospective, ongoing study started on November 2012 in our institution in order to evaluate the efficacy of palonosetron in the prevention of CINV in children with cancer.
Materials and Methods: Eight patients (M:F ratio 4:4), age 6-18 years, affected by solid tumors and treated with moderately emetogenic chemotherapy (CHT), received palonosetron 5 mcg/kg i.v., 250 mcg if weight $\geq$ 50 kg, 30 min before start of CHT. Palonosetron was administered on day 1 if CHT duration was less than 3 days, on day 1 and 3 if CHT duration was $\geq$ 3 days. Complete response (CR: no vomiting and no rescue therapy) was the primary endpoint, while complete control (CC: CR and no more than mild nausea) was the secondary endpoint. The endpoints were evaluated during the acute (0-24 hrs), the delayed phase (> 24-168 hrs) and overall phases (0-168 hrs) after start of CHT administration.

Results: A total of 44 courses of CHT was administered. CR during the acute phase was achieved in 98% of courses, in 100% during the delayed phase and in 98% during overall phases. CC rates were respectively 91%, 93%, and 89% during the acute, the delayed and overall phases. No side effects were observed.
Conclusions: Our preliminary data suggest that palonosetron could be effective in the prevention of CINV both in acute and in delayed phase in children receiving single and multiple day-based chemotherapy.

P-0518

APPLICATION OF EPIDURAL IMPLANTABLE ACCESS SYSTEMS FOR PAIN MANAGEMENT IN INCURABLE PATIENTS

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Purpose/Objective: Domiciliary chronic pain syndrome management in incurable patients with disseminated cancer is of paramount importance in improving their quality of life.
Materials and Methods: In the period of 2012-2013, 5 incurable patients with various types of cancer (aged 10 to 15 years; mean age 12.7 years) underwent epidural access system implantation. Epidural space catheterization at the L_3 * L_4 interspace was performed followed by x-ray to ensure the catheter proper placement. A 1 cm skin incision and blunt dissection of the subcutaneous tissue was made at the catheter exit site. A clip for catheter fixation was then inserted into the created subcutaneous space and sewn to the adjacent tissues. The port was implanted into the soft tissues above right ribs 10-12. The catheter was threaded through the subcutaneous tunnel up to the port. The incision above the clip and port was closed in layers. The choice of type and dosage of the analgesic was based on the pain syndrome severity, as well as cancer localization and stage.
Results: The patients noted the improvement in quality of life, improved emotional state, and almost complete pain relief. 1 patient (20%) is currently alive, 4 (80%) died due to cancer progression. The epidural implantable access system was used for up to 5 months. No infection or occlusion of the system was observed.
Conclusions: Epidural access systems facilitate pain syndrome management, improve the quality of life, and reduce the opioid dose. If administered otherwise, intravenously or through intramuscular injection, the opioid dose should be gradually increased. Besides, these routes of opioid administration are commonly associated with adverse effects. However the introduction of epidural access systems in the Russian medical setting is stalled due to the absence of qualified medical staff in hospices as well as in outpatient departments which provide in-home care for incurable patients.

P-0519

PERIPHERALLY INSERTED CENTRAL VENOUS CATHETER (PICC) ASSOCIATED COMPLICATIONS IN PEDIATRIC ONCOLOGY PATIENTS: A DEVELOPING WORLD EXPERIENCE.

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Purpose/Objective: To determine common complications in peripherally inserted central catheters (PICCs) among pediatric oncology patients in a developing world scenario.
Materials and Methods: Retrospective analysis of data of patients in whom PICC line was inserted at our centre from January- 2011 to January -2013.
Results: A total of 46 PICCs were inserted in 42 patients over the study period among 246 newly diagnosed cancer patients. Four patients had PICCs inserted twice. Thirty-three patients were males (71.7%) and 13 were females (28.3%) with a mean age of 6.7 years (range-0.8-18Y). 42 (91.3%) had hemato-lymphoid malignancies([ALL (38 out of 42) was the commonest] and 4 (8.7%) had solid tumors [neuroblastoma (3) was most common].The basilic vein was used most frequently (n = 38;82.3%) for PICC placement. The commonest indication for PICCs was chemotherapy and majority were inserted during induction-phase chemotherapy. The total duration in-situ for the 46 PICC in our cohort was 2,023 catheter-days (median-time 52.5 days; range: 4-120 days). PICC-associated blood-stream infection, in 20 PICCs was the most common complication in these patients (43.5%, n = 46; 9.88 episodes/1,000 catheter-days) with Gram-positive organisms isolated in 35% cases, Gram-negative organisms in 30% and fungi in 25% cases. Well-recognized hospital-acquired pathogens like Stenotrophomonas, Pseudomonas, Enterococci, Acenetobacter, Candida and Penicillium constituted 50% of isolated organisms. Other complications noted were catheter-occlusion (8.7%), accidental displacement (4.3%) and catheter-associated venous thrombosis (2.1%). No mortality attributable to PICCs was noted
Conclusions: Despite significant complications, PICCs are a relatively safe and cost-effective method of establishing long-term central venous access in pediatric-oncology patients. Catheter associated blood-stream infection (CABSI) remains a major morbidity in this patient cohort, often necessitating catheter removal. Pain relief was the major benefit and a tradeoff for increased risk of infection

P-0520

INTRAVESICULAR CIDOFOVIR AS A RENAL SPARING THERAPEUTIC OPTION IN THE MANAGEMENT OF VIRAL INDUCED HAEMORRHAGIC CYSTITIS IN A PAEDIATRIC TRANSPLANT POPULATION

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Purpose/Objective: Haemorrhagic cystitis is a recognised complication following Bone Marrow Transplantation (BMT) and aetiology is varied. Cases secondary to a viral infection (adenovirus/polyoma virus) are often managed symptomatically, though occasionally treatment with an anti-viral is necessary. Cidofovir is often the agent of choice. The drug is highly nephrotoxic when given systemically. We report the cases of two patients with renal impairment and severe haemorrhagic cystitis who received intravesicular cidofovir.
Materials and Methods: Two patients (6 and 16 yrs) developed severe haemorrhagic cystitis with concurrent renal impairment and shown to be positive by PCR for polyoma virus in the urine. Both patients required bladder hyperhydration and one was transfusion dependant due to the volume of blood loss. Systemic treatment was not possible due to renal impairment and the nephrotoxicity of the cidofovir. The patients received 5mg/kg topical cidofovir once weekly via a bladder instillation.
Results: Both patients tolerated the intravesicular cidofovir well with no adverse events noted. Twice weekly PCR was undertaken and a consistent reduction in titres correlating with symptom resolution was seen in both patients. Prior to treatment, both patients were receiving hyper bladder hydration; this was discontinued in both patients after 11 and 7 days respectively. Duration of therapy was 7 doses in one patient and 4 doses in the second patient. No further episodes of haemorrhagic cystitis were suffered by either patient.
Conclusions: Intravesicular cidofovir offers a novel, safe and effective approach to managing viral- induced haemorrhagic cystitis in patients with renal impairment or poor renal reserve where systemic treatment is not possible. It also offers a therapeutic option in other patients with preserved renal function and severe viral haemorrhagic cystisis.

P-0521

PROVEN INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH ACUTE LEUKEMIA: A SERIES OF 20 CASES

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Purpose/Objective: Invasive fungal infections in children with acute leukemia are associated with higher morbidity and mortality. Treatment of these infections poses a challenge, especially in resource limited setting. We aimed to study the etiological profile, predisposing factors, clinical presentation, and treatment outcomes of proven invasive fungal infections in children with acute leukemia.
Materials and Methods: Case records of children with acute leukemia diagnosed to have proven invasive fungal infections as per EORTC/MSG guidelines between August 2006 and March 2012 were reviewed.
Results: Twenty patients (20 episodes) with invasive fungal infection were identified. Acute lymphoblastic leukemia was the primary diagnosis in 17 (85%) and Acute myeloid leukemia in 3 (15%) children. The median age at presentation was 6.2 years (1.8-11years). Fifteen (75%) episodes occurred during induction phase, 4 (15%) during delayed intensification and 1(5%) during consolidation. More than one site was involved in half of the patients. The sites included: lungs in 14(70%), paranasal sinuses in 7(35%), gut in 5(25%) and skin in 3(15%). The commonest isolate was Aspergillus in 9 (45%) followed by Mucor in 6(30%), Candida in 3(15%) and Fusarium in 1(5%). Co-infection with Mucor and Aspergillus was seen in one child. Neutropenia was present in all patients. 17 (85%) patients were on steroids at the time of infection. Three (15%) patients took partial therapy. Conventional Amphotericin B was the main stay of therapy. Median duration and cumulative dose of Amphotericin B was 32 days (Range: 2-300 days) and 1174 mg (Range: 150-22000). Adjunct therapy with Voriconazole and Fluconazole was used in 7 (35%) and 3(15%) children respectively. Surgical debridement was done in 8 (40%). Of 20 patients,10(50%) died of progressive fungal infection and 10 (50%) survived.
Conclusions: Fungal infections are common during intensive phases of chemotherapy in children with acute leukemia. Fungal infections related mortality is deterrent to outcomes in cancer.

P-0522

YOUTH-FRIENDLY CANCER CARE: AYA BEST PRACTICE SUPPORTIVE CARE

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Purpose/Objective: Despite global interest in cancer service reform, evidence for best practice adolescent and young adult (AYA) care is scare. The aim of this study is to investigate on-treatment experiences of AYAs/parents to inform a program logic model of best-practice psychosocial supportive care.
Materials and Methods: Stage 1 was a qualitative telephone interview study. Identified from clinical databases, participants were 15-25 year olds, 6-24 months from a cancer diagnosis, together with a parent/carer. Nvivo and team discussions informed content and thematic analysis of interview transcripts.
Results: 55 AYAs with a range of diagnoses and from 6 Australian clinical healthcare settings (paediatric, adult, AYA specific), and 46 parents were interviewed. Focusing upon the subgroup of AYA's 15-19 years treated in paediatric and/or adult settings, several themes emerged. These included: *diagnosis delays* (often impacted by AYA, clinical and parent communication); *pathways to care settings* (sometimes multiple different hospitals); and, *the concept of an activated patient* (degree to which young people are participating in health care decision-making and management). A central finding was the variability in reported clinical efforts to elicit active AYA involvement. This in part may vary according to their location in paediatric or adult settings. We will illustrate these issues in relation to (i) fertility preservation discussions and (ii) consent processes.
Conclusions: Data indicate considerable room for improvement in many areas of AYA psychosocial supportive cancer care, with several themes not previously described in the literature. In particular, our data show we can make treatment experiences age- and developmentally-appropriate but questions remain about applying practices consistently regardless of treatment setting. These findings informed development of a quantitative survey currently being completed by a nationally representative sample. Both data sources will advance the articulation of a best practice model of AYA care.

P-0523

MEASURING SYMPTOM DISTRESS IN PAEDIATRIC ONCOLOGY SETTING: A SYSTEMATIC REVIEW OF ASSESSMENT INSTRUMENTS

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Purpose/Objective: Cancer- and cancer therapy-related symptoms can cause distress in paediatric oncology patients. The aim of the current review is to assess symptom distress instruments for use in paediatric and adolescent patients with cancer ($\leq$18 years old), and evaluate their psychometric properties for use in clinical practice and research.
Materials and Methods: A systematic search of the peer-reviewed English-language literature was performed using the CINAHL, PubMed, PsycINFO, Scopus, and Web of Science electronic database by two independent reviewers with the pilot tested search terms. Instruments designed to assess symptom distress were identified and screened with Kappa statistics to confirm the agreements between the reviewers. The eligible instruments were evaluated based on the psychometric criteria, and acceptability and feasibility.
Results: 1762 articles were screened, and 34 were eligible for inclusion of review and data extraction. Among these 36 articles, one study attempted to develop a new instrument for measuring distress while four studies attempted to validate a modified or translated instrument to measure distress. The remaining 31 studies reported on distress prevalence as the primary outcome using the instruments measuring distress. The most often used instruments among these 36 articles are Children Depression Inventory ($n = 7$) and Memorial Symptom Assessment Scale (10-18) ($n = 7$). Although Children Depression Inventory has established its psychometric properties in other populations, it has yet to be confirmed in paediatric oncology population. The Memorial Symptom Assessment Scale 10 * 18 appears to be more comprehensive and holistic in measuring physical and psychological dimensions of distress. In addition, it is well validated and demonstrates promising psychometric properties. Nevertheless, large scale studies are warranted to confirm its psychometric properties.
Conclusions: The available evidence suggests the Memorial Symptom Assessment Scale (10-18) could be an appropriate instrument to assess symptom distress in paediatric oncology setting.

P-0524

A TEN-YEAR SURVEY ON PARENTAL SATISFACTION TOWARDS PALLIATIVE HOME CARE SERVICES FOR THEIR CHILDREN WITH CANCER

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Purpose/Objective: To study the effectiveness and the parental satisfaction to the palliative home care service (PHCS) of Children's Cancer Foundation (CCF)
Materials and Methods: Children with incurable cancer and families were referred to the PHCS by doctors working in 5 different hospitals with paediatric oncology. A questionnaire was sent to bereaved parents who have child died of cancer after 6 weeks. Questionnaires were collected and examined from year 2000 to 2010. The questionnaire have fifteen 5-point forced choice questions and 4 open-ended questions. Qualitative and quantitative findings were analysed by SPSS version 17 and content analysis
Results: 123 questionnaire were administered to bereaved parents from year 2000 to 2010 with 121 questionnaire were returned. The mean score on the questionnaire satisfaction was high (4.55 out of 5). The parents were strongly agreed that the palliative home care service met their children's physical and psychological needs, particularly in relieving symptoms and preparing the family to face the death. 71.2% parents agreed that the PHCS can shorten the length of hospital stay. The majority of the parents wanted doctors to make referral earlier.
Conclusions: Parents feed back to the PHCS were positive, the service increased the quality of life of the children in their end stage of life. The doctor's awareness of the need of the family, and the use of PHCS needed to improve in the future.

P-0525

MEASLES OUTBREAK IN A PEDIATRIC ONCOLOGY UNIT AND THE ROLE OF RIBAVIRIN IN PREVENTION OF COMPLICATIONS AND CONTAINMENT OF THE OUTBREAK

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Purpose/Objective: Measles in immune-compromised children is a serious illness. We report a measles outbreak in children admitted in our oncology ward and the role of oral ribavirin in preventing complications and containing the outbreak.
Materials and Methods: Measles, diagnosed by clinical features and contact to a measles case, was seen in 15 children during March and April 2012. Anti-measles IgM ELISA was done in all and measles RNA by PCR in 7 patients. Oral ribavirin was given to all measles cases and to the patients exposed to them.
Results: Mean age of these 15 children was 4.36 ($\pm$ 2.68) years, 8 (53%) of them were under 5 and 11(63%) were unimmunised. Fever and rash were seen in all and pneumonia in 3(20%). Measles specific IgM ELISA was positive in 7 of 15 and measles RNA was detected in 2 of 7 tested children. Duration of illness was longer in unimmunised children (median 7, range 3-18 days as compared to those who were immunized (median 4, range 3-5 days) $p = 0.02$. Complications were higher in children with hematological malignancies (5 of 8 cases vs 0 of 7 cases; $p = 0.025$). Case fatality rate (CFR) was 13%. Delay in starting ribavirin was associated with fatal complications (2 of 2 vs 0 of 13, $p = 0.009$). Ribavirin prophylaxis prevented measles in all (21 of 21) exposed patients.
Conclusions: Measles in children with cancer has high CFR. Past immunization, though not fully protective, reduces disease severity. Early administration of ribavirin mitigated disease severity. Post-exposure prophylaxis with ribavirin was effective in preventing disease in contacts.

P-0526

A GLOBAL SURVEY OF PROCEDURAL SEDATION & ANALGESIA PRACTICES IN PAEDIATRIC ONCOLOGY

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Purpose/Objective: Children with cancer undergo frequent painful procedures during their treatment. This web-based survey was conducted to determine the sedation and analgesia practices for therapeutic lumbar puncture (LP) and bone marrow aspiration (BMA) in paediatric oncology settings across the world.
Materials and Methods: A 39-item self-administered online survey was distributed to 2051 SIOP members and Cure4Kids users (physicians and nurses) on 1st February 2013 and will continue to accrue subjects until 1st April 2013.
Results: 474 complete responses (23% response rate) from 87 countries have been received. 2% are from low (LIC), 17% lower-middle (LMIC), 36% upper-middle (UMIC) and 45% high income countries (HIC). Overall use of general anaesthesia (GA), dissociative anaesthesia (DA) or sedation + analgesia (S + A) was reported by 66%(LP) and 76%(BMA) of respondents.

For LP, NO SEDATION/ANALGESIA was reported by 13%, 6% and 0% of respondents from L/LMIC, UMIC and HIC respectively ($p < 0.0001$) while SEDATION ALONE by 17%, 11% and 3% ($p = 0.0002$). For BMA NO SEDATION/ANALGESIA was reported by

3%, 2% and 0% of respondents from L/LMIC, UMIC and HIC respectively ($p = 0.05$) while SEDATION ALONE by 11%, 8% and 0% ($p < 0.0001$).

Non-pharmacological methods were not commonly used and use of ADDITIONAL PHYSICAL RESTRAINT to complete LP was reported by 21%, 14% and 10% of respondents from L/LMIC, UMIC and HIC respectively ($p = 0.0.03$) while to complete BMA by 19%, 9% and 5% ($p = 0.0006$). 37% of respondents reported barriers to procedural sedation & analgesia, the principal of which were lack of staff, monitoring equipment and bed-space.

Conclusions: This survey provides the first description of procedural sedation and analgesia practices in children with cancer in L/LMIC and UMIC and contrasts this with that in HIC. There is a need for developing related evidence-based guidelines for resource-limited settings where GA is not widely available.

P-0527

THE EXPERIENCE OF USING CAPHOSOL FOR ORAL MUCOSITIS PROPHYLAXIS IN PEDIATRIC HIGH-DOSE CHEMOTHERAPY RECIPIENTS

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Purpose/Objective: Oral mucositis is one of the most common chemotherapy complications, especially in high-dose settings. The patients with oral mucositis are susceptible to systemic infection and prone to malnutrition, have higher demand for analgesia. Their inpatient period is generally longer and treatment more expensive due to more aggressive antibacterial and antifungal therapy employment.

Materials and Methods: One of the ways of oral mucositis prophylaxis and treatment is the employment of Caphosol solution containing monobasic and dibasic sodium phosphate, calcium chloride, sodium chloride and purified water. We analyzed the effectiveness of Caphosol prophylaxis in 23 pediatric (age 3-17, M:F ratio 17:7) patients receiving high-dose chemotherapy due tohigh-risk lymphoma (n = 10), Ewing sarcoma (n =), CNS tumors (n = 3), neuroblastoma (n = 1), osteogenic sarcoma (n = 1) and germ-cell tumor (n = 1). Seventeen patients received program therapy incorporating high-dose (> 1 g/m2) methotrexate, doxorubicin, cisplatin. Six patients received alkylator-based myeloablative regimen followed by autologous hemopoietic stem cell transplantation (auto-HSCT). All patients rinsed the mouth with Caphosol solution 4 * 8 times per day starting from the 1st day of chemotherapy. All patients had oral cultures examined before chemotherapy initiation, the following pathogens were discovered: Str. salivarius, Str. mitis/oralis, Str.anginosus, Str.viriolans, Staph.hominis, Candida albicans. In all the patients with systemic infection massive antibacterial and antifungal therapy was employed.

Results: Among all the high-dose chemotherapy recipients only 6 patients receiving the most dose-intensive regimens with auto-HSCT developed clinical signs of grade I oral mucositis. Therefore, Caphosol solution mouth rinse may be a feasible method of oral mucositis prophylaxis with promising preliminary results in pediatric high-dose chemotherapy recipients.

Conclusions: Therefore, Caphosol solution mouth rinse may be a feasible method oforal mucositis prophylaxis with promising preliminary results inpediatric high-dose chemotherapy recipients.

P-0528

MEROPENEM VERSUS PIPERACILLIN-TAZOBACTAM AS EMPIRIC THERAPY FOR FEBRILE NEUTROPENIA IN PEDIATRIC ONCOLOGY PATIENTS

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Purpose/Objective: Monotherapy has replaced combination therapy in empirical treatment of febrile neutropenic patients.In this randomized prospective study we compared the safety and efficacy of meropenem versus piperacillin tazobactam in febrile neutropenia of pediatric cancer patients.

Materials and Methods: This study included pediatric cancer patients hospitalised with febrile neutropenia at our center. patients were randomly selected to receive meropenem 60mg/kg/day and piperacillin-tazobactam 300mg/kg/day. Duration of febrile neutropenia, absolute neutrophil count,modification and success rate were compared between the two groups.Resolution fever with antibiotic change or death of a patients was defined as failure and resolution of fever without antibiotic change was defined as success.

Modification rate between two groups showed no significant difference ($P > 0.05$). No serious adverse effect occurred in either of the groups. Conclusion. CS and PIP/TAZO monotherapy are both safe and effective in the initial treatment of febrile neutropenia in children with cancer.

Results: Two hundred eighty four episodes were documented in 136 patients.In 198 episodes meropenem and in 86 episodes piperacillin tazobactam was used.Duration of fever and neutropenia,neutrophil count,age,sex and primary disease were not different between the two groups.Modification rate between the two groups was not significant($p = 0.58$)

Conclusions: Meropenem and piperacillin-tazobactam monotherapy is safe and effective in pediatric cancer patients with febrile neutropenia.

P-0529

A PILOT STUDY INVESTIGATING THE EFFECTS OF GLUTAMINE ON VINCRISTINE-INDUCED NEUROPATHY IN PEDIATRIC PATIENTS WITH CANCER

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Purpose/Objective: Vincristine (VCR) is associated with significant sensory and motor neurotoxicity. We conducted a pilot study describing the incidence of VCR- neuropathy and potential utility of glutamine for supportive treatment.

Materials and Methods: Fifty-six children (49 evaluable), aged 5-21, and treated with VCR > 6mg/m2, or > 6mg if dose capped, were recruited. Neurological status was assessed every three weeks by clinical exam (CTCAEv3), Purdue Peg Board (PPB) test, Symbol Digits (SD) Test, Grip Strength (GS) Test, and PedsQL 4.0 Quality of Life (QoL). Upon identification of neuropathy (T1), subjects were randomized to glutamine 6 grams/m2/dose BID (G) or placebo (P) for 21-days (T2), followed by a 21-day wash out (T3).

Results: All participants developed neuropathy: 53% by clinical exam, 22% by neuropsychological assessment, and 25% by both. No significant differences in demographics, degree or definition of neuropathy were observed between the groups. Following the intervention at T2, there was a significant difference between study arms in sensory ($P = 0.022$) but not motor neuropathy ($P = 0.559$), as defined by clinical exam. The G group was 3.48 times more likely to improve in sensory neuropathy score from T1 to T2 ($P = .030$). Children in the G group outperformed the P group by 8.42 points on QoL Self-Report Total Scale between T2 and T3 ($p = .031$). PPB but not SD or GS tests were correlated with the neuropathy exam. No significant side effects were associated with the administration of glutamine.

Conclusions: Vincristine induced neuropathy is highly prevalent in pediatric oncology patients. Glutamine may represent a clinically significant supportive care measure.

POSTER SESSION: POSTER SESSION - PSYCHOSOCIAL

P-0530

PROVIDER COMFORT IN DISCUSSING FERTILITY AMONG ADOLESCENT MALES NEWLY DIAGNOSED WITH CANCER

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Purpose/Objective: The American Society of Clinical Oncology recommends that health care providers discuss risk of treatment-related infertility and preservation options with all cancer patients of child-bearing age. Yet several barriers adversely impact the quality of these discussions, one of which is low provider comfort. The purpose of this study is to describe sociodemographic factors influencing provider (dis)comfort when conducting infertility and preservation discussions with adolescent males newly diagnosed with cancer and their families.

Materials and Methods: Information regarding infertility discussions was collected from providers ($N = 51$) treating adolescents newly diagnosed with cancer as part of a multisite, NIH-funded study investigating sperm banking practices. Health care providers (attending oncologists, nurses, fellows) completed a 12-item scale assessing their comfort when discussing fertility risk and sperm banking. A principle components factor analysis was performed to identify provider discussion comfort factors. Multivariate analyses of variance examined sociodemographic factors which may associate with provider discomfort.

Results: Factor analyses revealed four provider comfort factors: Discussion Comfort ($\alpha = .87$), Recommendation Conviction ($\alpha = .77$), Confidence in Risk Assessment ($\alpha = .81$), and Decision Help ($\alpha = .61$). Significant differences emerged for provider race (Wilks' Lambda $F_{(4,45)} = 2.68$, $p = .04$), age (Wilks' Lambda $F_{(4,45)} = 2.41$, $p = .06$), and professional role (Wilks' Lambda $F_{(4,46)} = 2.26$, $p = .08$), but not gender or religion. Post-hoc analyses revealed non-white providers were more comfortable than white providers ($p < .01$). Providers over 40 years of age were more comfortable during discussions than providers under 40 years ($p = .02$), and attending oncologists were more confident in their fertility risk assessment than other health care providers ($p = .04$).

Conclusions: Preliminary evidence suggests that sociodemographic factors differentiate provider comfort in conducting fertility risk-based discussions with adolescent males newly diagnosed with cancer and their parents. Specifically, provider race, age, and professional role associated with comfort in discussions. Implications for training and professional development will be discussed.

P-0531

HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA WHO WERE TREATED THE JAPAN ASSOCIATION OF CHILDHOOD LEUKEMIA STUDY ALL02-REVISED

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Purpose/Objective: Purposes of this study were to measure health-related quality of life (HRQOL) in children with acute lymphoblastic leukemia (ALL) who were treated by protocol of the Japan Association of Childhood Leukemia Study ALL02-revised (ALL02-R), and to explore relationship between HRQOL and disease specific health status.
Materials and Methods: Measurement time points were determined according to ALL02-R treatment phase; shortly after completion of the induction phase (T1), during the consolidation phase (T2), during the maintenance phase (T3), and after the completion of the treatment (off-TX). The Scores of HRQOL of children with ALL were compared with that of healthy children. The PedsQL Generic Core Scales and Cancer module were used.
Results: Thirty-five children aged 5*18 years were participated. Concerning to T1, School functioning of HRQOL of children with ALL was significantly lower than that of healthy children ($p = .02$). For T2, the scores of children with ALL were significantly lower than that of healthy children for overall HRQOL ($p = .036$), Physical ($p = .014$), and School functioning ($p = .011$). Similarly, HRQOL of children with ALL was significantly lower for Physical ($p = .001$) and School functioning ($p < .00$), but significantly higher for Emotional ($p = .039$) during T3. Similarly, the score of children with ALL was significantly higher than that of healthy children for Emotional domain ($p = .037$) for off-TX. Large value of correlations were found between overall HRQOL and Communication (T2), Procedural anxiety, Treatment anxiety, Worry, Cognitive problem, Perceived physical appearance, and Communication (off-TX) (Spearman ρ ranged from .806 to .857).
Conclusions: HRQOL of children with ALL were impaired for physical and school functioning during they were under treatment, however, improved after the completion of the treatment. Medical professionals should secure symptom management as well as provide educational support with collaboration with multidisciplinary team.

P-0532

IS SCHOOLING IN CHILDREN WITH MALIGNANCIES COMPROMISED?

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Purpose/Objective: Evaluation of school attendance and performance in children diagnosed with malignancy during and after completion of therapy.
Materials and Methods: A questionnaire with details of schooling including reasons for absenteeism, education & socio-economic status of parents and, attitude of teachers was put across by RJ & AT during oncology clinics to families and children with malignancies.
Results: Ninety seven children with a median age of 9.75(4-17) years were evaluated. Seventy had Acute Lymphoblastic leukemia, 27 had other malignancies. Sixty five children were on maintenance chemotherapy, 14 on intensive chemotherapy and 18 had completed treatment. Seventy eight children (80%) were enrolled in school. Nineteen children were not enrolled. Reasons included- 7: intensive chemotherapy; 5: parental apprehension for contracting infections; 3: distance from school; 3: refusal by school authorities; 1: financial constraints.

Attendance was 74% with 13 having below 50% turnout. Reasons for absenteeism included- 33: Intensive chemotherapy/ hospital admission/ongoing infection; 8: did not like school; 12: parental fear of child falling sick; 2: distance from school; 2: too much work. Sixteen children had full attendance. Seventy one percent had above average grades.

No association was noted between school enrolment and attendance with primary versus higher class, parental education, socio-economic status & rural/urban background.

School authorities knew of the child's diagnosis in 85 cases. In five cases, children/ parents felt that school authorities were unhelpful and uncooperative. Two children felt shunned & ostracised. Overall there was a loss/delay in schooling by 0.6 (0-3) years.
Conclusions: Educational disruption and loss of school years adds to anxiety in a child with cancer. Developing countries do not have school rooms in hospital or home tutoring facilities. Only 2/3rd of our children are able to attend school regularly. More awareness, better attitude and practices including a liaison between the schools and oncology units need to be established.

P-0533

PROVIDING CARE TO A CHILD WITH CANCER: A LONGITUDINAL STUDY ON PARENTS' EXPERIENCES WITH CAREGIVING DURING THE FIRST YEAR AFTER DIAGNOSIS

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Purpose/Objective: In order to assist parents with the difficult task to provide care to their child with cancer, it is important to know what they go through. Due to the cross-sectional nature of previous research, very little is known about variations in parents' caregiving stress over time. Therefore, this study longitudinally investigated the course, predictors and impact of caregiving stress on well-being in the first year after the child's cancer diagnosis.
Materials and Methods: Primary caregivers ($n = 95$, 100% mother) of consecutive newly diagnosed pediatric cancer patients (0-18 years) completed measures of caregiving stress, depressive symptoms, anxiety, and self-reported health at diagnosis, and 3,6 and 12 months thereafter.
Results: Results showed a significant reduction of caregiving stress over time, with a rapid decline in the first 3 months after diagnosis ($b = -4.80$; 95%CI -6.33 to -3.27). Predictors of caregiving stress were parental age, marital status, the ill child being the parent's only child, and treatment intensity. Multilevel analyses, controlled for sociodemographic and medical covariates, showed that, over time, the decline in caregiving stress was accompanied by a reduction in depressive symptoms and anxiety, and an improvement in self-reported health. The amount of variance explained by the full model was 55% for depressive symptoms, 36% for anxiety, and 5% for self-reported health.
Conclusions: Our findings suggest that the improvement of parental functioning reported in this research could be partly understood from a reduction of caregiving stress over time. Extra clinical attention should be paid however, to younger parents, single parents, parents whose ill child is their only child or whose child is on intensive treatment. Targeted support starting early in the disease trajectory might help them to cope better with the stressors of caregiving.

P-0534

THE EXPERIENCES OF PARENTS OF INFANTS IN PAEDIATRIC ONCOLOGY: A MIXED METHODS STUDY

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Purpose/Objective: Research examining the experiences of parents who have an infant within a paediatric oncology context is scarce. This study utilised semi-structured in-depth interviews and self-report questionnaires to examine the psychological wellbeing of parents and the influence of a paediatric cancer diagnosis on parent-infant relationships.
Materials and Methods: Two groups of parents were recruited: 1) parents of infants ($\leq$24 months of age at recruitment) with a cancer diagnosis, and; 2) parents of infants with a sibling who has a cancer diagnosis. Twenty parents (11 mothers & 9 fathers) completed interviews designed to investigate the stressors placed on, and the influence of, a diagnosis of paediatric oncology on their relationship with their infant. Fifty-two parents, 31 mothers and 21 fathers, completed questionnaires assessing anxiety, depression and post-traumatic stress symptomatology (PTSS).
Results: Interviews revealed a number of themes: emotional responses to diagnosis and treatment, treatment phases placing strain on the parent-infant relationship, the impact of time away from their infant, and identified positive and negative impacts upon family relationships. Preliminary results of questionnaire data indicated no significant difference between mothers and fathers scores on anxiety, depression and PTSS, although fathers were found to score higher than mothers on depression while mothers scored higher than fathers on anxiety and PTSS. Examination of PTSS scores revealed 9 (29%) mothers and 5 (24%) fathers self-reported clinically significant levels of symptoms. There was also a significant association between mother and father PTSS scores ($r = .49$, $p < .05$).
Conclusions: Our novel preliminary results highlight the importance of understanding the unique stressors, mental health strains and experiences of parents' of infants in families in

which there has been a paediatric cancer diagnosis. The results also emphasize the importance of including fathers in parenting research and clinical care.

P-0535

AN EXPLORATION OF PARENTAL SOCIAL SUPPORT: CAMP TRILLIUM'S PEDIATRIC ONCOLOGY FAMILY PROGRAM

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Purpose/Objective: When a child is diagnosed with cancer, the entire family is affected by the demands of the illness and its treatment. This paper aims to explore therapeutic camping programs as an avenue for providing social support for parents affected by childhood cancer. Camps are proven as effective modalities for reducing fear and anxiety in children with cancer by providing opportunities where they can interact with other children and learn ways to cope with cancer. This study aims to elucidate whether similar benefits may exist for parents attending family camps.
Materials and Methods: Qualitative mixed methods (questionnaires, interviews and observation) were used to better understand the perceptions and experiences of parents ($n = 85$) attending Camp Trillium's family summer program between June 26th and August 31st 2012 across two sites in Ontario, Canada. Data obtained was categorized using thematic analysis.
Results: Whilst parents documented a diversity of reasons for attending Camp Trillium, almost all reported personal benefit from their attendance. Particular reference was made to benefits derived from meeting other parents as well as the opportunity camp provided to escape from their everyday routine.

From the qualitative interviews, six distinct themes were explicated: (a) A sense of normalcy; (b) Reconnecting as a family; (c) Valuable interactions; (d) Group tensions; (e) Information sharing; and (f) Choice of participation. The themes identified were mirrored in the observations by both researchers on site.
Conclusions: The results of this study clearly demonstrate that residential family camp provides much more than respite and recreational support. Parents reported higher levels of perceived social support, hope, and increased ability to cope as a result of attendance at camp. The camaraderie and peer support at Camp Trillium functions as a surrogate source of intimacy and affirmation and as an expanded social network of support, unique to this context.

P-0536

THIS CHILD IS A PART OF ME . . . TOO! SUPPORT GROUP FOR GRANDPARENTS OF CHILDREN WITH CANCER

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Purpose/Objective: Cancer disrupts the wellbeing of the child, his nuclear family, and the extended family. Grandparents can offer a strong support for the sick child and his parents. In certain situations, grandparents are the main caregivers of the ill child. This support includes filling in the parents in caring for the child, tending the healthy siblings, and supporting the parents. Many times this involvement is limited due to the lack of access to medical information or due to the child's parent refusal for help or support. These confrontations and others give rise to fear, confusion, uncertainty and helplessness.
Materials and Methods: Usually the main recipients of professional care are the child, his siblings, and parents. What about the grandparents? This is the first time that a support group for grandparents of children suffering from Oncologic diseases, was formed in Israel. The support group enabled this unique population to share their experiences while receiving medical information and emotional support.

Three groups were formed. The grandchildren were in varying stages of treatment, but not nearing death. Each group had six sessions. The groups were led by two nurses from the unit.
Results: The issues dealt with were fear of the treatments, adverse effects, as well as facing the possibility of death. Another topic that surfaced was the feeling of helplessness. In the feedback, the participants expressed gratitude for the opportunity to share with similar grandparents and there was a request for an additional session.
Conclusions: Taking part in these groups empowered its members, and provided a feeling of belonging, and true partnership in coping with the family's problems. The group environment offered an opportunity to share experiences with similar grandparents coping with the same problems.

P-0537

DELIVERING BAD NEWS TO ANGRY ADOLESCENT PATIENTS - A LITERATURE REVIEW AND A CASE ILLUSTRATION

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Purpose/Objective: Delivering bad news is a core communication skill for oncologists. The patients' responses to bad news vary. Anger in adolescents or young adults (AYA) is clinically regarded as a particular challenge. The aim of this study is to review current knowledge about communication with angry AYA patients in cancer care. Further, a naturalistic observation of a consultation, where an oncologist presents a cancer diagnosis with uncertain prognosis to an adolescent who responds with anger, is presented.
Materials and Methods: Selection of articles for review was based on search in Medline, Cinahl and PsychInfo (keywords anger, adolescents, young adult, physician-patient relations and communication), on inspection of reference lists of the papers identified in the searches and on interviews with experts in the field. An audio-tape of a consultation from an ongoing study of the communication of diagnostic and prognostic information to a young cancer patient was analyzed using conversation analysis.
Results: There is a scarcity of empirical knowledge and guidelines on how to adequately handle angry AYA patients in clinical oncology. There appears to be a consensus that effective communication with angry AYA patients requires an understanding of anger in adolescents from a psychological developmental perspective, acknowledgement of the emotion and facilitating of coping and social support. The consultation provides examples of challenging expressions of anger of an AYA patient and physician approaches to give information and relate to him for instance in terms of skills to prevent further escalation and at the same time straightforward and direct speech.
Conclusions: There is little evidence-based knowledge on how to deliver bad news to angry AYA cancer patients, but some general recommendations are provided in the literature. The real-life examples from the consultation indicates that skills needed for dealing with angry patients differ from those needed to meet other common emotional reactions such as uncertainty, sadness and anxiety.

P-0538

". . .AND THEN I GOT CANCER": EXAMINING THE LIFE NARRATIVES AND IMAGINED FUTURES OF ADOLESCENTS AND YOUNG ADULTS WITH CANCER, COMPARED TO HEALTHY AGE-MATCHED CONTROLS

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Purpose/Objective: Cancer during adolescence and young adulthood disrupts a developmentally formative life period. A key milestone during this time is for young people to develop a sense of self, and sense of purpose with regards to future life goals. Traumatic events, such as cancer, may shatter an individual's core assumptions about themselves, the world, and the future. Survivors of these events may therefore carry with them potential grief, anger, depression, and anxiety about the future. This study explored how young people think about their cancer experience in the context of their 'life story', and how this impacts upon their imagined future lives. The two aims were to examine: how the life stories of young people with, and without, cancer differ; and explore the relationship between adolescent and young adults' (AYAs) current psychological distress, life stories and imagined future events.
Materials and Methods: Sixty healthy AYA controls and 20 AYAs with cancer completed structured interviews involving the validated *Life Narrative Task* and *Future Imaginings Task*. Interviews were audio-recorded and coded for content, specificity, and continuity by two raters. Participants also completed the *Depression, Anxiety, Stress Scales-Short Form* to correlate memory/future imaginings results with current psychological adjustment.
Results: AYAs with cancer showed more illness-focused life narratives and future imaginings compared to healthy AYAs. In addition, AYAs with cancer who also showed elevated depression, anxiety or stress symptoms showed less specific future imaginings, and a less continuous life narrative, compared to healthy young people.
Conclusions: How young people 'fit' their cancer experience into their life narrative may significantly impact how they imagine their future lives, and this appears to be related to current levels of distress. Assisting AYAs to process their cancer experience, and understand how it fits into their continuous life narrative into the future, may promote adjustment as young people transition to cancer survivorship.

P-0539

ESTABLISHING A NEEDS ASSESSMENT TOOL FOR PAEDIATRIC CANCER PATIENTS

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Purpose/Objective: Paediatric cancer patients have unique biological, psychological and social needs during treatment, distinct from other groups including adolescents. This pilot

study aims to assess the feasibility of a needs assessment tool for paediatric cancer patients in enhancing the quality of care received from a multi-disciplinary team.
Materials and Methods: We developed the needs assessment tool based on one used for adolescent cancer patients, and incorporated the treating multidisciplinary team's recommendations. Children with solid tumour malignancies (n = 10) and their parents (n = 15) who were treated in the UCH paediatric oncology ward were consented to participate in this study. Their distress level and areas of concern were assessed via a self-administered checklist. In addition, a structured interview explored biological, psychological and social issues. They were asked to recapitulate their experience with cancer and its treatment, along with their familial, educational, cultural and spiritual background, and how their experience with cancer impacted significant people in their lives. These answers were rephrased in second person to address the patient when they reread their responses. The treating team then used this information to address the areas of concern for the patient.
Results: The assessments were completed in an average of 45 minutes, and were conducted by a range of people, including medical students and psychologists. These assessments were useful in uncovering levels of distress in children who might have not expressed it otherwise, and also particular areas of concern which have not been explored adequately. These assessments identified information gaps and needs not recorded elsewhere.
Conclusions: This tool resulted in repeated tailoring of our MDT support to our patients' needs. Future considerations include timing of repeat assessments and assessment of impact on distress levels.

P-0540

FACTORS WORSEN THE POSTTRAUMATIC STRESS SYMPTOMS IN CHILDHOOD CANCER PATIENTS: A LONGITUDINAL STUDY

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Purpose/Objective: Children, who experience cancer diagnosis and treatment, become emotionally traumatic with responses to horror, intense fear and /or helplessness, and may develop symptoms of posttraumatic stress disorder. The purpose of this study is to investigate factors that worsen the posttraumatic stress symptoms in childhood cancer patients by using a longitudinal design.
Materials and Methods: Forty-seven patients were asked to complete the Posttraumatic Stress Reaction Index (PTSD-RI) at the completion of therapy (T1) and the follow-up care (T2). There were 30 males and 17 females, mean age of diagnosis was 6.4 years (range, 0-14), mean age of T1 was 11.1 years (range, 5-22), and mean age of T2 was 15.8 years (range, 8-34). Analysis of covariance (ANCOVA) was conducted to investigate the relationships between PTSD and demographic characteristics. Difference of time interval between T1 and T2 were used as the covariate in this analysis.
Results: The results of ANCOVA revealed that female showed significant increase in the score of PTSD-RI than male (F (1,46) = 5.86, $p < .05$). In addition, significant increase in the score of PTSD-RI was observed in patients diagnosed in early childhood (F (1,46) = 3.74, $p < .05$) and completed a treatment in younger age (F (1,46) = 4.59, $p < .01$).
Conclusions: Previous research showed that posttraumatic symptoms became milder over the years. However, this study indicates that female patients, patients diagnosed or completed a treatment in early age are risk factors for worsening of the PTSD. It is necessary to pay attention to the change of their posttraumatic symptoms.

P-0541

LONGITUDINAL STUDY OF POSTTRAUMATIC STRESS SYMPTOMS AMONG PARENTS OF PEDIATRIC CANCER PATIENTS DURING TREATMENT AND AFTER TRANSITION TO OUTPATIENT SETTINGS

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Purpose/Objective: To investigate longitudinally the association between parental posttraumatic stress symptoms (PTSS) and related variables during pediatric cancer inpatient treatment and after discharge.
Materials and Methods: This is a longitudinal follow-up study of 15 parents of children treated for cancer. Mothers (N = 15) and fathers (N = 13) of 15 children diagnosed with cancer completed questionnaires. We evaluated these questionnaires at the end of inpatient treatment and one year after discharge. The disease status of patients was remission at the time of investigation. The Impact of Event Scale-Revised (IES-R), the Family Assessment Device (FAD), the Zung Self-rating Depression Scale (SDS), and the State-Trait Anxiety Inventory (STAI) were used to assess PTSS, family functioning, depression, and anxiety respectively. We also assessed medical and demographic variables.
Results: Descriptive statistics and univariate analysis were performed to examine factors related to PTSS. The total scores on the IES-R of mothers and fathers changed from 22.1 ± 10.4 to 18.7 ± 9.6 and from 25.5 ± 10.7 to 16.9 ± 11.5 respectively. The percentage of mothers with an IES-R score ≥ 25, which indicates the presence of severe PTSS, notably decreased from 46.7% to 26.7%, and the percentage of fathers with an IES-R score ≥ 25 decreased from 46.2% to 15.4%. The scores on depression and anxiety significantly improved in mothers. Moreover, the scores on depression, anxiety, PTSS, and family functioning significantly improved in fathers.
Conclusions: Although parental distress decreased with time, some parents showed clinically significant levels of PTSS even if the children were in remission. Pediatric medical teams should be aware that parental distress could be extended for a long period. Alleviating anxiety and depression about cancer and its treatments is suggested as possible approaches for supporting parents after their child's discharge.

P-0542

THE RELATIONSHIP BETWEEN HOPE,RUMINATION RESPONSE STYLES, RUMINATION CONTENT AND PSYCHOLOGICAL ADJUSTMENT AMONG CHILDHOOD CANCER PATIENTS AND SURVIVORS

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Purpose/Objective: Two types of rumination response styles, brooding and reflective, were widely studied among trauma survivors but had not been investigated among childhood cancer survivors and patients. This study aimed at investigating whether hope, rumination response styles and rumination content were related with childhood cancer patients' and survivors' psychological adjustment after treatment.
Materials and Methods: 89 childhood cancer survivors, aged 17.2 to 31.3, were recruited from Children's Cancer Foundation Survivors' Club to complete The Hope Scale, The Chinese Cancer-related Rumination Scale (CCRRS), Chinese Responses Styles Questionnaire-Rumination sub-scale (RSQ-Rum), Beck Depression Inventory and Beck Anxiety Inventory through mailing survey. 18 childhood cancer patients, aged 8 to 16, who had just completed acute cancer treatment no more than three months and were in remission were recruited from hospital out-patient clinics to complete Children's Hope Scale, Children's Depression Inventory, State-Trait Anxiety Inventory for Children, CCRRS and RSQ-Rum.
Results: Correlational studies on survivors found that brooding but not reflective rumination correlated with depression (r = 0.47, p < 0.01) and anxiety (r = 0.358, p < 0.01). Rumination on negative cancer-related content correlated with depression (r = 0.376, p < 0.01) and anxiety (r = 0.333, p < 0.01). Hope correlated negatively with depression (r = -0.525, p < 0.01) and anxiety (r = -0.347, p < 0.01).Correlational studies among patients suggested brooding (r = 0.585, p < 0.05) and negative content rumination (r = 0.487, p < 0.05) correlated with anxiety but were unrelated to depression. Hope again correlated negatively with depression (r = -0.605, p < 0.01) and anxiety (r = -0.535, p < 0.05).
Conclusions: Brooding and negative content rumination were associated with depression and anxiety among survivors and were related to anxiety among patients. Hope served as a protective factor for both survivors and patients. This finding would support fostering of hope and reduction in brooding and negative rumination in psychotherapy.

P-0543

POSTTRAUMATIC STRESS IN SURVIVORS OF CHILDHOOD CANCER WHO HAVE NOT RECEIVED COMPREHENSIVE SURVIVORSHIP CARE

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Purpose/Objective: Posttraumatic Stress Disorder (PTSD) is a potential problem in pediatric and young adult survivors of childhood cancer, but has not been well characterized, particularly in patients not yet enrolled in survivorship care.
Materials and Methods: We identified a total of 68 patients who were diagnosed with invasive cancer at age < 18 years at the Yale-New Haven Hospital during 2000-2010, but had not previously received survivorship care. The patients responded to posttraumatic stress-related questions included in the well-validated UCLA PTSD Reaction Index (PTSD-RI) instrument. For each patient, we calculated the PTSD-RI Severity Score, which ranges from 0 to 68, with 20-38 categorized as *partial* PTSD and > 38 consistent with *clinical* PTSD.
Results: The 68 participants had a mean age at diagnosis of 9.9 years (range 0.4-18.0), mean current age of 16.8 years (range 6.0-27.0), and mean elapsed time since diagnosis of 6.7 years

(range 2.1-11.7); 59% were female and 50% >18 years at evaluation. The mean PTSD-RI Severity score was 17.5 $\pm$ 10.2 (range 4.0-47.0) with 28% of patients having *partial* PTSD and 4% *clinical* PTSD. PTSD scores were significantly higher in patients currently >18 years, 22.7 $\pm$ 10.2, compared to 12.4 $\pm$ 7.2 ($p < 0.001$). Older current age ($r^2 = 0.27$, $p < 0.001$) and older age at diagnosis ($r^2 = 0.27$, $p < 0.001$) were each significantly associated with higher PTSD score. Sex, time since diagnosis, and diagnostic category were not significantly associated.
Conclusions: In our study of childhood cancer survivors not enrolled in survivorship care, 32% meet criteria for at least partial PTSD. Those diagnosed at a later age are particularly vulnerable, especially as they approach young adulthood. Clinicians should screen for this adverse outcome in survivors, and further studies should examine possible interventions to mitigate PTSD symptoms.

P-0544

NEUROCOGNITIVE ASSESSMENT IN CHILDHOOD CANCER SURVIVORS – OUR EXPERIENCE IN TERTIARY CARE CANCER CENTER IN INDIA

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Purpose/Objective: Neurocognitive problems are a frequent long-term outcome following treatment of pediatric cancer with cranial irradiation and/or antimetabolite chemotherapy. Cranial radiation is known to adversely affect the developing central nervous system (CNS), which subsequently leads to neurocognitive deficits. Existing researches have shown that impairments within the domains of memory, processing speed, and attention occur very commonly in pediatric cancer patients and this can adversely affect academic, social, and vocational success, thereby impacting quality of life from childhood to adulthood.
Materials and Methods: This study is a retrospective analysis of childhood cancer survivors who were attended in multidisciplinary clinic on regular annual follow up. Those who had scholastic adjustment issues were assessed on neurocognitive testing. A proforma was designed to note demographic variables & referral patterns. Neurocognitive testing details were also evaluated. Descriptive statistics are used.
Results: A total of 90 childhood cancer survivors were assessed on neurocognitive tests between 5-19 years of age. All were assessed on standardizes tests. Majority were referred by mainly for scholastic difficulties and adjustment issues. Overall, approximately 26(28%) patients had average intelligence and 24(26%) had mild to moderate retardation. 7(8%) had sever impairment and poor performance on neurocognitive domains. 15(17%) patients were of borderline intelligence and 18(20%) with above average intelligence who scored high on assessment. Details of domain impairments are discussed.
Conclusions: Majority of survivors had scholastic difficulties along with adjustment and behavioral problems despite average and borderline intelligence. There is a need for therapeutic psychosocial interventions to address the difficulties and issues of the childhood cancer survivors.

P-0545

INFLUENCE OF RELIGIOUS AND SOCIOECONOMIC BACKGROUND OF PARENTS OF DYING PEDIATRIC CANCER PATIENTS ON (DO NOT RESUSCITATE) DNR ORDER

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Purpose/Objective: To evaluate the influence of socioeconomic status and religious background on decision made by parents of children with incurable cancer regarding DNR order
Materials and Methods: Retrospective analysis of medical charts of patients (pts) who died between 01.01. 2000 and 31.12.2010. The following data were looking for: written evidence for DNR discussion with parents; religious background, educational level (more or less 15 years of formal education), monthly income in Israeli shekels (>10000 vs. <10000 per family), patients' age, sex and diagnoses
Results: We found written evidence of discussion on DNR in 73 charts. In 14 cases both parents had higher education (10 Jewish families, 2 Muslim and 2 Christian). Totally, in 14/17 (82.4%) of at least one parent with more than 15 years education DNR consent was obtained. In contrast, among parents with less years of education, positive response to DNR order was obtained only in 24 cases (53.3%) and in 21 (46.7%) cases request for DNR permission was not obtained, $p = 0.03$. In 11 remaining cases data regarding parents' education were not mentioned. There were data about monthly income of both parents in 68 cases. With income <10000 NIS (38 families) 20 (52.6%) gave their consent to DNR. The percentage of positive responses to DNR request was higher 24 of 30 (80.0%) among families with income >10000 NIS, $p = 0.013$. Percentage of positive responses to DNR request was approximately equal among Jews, Muslims and Christians (22/30 [73.3%], 16/26 [61.5%], 8/9 [88.9%], respectively). Consent to DNR request was obtained significantly rarely among Druze families (2/8 [25.0%]).
Conclusions: In our group of pts process of decision on DNR order was influenced by level of parents' formal education and by monthly family income level and not by religious background

P-0546

SOCIOECONOMICAL DESCRIPTION OF ONCOLOGY PATIENTS IN A CHILEAN HOSPITAL.

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Purpose/Objective: Chile is considered of median-high income country; however, the income distribution is inequitable. In the last years the diagnosis and treatment of oncology diseases in the country has undergone advances. Exequiel Gonz‡lez Cort*s Hospital (EGCH) is one of 12 public Oncology Units, treats 10-12% of infantile cancer (average 50 under 15 years old new patients yearly). The median survival is near 70% at 5 years follow-up. Fundaci—n Nuestros Hijos (FNH) is a foundation that provides medical and social support to the kids diagnosed of cancer and their families.
The purpose is to describe the socioeconomic status of patients undergoing oncology therapy for cancer in EGCH.
Materials and Methods: Retrospective analyses of the charts of patients diagnosed of cancer between January to December 2011. The dates were taken from the Social Worker«s report when the patient is diagnosed.
Results: 53 families were included. The diagnoses were: 56.6% leukemia, 32.1% solid tumors and 11.3% lymphoma. 52% live in the traditional model of a nuclear two-parent family and 49% are owner of the house where they live. 8,1% of fathers and 70,2% of mothers are unemployed. Education levels are equal between fathers and mothers. The mean monthly family and per capita income are USD 655 and 143 respectively.
Conclusions: Families of kids under treatment of cancer are in socioeconomic risk. Interventions should be maintained in term to support them while the kids are under treatment and advocate for a special government financial assistance during this period of time. We think that the goods clinical results are a consequence of the good public politics and also because of the complementary medical and psychosocial support given by FNH. Projection of the present study is to survey the condition of the family 6 months after the diagnosis in terms to evaluate the impact of the illness in the socioeconomic status

P-0547

THE EFFECT OF CANCER ON CHILDREN'S PHYSICAL, EMOTIONAL AND PSYCHOSOCIAL WELLBEING IN ACCRA, GHANA

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Purpose/Objective: The diagnosis of cancer is a stressful and threatening experience which can be emotionally devastating to children. This study aims to examine the impact of cancer on physical, emotional and psychosocial well-being of children receiving treatment at the Paediatric Oncology Unit, Korle Bu Teaching Hospital, Accra.
Materials and Methods: Thirty Ghanaian children, aged eight to thirteen years, admitted for treatment of cancer at the Paediatric Oncology Unit of the korle-bu teaching hospital were invited to participate in the study. A questionnaire was administered to both children and guardians after consent had been obtained from the guardian and assent from the children.
Results: Males formed 66.6% of those interviewed. 60% were less than 12 years of age and 73% were living with both parents. About 60% were aware that they had cancer. School performance was stated as good in 86.6%. Sleep problems were reported in 60% and pain in 93% of children. Complaints of undesirable physical effects were mentioned in 93% including hair loss, darkening of palms and mouth ulcers. Fears were expressed by 77% of children examples included death, loss of vision, not looking normal in appearance again. 47% stated that their friends had deserted them mostly because of the physical appearance.
Conclusions: Children with cancer suffer from physical, emotional and psychosocial problems. There is an imperative need for nurses to institute appropriate nursing interventions, particularly in developing countries, to help ease the physical, emotional and psychological burden of life threatening disease. This will help affected children resume their normal growth and development.

P-0548

HEALTH KNOWLEDGE AND BELIEF OF PRIMARY HEALTH CARE PROVIDER ABOUT CHILDHOOD LEUKEMIA IN MANADO

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Purpose/Objective: Referral of childhood leukemia case from Primary Health Center in Manado is still lack. Therefore, we would like to explore the health knowledge and belief of Primary Health Care Providers (HCPs) about leukemia in children.
Materials and Methods: A structured questionnaire about suspected sign and symptoms, etiology, treatment and curability of leukemia was used. Correct answer of more than 70% was considered as good level of knowledge. Primary HCPs were selected by clustered random sampling from 15 Primary Health Center in Manado.
Results: One hundred and fourteen Primary HCPs were participated. The questionnaire was validated with Cronbrach Alpha of 0.969. Most of responders (69.3%) have a good level of knowledge. However, 40.4% of the Primary HCPs did not believe that leukemia in children can be cured and 43% of them believed that children with leukemia will die in spite of the treatment.
Conclusions: The majority of Primary Health Care Providers in Manado has good knowledge about leukemia, but many of them still doubt about it's curability. Continuing education is needed to convince the HCPs about the curability of childhood leukemia.

POSTER SESSION: POSTER SESSION - NURSING

P-0549

CARE COMPLEXITY IN AFRICAN SICKLE CELL ANAEMIA PATIENTS. SCA VS ONCO HEAMATOLOGY PATIENT

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International Centre of Bone Marrow Transplantation, BMT, Rome, Italy

Purpose/Objective: Sickle Cell Anaemia (SCA) is an autosomal recessive genetic disorder predominantly affecting Africans. In Nigeria, the prevalence is 20 per 1000 births and about 150 000 children SCA patients born annually with carrier rate 24%. The SCA has many complications, and bone marrow transplantation (BMT) is the only cure. In patients with SCA and sibling HLA donor, BMT improve a better quality of life, and has a large social impact. In our centre we have performed 37 BMT for SCA with success rate: 96% survival and disease free survival.
Materials and Methods: We have evaluated a multiethnic group of SCA patients during and after the phase of BMT using clinical data. The evaluation period is based from January 1st 2005 to July 31, 2012. The entire donors were the HLA sibling.
Results: During the aplastic phase great attention was given to the patient's systemic and local infections. In our centre we have a few cases that demonstrate after BMT, complication like: Skin GVHD grade IV, seizures, gut GVHD, rectorrhagia, diarrhoea, systemic infections, intermittent abdominal pain, ascites and pancreas inflammation. In addition, those patients having had embolic, ischemic, vessel occlusive, renal and pulmonary events in different organs as infants represent most clinical complications at the same time during the BMT. I would like to say that the treatment with a radical cure of a hemoglobinopathy such as SCA presented a series of complications, sometimes such that patients with leukemia. In these clinical cases, the implementation of immediate action, can lead to a better outcome for patients.
Conclusions: By uniting specialized professionals and using new drugs and technology the best quality treatment was achieved. In our case, the patient had several BMT-complications that only experienced professionals can handle. Also based on our experience, we are convinced that the SCA patient undergoing BMT can promote very fast several fatal compliances.

P-0550

BMT FOR SICKLE CELL ANAEMIA. NURSE'S EXPERIENCE WITH GRADE IV SKIN GVHD

M. Dubali

International Centre of Bone Marrow Transplantation, BMT, Rome, Italy

Purpose/Objective: Sickle cell anaemia (SCA) is an autosomal recessive genetic disorder predominantly affecting Africans. In Nigeria, the prevalence is 20 per 1000 births. The SCA has many complications, and bone marrow transplantation (BMT) is the only cure. In patients with SCA and sibling HLA donor, BMT improve a better quality of life, and has a large psycho-social impact. In our centre we have performed 37 BMT for SCA with success rate: 96% survival and disease free survival.
Materials and Methods: The 12 year old patient was diagnosed with SCA at 1 year of age. Treatment protocol with: Bu 3.7- Cy 200- Fludara 30. GVHD prophylaxis was: CyA I.V; six short MTX 10mg /m^2 and CTX 7.5 mg/kg. The donor was the HLA identical patient's sister. Chimerism reached 100% donor. In post BMT period, clinical complications were: intestinal GVHD III; fever (streptococcus gram +), skin GVHD IV; diarrhoea (> 10 times/day).
Results: The cetaceous GVHD was presented erythematous bullous, spreading all over the surface of the back, even with blood loss. During the aplastic phase great attention was given to the patient's systemic and local infections. Nursing management included: skin dressings, intensive blood/platelets transfusions, photo- aphaeresis, intensive pain control and infection control applying platelet gel to bleeding surfaces with use of sterile drip. During skin GVHD accompanied with aplasia, protecting skin was carefully done. Back dressings were done in total aseptic conditions changing them twice a day. After intensive treatment, both pharmacological and cutaneous, application of medication with paraffin gauze and platelet gel was done. During BMT hospital admission days dressings were carried twice a week applying the regenerative products. Currently, total skin epithelisation is achieved and the GVHD is resolved.
Conclusions: By uniting specialized professionals and using new drugs and technology the best quality treatment was achieved.

P-0551

STRATEGIES TO INCREASE THE ACCOMPLISHMENT RATE OF CLINICAL NURSE LEVEL ACHIEVEMENT IN A PEDIATRIC ONCOLOGY UNIT

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Purpose/Objective: According to the continuous education policy of Taiwan Nurses Association (TWNA), all clinical nurses in Taiwan are encouraged to complete certain assignments to receive a higher clinical nurse level.

Nurses with higher clinical level may have better knowledge, practical skills, teaching and research abilities, and are able work with other medical providers to provide high quality care to the patients. However, the accomplishment rate of clinical nurse level achievement in our pediatric oncology unit was only 20% in 2011, so the purpose of this projet is to increase the accomplishment rate.
Materials and Methods: The step-by-step strategies were developed conducted from Jan. 2012:

Guide: A suggested schedule to achieve a higher clinical level was provided to all nurses.

Pair: Nurses were paired as preceptors and trainees, the senior nurses (preceptors) would help the junior nurses (trainees) on searching, reading and writing journal reading articles related to pediatric oncology nursing.

Share: The nurses need to do an oral presentation about their journal reading articles before achieving the next level, once the nurse completes the presentation, a bonus of salary would be provided immediately.
Results: Through the step-by-step strategies, the accomplishment rate was increased from 20% to 91% in one year. Ten out of eleven nurses were achieved a higher clinical nurse level, and most of them are working on achieving the next level.
Conclusions: Topics of journal reading by nurses were included assessment and management of pediatric oncology complications such as disseminated intravascular coagulation (DIC), Pneumocystis jiroveci pneumonia (PJP) infection, and Post-Lumbar Puncture Headache (PLPH). When nurses presented in the monthly staff meeting, other nurses may learned new knowledges and skills. A positive learning atmosphere was successfully created in our unit.

P-0552

SUPPORTIVE INTERVENTIONS FOR PARENTS OR CAREGIVERS WITH CHILDREN DIAGNOSED WITH CANCER: A SYSTEMATIC REVIEW

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Purpose/Objective: Childhood cancer not only affects the children, this traumatic event also significantly affects the whole family. Studies had well documented that caregivers or parents experienced depression, anxiety and post-traumatic stress symptoms after the diagnosis of children's cancer. This imposed negative impact on the physical and psychosocial quality of life in the caregivers, and thus affected the overall care provided to their children with cancer. Different supportive interventions had been implemented to help caregivers cope with this traumatic event. This systematic review aims to evaluate the best available evidence on the effects of supportive interventions on the psychosocial outcomes in parents or caregivers of pediatric oncology patients.
Materials and Methods: Relevant studies were searched in 13 databases, such as MEDLINE, CINAHL, PsycINFO, Embase and China Journal Net. All databases were searched from inception to January, 2013. Searching in grey literatures and unpublished studies was also conducted. Hand searching of the reference list of all identified articles was performed for identifying additional studies. The following keywords were used in each electronic database search, including: pediatric, child, caregiver, parents, cancer, intervention, educat*. Experimental studies will be included if they are a) written in English and Chinese, b) conducted in parents or caregivers of children aged 0 -18 years and diagnosed with any form of cancer. Studies will be excluded if the participants were pre-diagnosed with psychiatric disorders.
Results: A total of 14 studies met the inclusion criteria and have been included in the analysis. All the studies would be critically appraised according to Cochrane review protocol by two reviewers independently.

Conclusions: Supportive interventions play an important role in improving health outcomes of caregivers, thus it might be incorporated in pediatric oncology care.

P-0553

EXPERIENCES AND GROWTH OF SIBLINGS OF PEDIATRIC CANCER PATIENTS

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Purpose/Objective: The purpose of this study was to clarify the experiences of siblings of pediatric cancer patients and develop an intervention model.
Materials and Methods: Using our method, based on the philosophical method proposed by A.P. Giorgi, a phenomenological psychologist, we analyzed the date through adopting a qualitative descriptive approch and trajectory equifinality model(TEM).Siblings of pediatric cancer patients were affected both physically and mentally by their brothers' and sisters' lives under medical treatment and their parents' speech and behavior, causing the siblings to perform.As our subjects,we conducted a survey of siblings and parents of pediatric cncer patients.
Results: As our subjects, we conducted a survey of 11 people comprised of 7 siblings and 4 parents of pediatric cancer patients. As the results, we identified 394 phenomena, 66 elements, and 27 essential elements.Siblings of pediatric cancer patients were affected both physically and mentally by their borthers' and sisters' lives undre medical treatment and their parents' speech and behavior, causing the siblings to perform 'self-restraint and suppression' and experience abrupt somatic symptoms.
Conclusions: The results suggested the necessity of supporting siblings of pediatric cancer patients and intervening specifically so as to allow the siblings to have places to express their feelings, establish their identity through new relationships, and 'live their own lives' by answering the questions and solving the conflicts regarding their relationships with their deceased brothers and sisters.

P-0554

WE SUPPORT YOU ALL THE WAY... THE PEDIATRIC COORDINATING NURSE'S ROLE

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Purpose/Objective: Children diagnosed with cancer as well as their families are subjected to great stress. Experiencing physical and emotional difficulties, children and their families confront a whole new world of content that can easily shake their foundation. Facing this new complex situation they strive to cope.
Materials and Methods: The pediatric Nurse Coordinator's (PNC) role developed recognizing the importance in accompanying and supporting the child and his family throughout the process of adapting to the new situation, coping with the disease and providing them with holistic long term response. Furthermore, the PNC identifies the needs and challenges of the patients, families and professional staff, and provides for them.
Results: To accompany and support the child and his family throughout the disease stages; from the intensive treatment phase to long term follow up or end of life.

They serve as the main point of contact for all needs: information, support, guidance, instruction and coordination. The PNC role features work according to structured treatment protocols, enabling independent work without doctor's intervention. This practice shortens and simplifies procedures, solves urgent problems, maintains child's social and academic support while connecting and coordinating all care givers in efficient use of resources within the hospital and the community.

Alongside serving as a source of information, she leads nursing research.

Hundreds of children and their families are closely cared for, nursed and accompanied in every possible way, each year at our medical center.
Conclusions: The role of the PNC enables nurses to develop clinical expertise, broaden their professional horizons and provide holistic care supported by comprehensive professional knowledge. The PNC offers useful tools to enhance adaptation of the child and his family. Focused on high quality of care, we see the establishment of our role implementing and enhancing it, our professional credo.

P-0555

EXPERIENCES OF SIBLINGS OF PEDIATRIC CANCER PATIENTS

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Purpose/Objective: The purpose of this study was to clarify the experiences of siblings of pediatric cancer patients and develop an intervention model.
Materials and Methods: Using our method, based on the philosophical method proposed by A.P. Giorgi, a phenomenological psychologist, we analyzed the data through adopting a qualitative descriptive approach and trajectory equifinality model (TEM).Siblings of pediatric cancer patients were affected both physically and mentally by their brothers' and sisters' lives under medical treatment and their parents' speech and behavior, causing the siblings to perform.As our subjects,we conducted a survey of siblings and parents of pediatric cancer patients.
Results: As our subjects, we conducted a survey of 11 people comprised of 7 siblings and 4 parents of pediatric cancer patients. As the results, we identified 394 phenomena, 66 elements, and 27 essential elements. Siblings of pediatric cancer patients were affected both physically and mentally by their brothers' and sisters' lives under medical treatment and their parents' speech and behavior, causing the siblings to perform 'self-restraint and suppression' and experience abrupt somatic symptoms.
Conclusions: The results suggested the necessity of supporting siblings of pediatric cancer patients and intervening specifically so as to allow the siblings to have places to express their feelings, establish their identity through new relationships, and 'live their own lives' by answering the questions and solving the conflicts regarding their relationships with their deceased brothers and sisters.

P-0556

NURSE LED PALLIATIVE CARE AT HOME - WEST OF SCOTLAND EXPERIENCE

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Purpose/Objective: Yorkhill Hospital's four Paediatric Oncology Outreach Nurse Specialists (POONS) provide a 24/7 palliative care on-call service for Glasgow & the West of Scotland. 81% of palliative families wished home to be the place of death for their child * did the service facilitate this?
Materials and Methods: A retrospective analysis of numbers, place of death and families choice was performed using the notes kept by the POONS. When a child or young person is deemed to be palliative, options for care - Home, Children's Hospice, Ward, Teenage Cancer Trust unit - or a combination of all - are discussed. There follows a Primary Care Multidisciplinary Meeting at the local GP surgery, attended by the Consultant and named POON (who has known the child since diagnosis) to discuss the continuing care of the patient.

On disease progression a Just-in-Case Box is placed in the house containing intravenous Cyclizine, Levomepromazine, Diamorphine, Midazolam, Hyoscine patches and buccal Midazolam; necessary sundries and a McKinley Syringe Driver. An Individualised Symptom Care Guideline & Prescription ensure timely interventions. The family is given the POONS mobile phone numbers and on-call rota. Daily visits, distances permitting, are arranged depending on the child's condition, need for parental support, changes in medication and input from community services. If the family wish the POON attends at the time of death. There is direct Consultant back-up throughout.
Results: The unit sees 70-80 new patients a year. Over the past 6 years, 475 patients were treated and there were 104 deaths (22%). Of the 78 'planned' palliative families (excluding on treatment, sudden & intensive care deaths) 63 (81%) choose home as their preferred place of death for their child. This was attained for 61/63 (95%).
Conclusions: POONS led care facilitated, with continuity and familiarity, specialist palliative care that enabled 95% their first choice.

P-0557

NURSING FOR 12 PEDIATRIC CASES OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN NEWLY DIAGNOSED TYPE 1 DIABETES MELLITUS

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Purpose/Objective: To determine the nursing effects of high-dose immunosuppression followed by autologous hematopoietic stem cell transplantation(AHST) in pediatric newly diagnosed type 1 diabetes mellitus(DM).
Materials and Methods: 12 pediatric patients with type 1 DM (aged 3-13 years) diagnosed within the previous 6 weeks by clinical findings and hyperglycemia and confirmed with positive antibodies against glutamic acid decarboxylase. Enrollment was October 2009-February2012 with observation until December 2012 at the Hematology/Oncology Unit of Children's Hospital of Fudan University. Hematopoietic stem cells were mobilized with cyclophosphamide (2.0 g/m^2) and granulocyte colonystimulating factor (10 μg/kg per day) and then collected from peripheral blood by leukapheresis and cryopreserved. The cells were injected intravenously after conditioning with cyclophosphamide (200mg/kg) and rabbit antithymocyte globulin (4.5 mg/kg). Other than some typical AHST nursing practice, for DM

patients, every step we concerned a lot witht their blood sugar lever and the toxicity reaction which they never experienced.
Results: During a 10 to 38 month follow-up, 1 patients became insulinfree, 1 patient resumed insulin use 2 years 1 month after insulinfree. Other patients are in insulin tapering. During the AHST, there were no severe nursing issues, no mortality.
Conclusions: High-dose immunosuppression and AHST were performed with acceptable toxicity in a small number of pediatric patients with newly diagnosed type 1 DM. Our nursing interventions do good work during the AHST.

P-0558

COUNSELLING PARENTS ON TREATMENT FAILURE AT BANSO BAPTIST HOSPITAL, CAMEROON

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Purpose/Objective: About 40% of our annual patients with Burkitt lymphoma are not cured, and require palliative care.
Materials and Methods: On first admission, the seriousness of the disease, investigations, treatment, need for hospital visits, follow * up, uncertainty of the outcome and available financial support are carefully explained, and informed consent for treatment is obtained from the parents of the child.

When the tumor responds to treatment, and parents rejoice, they are reminded to pray and hope for a confirmed cure one year later.
Results: On relapse, the clinical nurse practitioner, oncology nurse, chaplain and caregiver together discuss the situation with the patient and their family. Pre - treatment counselling and treatment are reviewed, the recurrence of disease confirmed, and the futility and side effects of further chemotherapy explained.

Expected symptoms (e.g. pain) are explained, and palliative care including home visits are offered. Palliative care is provided by a Burkitts lymphoma program-specific palliative care nurse.

Finally parents are questioned about their understanding of the proposed plan, and given the opportunity to ask questions and express their feelings. This is a difficult time for both the child, family and healthcare team. However, open communication and consideration of symptom management to the end of life can help ease the child and family's burden.
Conclusions: The above approach provides comprehensive family-centred care that includes the nurse practitioner as a significant team member.

P-0559

TREATMENT OF CHILDREN WITH DRUG-RESISTANT GRAFT-VERSUS-HOST-DISEASE BY EXTRACORPOREAL PHOTOPHERESIS.

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Purpose/Objective: We reviewed the clinical experience of performing extracorporeal photopheresis (ECP) for the treatment of children with drug-resistant graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation.
Materials and Methods: This is a retrospective review of children who received ECP at Queen Mary Hospital in Hong Kong since 2011.
Results: We performed ECP 79 times (discontinuous flow 16 times and continuous flow 63 times) in 3 children (body weight 26 to 35 kg) who suffered from severe extensive sclerodermatous chronic GVHD with pulmonary fibrosis (patient 1, beta-thalassemia major girl, matched unrelated stem cell transplant), steroid refractory grade 4 acute gut and liver GVHD (patient 2, AML boy, 5/6 HLA-matched unrelated cord blood transplant), and progressive bronchiolitis obliterans (patient 3, AML boy, matched sibling bone marrow transplant) respectively. Blood priming and prior hypertransfusions were required to minimize fluid shifts in these underweight patients. ECP was performed 1-3 times per week. The anticoagulant:blood ratio (heparin saline 20 units/ml) was adjusted according to the patients' hemostatic status between 8:1 to 12:1. Problems including machine failure possibly caused by poor inlet blood flow, blood clots or air in the circuits were encountered. Transient hypertension and cold sensation had been reported during discontinuous flow but not in continuous flow ECP. There were no adverse hemodynamic events noted. Patient 2 and 3 had significant improvement in their GVHD resulting in reduction of the immunosuppressive drugs. Patient 1 started ECP at a relatively late stage and she died of pulmonary aspergillosis and atypical mycobacterial infection, unrelated to the procedure.
Conclusions: ECP was well tolerated in these underweight patients by using the continuous flow photopheresis system. Technical problems are common and require trained and experienced nurses to perform the procedures. It seems to be an efficacious and safe alternative therapy for drug-resistant severe acute or chronic GVHD.

P-0560

SURVEILLANCE ON CENTRAL VENOUS CATHETER COMPLICATIONS IN PAEDIATRIC HAEMATOLOGY-ONCOLOGY UNIT

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Purpose/Objective: To determine the incidence of central venous catheter (CVC) complications in haematology-oncology paediatric patients.
Materials and Methods: This is a prospective surveillance study of the CVC complications in January 2010-June 2012. Rate of catheter-associated infection was calculated base on the Centers for Disease Control and Prevention guidelines.
Results: There were 151 CVC for a total of 36634 catheter days were monitored during the study. Patients belonged to 4 major disease groups: leukaemia/lymphoma (57%), solid tumor (27%), other hematological diseases (13%), and primary immunodeficiencies (2%). Median age of the patients was 4.5 years (range 1month -18 years). Twenty-eight catheter-associated infections were detected, with 18 CVC associated bloodstream infection (CLABSI) and 10 exit site infection (ESI). Overall infection rate was 0.76 per 1000 CVC days (0.49 for CLABSI and 0.27 for ESI). Organisms responsible for CLABSI included Escherichia coli (22%), Bacillus (22%), Coagulase negative Staphylococcus (CNS) 22%, Pneumococcus (11%), and others (22%). Organisms cultured in ESI included Methicillin sensitive Staphylococcus aureus (MSSA) ($n = 5$), CNS ($n = 4$), and MSSA and CNS ($n = 1$). Fifty-one non-infective CVC complications (0.14 per 1000 CVC days) were detected which included blockage (56.9%), slipped out (15.7%), leakage (9.8%), cuff exposure (7.8%), malposition (7.8%), and others (2.0%). Twenty-nine CVC removed before end of treatment due to infection (24%), slipped out (24%), malposition of CVC (14%), blockage (10%), leakage (10%), and others (11%).
Conclusions: Catheter-associated infections and catheter blockage were the most frequent complications in our paediatric patients with CVC. Despite of the low CLABSI rate when compared with pooled mean CLABSI rate (1.7 per 1000 CVC days) for all paediatric haematology-oncology units reported in 2010 National Healthcare Safety Network, staff training and patient education on CVC care should be reinforced to minimize infection. Moreover, continuous surveillance of the CVC complications is essential to improve infection control and quality of patient care.

P-0561

THE STATE OF DENTAL VISIT AND ORAL HEALTH CARE IN CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: To research the state of dental visits * dentists' attitude/response when they are reported patients' cancer experience, their knowledge in childhood cancer/ treatments and late effects, and managing skills for cancer survivors, how survivors manage their dental health care as well.
Materials and Methods: Mailed questionnaires to 204 survivors who live in a district (Chiba prefecture) in Japan.The questionnaire was prepared drawing on some literatures about the state of dental visits, late effects related to mouth from childhood cancer treatments, and pediatric dental health.
Results: 79 respondents including hematological malignancy. Age; 29 school children, 16 in 20's, 11 in 30's, 18 in adolescence. Time from completion of treatment; 29 are $\geq$11 years and 28 are 3 years - 10 years.

50 visit dental clinics (46 for dental check, 44 for tooth decay, 9 for hypotrophy of dental root, 9 for missing teeth and 2 for enamel hypoplasia). They reported some troubles including 'being easy to have a decay ', 'hypotrophy of dental root' 'poor secretion of saliva' and 'irregular teeth'. A 30 years old survivor reported he had milk teeth still now. 54 reported to dentists that they were cancer survivors and most of them received treatment without any uncomfortable response and uneasiness, although some were rejected treatment from the dentists or were referred to other medical institutions.

78 keep brushing teeth every day including 20 who have been careful dental health care after childhood cancer experience.
Conclusions: Need for education of dental health care to patients and their families during hospitalization.Need to give information about childhood cancer treatments and late effects to dentists because more than 60% visit dentist's office.They visit a dentist whom they used to visit before diagnosis of cancer and keep good communication with the dentist. It is important to confirm if patients have trustworthy dentist at the time of discharging from the hospital.

P-0562

UNRELATED BONE MARROW DONORS NURSE COORDINATOR

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Purpose/Objective: Stem cell transplants are a significant treatment option for curing blood and bone marrow diseases. Since 1999, Schneider Children's Medical Center of Israel has been harvesting hematopoietic stem cells from unrelated donors. In 2012 we screened 202 donors and performed 179 stem cells collections (11 of them bone marrow harvests) for the Ezer Mizion bone marrow Donor Registry.

Donors voluntarily and altruistically submit to a process that involves side effects and invasive intervention. Despite their motivation donors and their families often experience ambivalence regarding donation and its impact on their health. To better serve this unique population, a nurse coordinator (NC) position was established.

Materials and Methods: *Donor education* *Explaining the process of marrow or peripheral blood donation, providing information about management of common side effects, teaching self-injection of NEUPOGEN.

Emotional support - Telephone and face to face communication, support and encouragement throughout the process, allaying concerns of the donor and family members.

Medical procedures- Insertion of intravenous lines, support and treatment of the side effects throughout the process, coping with medical issues after the donation.

Learning * constant improvement of the donation process to ensure compliance with international standards, participation in the Transplant Unit's quality management, use of feedback from donors to improve the process.

Results: N/A

Conclusions: This model for a stem cell donation NC emphasizes the contribution of the nursing profession in this process. The NC is uniquely positioned to provide technical education and emotional support for the donor. This challenging position requires professionalism, familiarity with the most recent research literature and the ability to match the right process to each donor, while complying with international standards.

P-0563

HEALTH TEACHING AS A NURSING TOOL TO EDUCATE PARENTS AND CAREGIVERS ON INFECTION PREVENTION AND CHILD CANCER

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Purpose/Objective: Health Teaching is an integral part of nursing care in specialized and multidisciplinary settings like pediatric oncology. This study describes the health education sessions conducted by pediatric oncology nurses at the Southern Philippines Medical Center Children's Cancer and Blood Diseases Unit (SPMC-CCBDU).

Materials and Methods: Health education sessions are conducted weekly for parents and caregivers at SPMC CCBDU using powerpoint presentations. The health education lectures are in English and translated to the vernacular dialect by pediatric oncology nurses conducting the lectures. Participants are encouraged to ask questions and important points on hygiene and sanitation to prevent infection are emphasized. An attendance sheet is collected to record number and names of participants.

Results: There were 289 patients/caregivers who attended the health teaching sessions from January to December 2012. The lectures compose basic personal cleanliness for patients and caregivers; hand hygiene; food choices, handling and preparation; waste disposal and child cancer information.

Conclusions: Structured health teaching lectures can be conducted by nurses as part of regular pediatric oncology activities to promote infection prevention and child cancer education. The use of feedback forms is recommended to assess parent/caregiver understanding and response as well as parameters to measure the impact of these lectures in future studies.

P-0564

ADAPTING THE INNOVATIVE UNIT SPECIFIC GUIDEBOOK AND TECHNOLOGY IMPROVES WORK SATISFACTION AND EFFICIENCY FOR PEDIATRIC HEMATOLOGY/ONCOLOGY/BMT NURSES.

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Purpose/Objective: Adapting the Innovative Unit Specific Guidebook (IUSGb) framework, as a mobile resource tool to improve nurse satisfaction and efficiency in the clinical nursing practices areas, specific to a Pediatric Hematology/Oncology/Bone Marrow Transplant (BMT) Unit.

Materials and Methods: The IUSGb is a paperless guide providing unit specific comprehensive information to the target users. By structuring this framework to house in touch screen and mobile devices, allows the use to be accessible within and outside of the clinical practice units, allowing time to retain information. By adding hyperlinks to abstracted data linked to visual cues, allows for quicker access to institutional resources, therefore changes the way the user interacts with the device and content.

IUSGb to include relevant content to clinical nursing practices on a Pediatric Hematology/Oncology/BMT Unit:

1. Collaborative and reduction of Central Line Associated Blood Stream Infections (CLABSI) with Central Line Care Bundle on a Pediatric Hematology/Oncology/BMT Unit
2. Line set up and administration of hazardous/chemotherapy medications
3. Handling and waste of hazardous materials with personal protective equipment (PPE)
4. Isolation Precautions and decision trees
5. Administration of common IV medications used on a Pediatric Hematology/Oncology/BMT Unit
6. Blood product lines and administration
7. Standardized Nursing Intervention on a Pediatric Hematology/Oncology/BMT Unit

Results: Information and communication technology can help be efficient at work. Response (61): strongly disagree 0% (0), disagree 0% (0), moderate 6.56% (4), agree 49.18% (30), strongly agree 44.26% (27).

Information, communication, and preventive technology can improve work satisfaction. Response (65): strongly disagree 0% (0), disagree 1.54% (1), moderate 18.46% (12), agree 46.15% (30), strongly agree 33.85% (22).

Conclusions: Adapting IUSGb on mobile devices and technology can improve work satisfaction and efficiency by providing information easily accessed by nursing staff within and/or outside of the clinical nursing practice areas.

P-0565

A GLOBAL WEB-BASED PROGRAMME ABOUT CANCER IN LANGUAGE SPECIFIC FOR STAFF, A SICK CHILD AND THEIR FAMILY

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Purpose/Objective: To have expert paediatric oncology nurses to inform and explain childhood cancer diagnoses, treatments, side effects, situations and feelings, by developing a web-based programme.

Materials and Methods: The programme will be developed and tested in three steps. Step 1 is to develop a web portal with animated pictures of cancer themes based on the 'See Hear Do' programme in Sweden and Norway. Step 2 is to add text and audio in several languages for each theme (such as Arabic, English, Spanish). Step 3 is to develop two informational sections on the web portal: one section for staff and for the patient and family. The staff, children and families will evaluate each section as appropriate before the programme is published on the web portal. A participatory design method is going to be used. The programme will also be offered to nurses in the International Society of Paediatric Oncology and nursing working group of the Pediatric Oncology in Developing Countries committee for translation into their native languages.

Results: Expected result is that the web portal can easily be downloaded via computer, iPad or mobile and can be used twofold. Staff can use this programme for self-education and for working with the child and family. The child and family can use the web programme in various situations during the child's cancer treatment, e.g., explaining the diagnosis to family members, schoolmates, families' networks, during phone calls using an interpreter or for persons with a visual or auditory disability.

Conclusions: Goal of the project is to globalize childhood cancer education and information with a web-based programme including pictures, text and audio in various languages. The programme is designed to consider the professional's information and the child and family's needs and participation. The active role of all stakeholders to ensure cultural relevance is key to this project.

P-0566

NURSING ORIENTATION IN PEDIATRIC ONCOLOGY: A COLLABORATION BETWEEN BUENOS AIRES, ARGENTINA AND HANNOVER, GERMANY

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Purpose/Objective: Following the SIOP 2012 meeting, two nurses (one from Argentina and one from Germany) began collaborating on the development of a pediatric oncology curriculum module for nursing orientation in low- and middle-income countries (LMIC). The Hospital Garrahan in Argentina is a tertiary pediatric hospital with approximately 350 children diagnosed with cancer annually. Since the number of patients is increasing, more nurses are hired, but generally lack knowledge about caring for children with cancer.

Annually, in Hannover Medical School (MHH) in Germany approximately 100 children are diagnosed with cancer and only two new nurses are hired.
Materials and Methods: At present, new Garrahan nurses are given a written guide to the procedures and rules of the institution; didactic classes are divided in five modules (45 minutes bimonthly) for three months. Other days are practical clinical work with a nurse mentor. Garrahan nurses also cooperate in pediatric oncology nursing training in a northern Argentinean hospital. In the MHH, nursing orientation is 2-6 months and clinically based as one-to-one training. Didactic teaching is offered as needed. The orientation guideline includes links for diagnostic information and nurses have access to all protocols.
Results: Currently, the Garrahan Hospital is in the initial phase of their orientation program due to dramatic increase in patients. Consultation with a long-time pediatric oncology nursing educator at MHH is on going and an evaluation of the pilot nursing training module at Garrahan is expected in September.
Conclusions: The orientation of new nurses is challenging in Argentina (and also in many LMIC where specialization education is non-existent), particularly since the service is expanding for another three years. We believe that this collaboration with MHH to develop and test a new orientation module will strengthen the programs in both sites and provide a model for other LMIC to adapt for their local context.

P-0567

THE EVALUATION OF THE TV CONFERENCE SYSTEM (TVCS) WITH THE NET TO LINK THE HOSPITAL CLASS AND THE REGULAR SCHOOL CLASS OF CHILDREN UNDERGOING CHEMOTHERAPY

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Purpose/Objective: The aim of this study was to evaluate the TV Conference System (TVCS) with the Net to link a child undergoing chemotherapy, who was enrolled in the hospital class, and his/her classmates in regular school, and to evaluate relationship of class development through the TVCS.
Materials and Methods: Research period: March 2009 to Jan. 2013. The 2 classes in the regular school and in the hospital were linked by optical broadband network on the TVCS over period of 3 to 5 months. We conducted 30-minutes interview for 5 children, their mothers and teachers.
Results: The participant ware 6 to 9-year-old males/girl who ware undergoing chemotherapy for tumor or leukemia. Intervention began at the point where they transited from bedside learning to walking to the hospital classroom. The TVCS linked their home classmates allowing them to talk via the TV screen. Such sessions as enjoy talking time and recorder playing were held. In total, 3 to 9 sessions were held. Evaluation by their parents: Initially, they were worried about When and how to contact with school, but was happy to be able to see friends from his/her classmates. After leaving the hospital, he had no problems in relations with friends, and enjoys playing and participating in other activities with classmates. Evaluation by their teachers: All of the teachers had never experiences take care of children with cancer. After used TVCS, they are pleased very much, and the operation of the machine was very easy.
Conclusions: The establishment of bidirectional system strengthened communication between the school and hospital. Parents and teachers evaluated the TVCS with satisfaction. Children were able to participate in classes in his regular school via the system facilitated friendships and reduced psychological isolation from the school, enabling him/her to form an image of returning to school after leaving hospital.

P-0568

EDUCATION WITH A SUPPORTIVE TWIST– EXPERIENCE SHARING BY A CLINICAL NURSES EDUCATOR

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Purpose/Objective: Utilizing adult learning model to deliver consistent professional education along with psychosocial and spiritual support to paediatric oncology nurses in Children's Cancer Centre (CCC). Assist healthcare professionals in decreasing the sense of burnout, exhaustion and depersonalization from stressful and challenging working environment and help improve job satisfaction.
Materials and Methods: The key differentiator between this plan and other education methodologies in use today is the combined delivery of Education and Psychosocial Support through segregated sessions (in co-operation with the psychosocial service team at least thrice a week). The plan is carried out in four stages and delivered over a period of five months.

Stage1: Collection of topics of interest from every nurse in the ward through E-mail or through anonymous entries on survey posters. Allowing nurses to select topics of interest to them and request experts in those fields to lecture;

Stage2: Finalizing topics and speakers engagement;

Stage3: Scheduling 45 minute sessions per day for five days a week with appropriate re-occurrences. Time management is important due to the 24×7 work environment.

Stage4: Feedback collection.

The topics covered were diagnosis, treatment regimes, clinical interventions, case study, pharmacological update, nutrition issues and technology skills updates.
Results: Overall 95% of in service sessions were successfully delivered. Although feedback at the start received regarding topics arrangement was 22% of nurses being uncertain. At the end of project however it changed to 90% of nurses being satisfied with the change and support provided. Most importantly, the nurses are now keen to participate in education sessions as their ongoing professional development.
Conclusions: This project provided opportunities for nurses to prioritize their education needs in order to improve their professional skills in conjunction with psychosocial support. It also empowered them to prudently deal with everyday challenges.

P-0569

KNOWLEDGE, ATTITUDE AND PRACTICE METHODS ON PAIN: SURVEY ANALYSIS AT CHILDREN CANCER HOSPITAL KARACHI PAKISTAN

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Purpose/Objective: To assess knowledge, attitude and practice of health care team about pain assessment and management at Children Cancer Hospital Karachi (CCH) Pakistan.
Materials and Methods: A survey was done on 20 members of health care team including doctors (4), nurses (10) and nurse technician (6) through a structured questionnaire focusing on knowledge and attitude about pain. Practice review was done by close audit of files of patients
Results: According to the data collected, 18/20 (90%) of the staff at CCH was aware of pain assessment. 100%, 50% and 16.7% doctors, nurses and technicians respectively said to have sufficient skills to assess pain. Pain was recognized as fifth vital sign by 18/20 (90%) staff. They all also agreed that pain control is the primary objective in patient care. 17/20(85%) agreed to intervene on every pain complain of pain. 70% re-assess pain score after administration of pain killer while 30% do not. 50% staffs were of the view that patients get addicted if narcotics are used. Only nurses and technicians concluded that morphine causes respiratory depression. 40% did not agree that morphine could be used safely
Conclusions: The hospital staff at Children Cancer Hospital is aware of pain assessment but technician need further training to be competent. Suitable drugs are available for proper pain management, but myths related to morphine needs to be eliminated to improve pain management.

P-0570

LOW COST INNOVATIVE SIMULATORS FOR SKILL TRAINING OF HEALTH CARE TEAM IN RESOURCE LIMITED INSTITUTE

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Purpose/Objective: Children Cancer Hospital (CCH) is a tertiary care hospital dedicated to treat children with cancer free of cost. Its 28 bedded hospital with census of 60 patients/day for day care chemo and an out-patient clinic of 80 per day. Capacity building is one of the main focus of CCH .With My Child Matter Grant of UICC we have started several educational courses for nurses and doctors .Clinical skills are basic part of nursing profession and teaching. It requires several resources including mannequins and models but they are too expensive for institution like us. Single mannequin for naso gastric tube insertion cost about 680$ (aprox)and above and buying simulator for every skill teaching will cost several thousand dollars.
Materials and Methods: We have created our own simulators in very low cost. For N/G insertion we searched the web for appropriate picture had it printed on panaflex 2×4 feet, pasted it on a thermo pole sheet. GI track was compressed to accommodate tube then had it framed with plastic cover. It costed us only 4$. For I/V cannulation and Port-a-cath needle insertion practice we brought a cotton filled soft doll, placed I/V tubing's in limbs and stitched it inside which served as veins and in same doll Port-a-cath was stitched in left upper torso Commercial simulator cost 425$(I/V) our cost was 5$
Results: We have used low cost self made simulators very effectively for skill training of our nurses. Up till now 285 students have been trained on these manikins.
Conclusions: Clinical skills teaching requires demonstration and return demonstration on simulators and manikin's. Commercial manikins are too expensive for a low resource teaching institute .Few innovative and creative ideas reduced the expense to minimal and several groups of students are taught skills on self made simulators.

P-0571

TOXIC DEATHS AMONG CHILDREN TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA AT CHILDREN CANCER HOSPITAL PAKISTAN.

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Purpose/Objective: To document rate and causes of toxicity death among children treated for acute lymphoblastic leukemia at children cancer hospital Pakistan.
Materials and Methods: Charts of all newly diagnosed children treated for Acute Lymphoblastic Leukemia from Jan 2008 to Dec 2012 were reviewed. Causes of death were documented to find rate and causes of toxic deaths.
Results: Total registered patients of acute lymphoblastic leukemia at children cancer hospital were 449 during the period of five years. Total mortality was 31% (152,) toxicity 18% (88). Among toxic deaths infection was major cause (88%). Majority infections were related to bacterima and septicemia. However 8 deaths were due to chicken pox and measles and 11 children died to fungal infections. The yearly toxic deaths were 2008 19%(13/67), 2009 24% (17/71), 2010 22% (20/91), 2011 19% (24/124), 2012 15% (21/141). There has been decline in infected mortality
Conclusions: Toxic death in our study is very high. This could be due to multiple challenges associated with cancer care in developing countries like, illiteracy, poor socioeconomic condition, compromised hygiene, malnutrition, and distance from treatment center and overcrowding. Mortality rate could be reduced by improving supportive care,, intensive health education of patients and parents comprehensive multidisciplinary team approach and satellite centers.

P-0572

NURSING CARE ISSUES DURING 131I-MIBG TREATMENT FOR ADVANCE NEUROBLASTOMA

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Purpose/Objective: ^{131}I-MIBG treatment is a target therapy for advanced Neuroblastoma. ^{131}I-MIBG kills neuroblastoma cells by binding MIBG to a radioactive isotope of iodine (^{131}I) and then administer to the child intravenously. The safe care for patients and exposure to radiation of caregivers imposed challenges on caring of these patients.
Materials and Methods: From 2003 to 2013, 23 patients aged between 25 months to 15 years old underwent ^{131}I-MIBG treatment. All patients received a standard dose of ^{131}I-MIBG 12 mCi/kg.

After the^{131}I-MIBG infusion, the patient was isolated for 5 to 7 days due to radioactive burden. Detail explanations and instructions were given to the caregiver when taking care to the patient. They would use a radiation dosimeter to measure radiation dose they were exposed. Lead apron, shielding and full personal protective equipment would also be used. Treatment side-effects and radiation exposed through different nursing procedures were evaluated.
Results: Nurses would provide food to the child routinely and emptying the urine bag at the same time for all the patients, the highest dosimeter reading was 48 μSv. Within 23 patients, 4 had vomit during the procedure, when nurses were handling the vomitus, the highest dosimeter reading was 134 μSv. Diarrhea was affecting 9 patients, the highest dosimeter reading was 60 μSv when changing napkin. 2 of the patients fever during the procedure, 164 μSv was the highest measured dose when caring the patient.
Conclusions: The I-131 MIBG treatment was well tolerated by patients. Care focus on patient's comfort, management of side-effects, radiation precautions and safety of both patient and caregivers were vital. The radiation exposure measured was within safety for health care providers. The patient safety and staff occupational safety were ensured.

P-0573

A STUDY ON CHILDREN RETURNING TO THEIR ORIGINAL SCHOOLS ON THEIR RELEASE FROM HOSPITAL AFTER TREATMENT FOR CANCER

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Purpose/Objective: A long-term hospital stay for treatment with chemotherapy, radiotherapy and surgical remedy is necessary for children with cancer. Most of children at school age change their school to the hospital school in Japan. Therefore, children at school age may often encounter the difficulties such as delay of the school study, poor physical activity, psychological disturbance by changed appearance, when they return to their original school. The purpose of this study is to clarify the contents and correlation of difficulties at hospital school and after returning to their original school, and to obtain the suggestion for smooth returning to their original school in children with cancer.
Materials and Methods: We investigated by the questionnaire to guardians of children with cancer in Aichi prefecture, Japan. The investigation period was from October 2009 to March 2010. The questionnaire consists about patient's background, hospital stay period, hospital school life, and difficulties of school life in the hospital and at the original school after release from hospital.
Results: One hundred and four guardians whose children with cancer at school age or older answered the questionnaire. Patients' average age was 12.7 years old (SD 3.58 range 6-20), The duration of hospital stays were 8.4 months on the average (SD7.08 range 1-60). Difficulties of school life in the hospital correlated to loss of connection with the teacher of original school, to loss of communications with the classmates, and to discontinuous study in the hospital.
Conclusions: The connection with the teacher of original school, the connection with the classmates, and the continuous study in the hospital are very important for children with cancer to smooth returning to their original school. It is necessary to look for the ideal way of good communication between the hospital school and the original school.

P-0574

SEARCH FOR A GOOD FIT BETWEEN NURSING PRACTICE AND ELECTRONIC NURSING RECORDS: BENEFITS AND LIMITATIONS OF NURSING RECORDS ON A PEDIATRIC HEMATO-ONCOLOGY WARD.

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Purpose/Objective: Nowadays, electronic charting is widely used in healthcare. The electronic patient file has been introduced on our ward since May 2011 to improve workflow and quality of documentation.

Two years after implementation, the benefits and limitations of electronic nursing records are identified. This will contribute to the accurate selection of a future electronic system in our hospital.
Materials and Methods: Benefits and limitations are gained by individual interviews with all nurses on the pediatric hemato-oncology ward. Simultaneously, a retrospective analysis of 20 electronic nursing records during a two-week period is performed.
Results: The obtained patient information is correct, actual, traceable and linked to electronic medical records, imaging, online databases and lab results. It improves standardization and uniformity within the hospital. Although trends and graphics of some important vital signs are available, more extended data extraction is devious and an adequate search function is lacking.

Different health-care providers in the hospital have access to all relevant patient information without re-questioning the patient, which simplifies communication and consultation and facilitates decision making.

Retrospective analysis of nursing records revealed a lack of structure and difficulties to get a quick general view of the patient's condition and needs.

The use of electronic nursing records results in a fragmentariness of care items which results in incomplete nursing records and is time-consuming. This is mainly due to gaps in the electronic system: input of essential data is not exceeded over time and has to be completed upon each admission.
Conclusions: The results of this survey indicate that the workflow can be improved on our ward. Progress in this area is strongly recommended in our future electronic nursing platform as this is an important daily used tool for accurate patient care.

ABSTRACT SUBMISSION: PUBLICATION ONLY

PUB-0001

CLINICAL FEATURES AND PROGNOSTIC SIGNIFICANCE OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA WITH E2A/PBX1 FUSION GENE

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Purpose/Objective: To explore the clinical characteristics and prognosis of childhood acute lymphoblastic leukemia (ALL) with E2A/PBX1 fusion gene.
Materials and Methods: The E2A/PBX1fusion gene was detected by reverse transcription *polymerase chain reaction (RT-PCR).E2A/PBX1 was found in 20 pediatric patients with ALL,accouting for 4.76% in total 420 patients since Jan. 2006 to Dec. 2011 in our hospital.According to the risk stratification of ALL, patients with E2A/PBX1 gene were classified as intermediate risk. 85 cases with negative E2A/PBX1 gene in ALL from intermediate risk group were regarded as control group. Clinical characteristics, event-free survivial (EFS) rate and over all survivial (OS) rate by Kaplan-Meier curves were compared.
Results: No statistic difference was found in the distribution of age,gender ratio,initial leukocyte count. The 5-year EFS rates of two groups were (84.4 $\pm$ 15.6)% and (73.5 $\pm$ 15.6)% respect tively,and the OS rates were (86.0 $\pm$ 17.6)% and (81.8 $\pm$ 17.6)% respectively ($P > 0.05$).Their relapse rates was 10.5% and 12.8% respectively ($P > 0.05$).
Conclusions: There was no significant difference between E2A/PBX1 gene postive and negative group in pediatic B-ALL.E2A/PBX1 gene is not regarded as a bad factor in clinical risk stratification for pediatric B-ALL.

PUB-0002

GASTROSTOMY PLACEMENT IN VERY HIGH NUTRITIONAL RISK PAEDIATRIC ONCOLOGY PATIENTS – A RETROSPECTIVE AUDIT

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Purpose/Objective: Medulloblastoma, primitive neuroectodermal tumour (PNET), osteosarcoma, or oro-nasopharyngeal tumours are considered very high nutritional risk diagnoses due to the toxicity and duration of their treatment. The audit aims were to determine if this patient group initiated artificial nutrition using nasogastric tubes (NGT) when they reached their predetermined lower weight limit (typically ∼5% weight loss), and were given a gastrostomy within 2-months from diagnosis, in line with local standards.
Materials and Methods: Data was collected from dietetic record cards on patients diagnosed between January 2010 and December 2011, who received active treatment with a curative intent. Diagnosis and anthropometry data (age, gender, weight height, BMI) was collected at various time-points (at diagnosis, pre-gastrostomy placement, 2-months, 4-months, 6-months post-gastrostomy placement, end of treatment). Anthropometry data was compared to World Health Organisation (WHO) descriptors for malnutrition.
Results: Ten patients were labelled for this audit. There was no missing data. Mean age at diagnosis = 9.8years (SD = 4.6years). Eighty percent were diagnosed with medulloblastoma, 20% with osteosarcoma. Ten percent were malnourished at diagnosis. All 10 patients required NG feeds, but only 70% had a gastrostomy inserted, and only 30% had a gastrostomy inserted within 2-months of diagnosis. Eighty-six percent of these patients experienced >5% weight loss prior to gastrostomy insertion, even with NGT feeding preceding their gastrostomy. Having a gastrostomy stabilised their weight, but weight loss was not fully recovered.
Conclusions: Gastrostomy placement delays included neutropaenia or acute illness. Our sample size was small, but other larger studies which compare proactive enteral feeding versus reactive enteral feeding support show that early intervention results in less unintentional weight loss. Our results suggest that a reactive approach to initiating NGT feeds is not effective at preventing weight loss, yet a gastrostomy may be more effective. So it has been proposed that this patient group have a gastrostomy inserted at diagnosis.

PUB-0003

A PROFESSORSHIP AND PROGRAM OF RESEARCH IN CHILD AND FAMILY CENTRED CANCER CARE

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Purpose/Objective: Illness is a family affair and no more so than in pediatric oncology. When a child is diagnosed with cancer, the family is handed a diagnosis in which no member goes unaffected, unchanged, or untouched. A child diagnosed with cancer is a *family* experiencing cancer. While commendable research in the natural and biological sciences has resulted in significant decreases in morbidity in childhood cancer, long term cure, and exponential longevity of life, the experiences of family members and ways in which health care professionals can be most effective in mitigating family and child suffering has received relatively smaller attention in the research arena.

There are many research questions and objectives in this qualitative program of research but, at the heart of each, is the intent to understand and mitigate child and family suffering in childhood cancer.
Materials and Methods: Dr. Nancy Moules has developed a program of qualitative research in family, relational, and psychosocial study in pediatric oncology and has a group of masters and doctoral students who have joined her. She has been awarded the first Nursing Professorship in Child and Family-Centred Cancer Care, a joint collaborative between Calgary, Alberta, Canada's Alberta Children's Hospital Foundation, Alberta Children's Hospital Research Institute, and the University of Calgary. In this presentation, I describe the purpose of the Professorship, its groundbreaking mark on recognizing family nursing research, studies in progress and in application, and research studies that are being enacted by doctoral students who are being funded by Alberta Children's Hospital Foundation. Methods for each will be described.
Results: All studies completed, in progress, and in application will be described along with completed and emerging findings.
Conclusions: Understanding the impact of childhood cancer on the family system and the larger system is an obligation of nurses, which must then translate to practices and innovations that make a difference.

PUB-0004

SEXUALITY AND ADOLESCENTS WITH CANCER: THE REFRACTIVE CAPACITY OF THE DISEASE LENS

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Purpose/Objective: During adolescence, a large portion of self-esteem is derived from the active crafting of sexual identity. Cancer treatment regimes may compromise individual physical appearance, self-esteem, body image, and emerging sexuality. For adolescents with cancer, establishing a positive sexual identity is further complicated by obtaining sexual health knowledge, developing interpersonal relationships, and dealing with body image concerns in a manner that is not typical of peers without cancer. How sexuality is conceptualized and practiced by this population is poorly studied and understood, and even more poorly addressed in practice.
This project is two faceted. It involves a pilot study seeking advice from adolescents about how to best approach other adolescents with cancer. At the heart of this pilot study is the intent to discern how best to approach adolescents with cancer around the potentially sensitive, disquieting, and often even taboo issue of sexuality.
The goal of the larger study is to discern knowledge of the topic that will help to provide a counter-discourse or alternate view of the body to the one offered to us through the disease lens. As a result, clinicians will gain access to insights that can promote sensitive, effective therapeutic working with young people with cancer.
Materials and Methods: The pilot study involved the use of focus groups and the larger study has a mixed qualitative design using hermeneutics and narrative inquiry.
Results: Completed results of the pilot study and emerging results of the larger study will be available for discussion in this presentation.
Conclusions: Sexuality and the development of a sexual identity is a pivotal issue and task in adolescence, and a cancer experience can offer a refractive lens that have effects lasting into adulthood. Understanding how to best address this issue with adolescents experiencing cancer is an obligation in pediatric oncology.

PUB-0005

COPING WITH THE EXPERIENCE OF HAVING A CHILD WITH CANCER; A LEBANESE PERSPECTIVE

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Purpose/Objective: To gain more in depth understanding of the coping strategies of Lebanese parents with a child with cancer.
Materials and Methods: Purposeful sampling and saturation principles were followed in which 12 parents of a child were interviewed. Data were analyzed following the Utrecht School of Phenomenology.
Results: Five core themes emerged describing the coping strategies of Lebanese parents with a child with cancer: The communication style; couple's relationship; social/family support; dependence on God and sibling's reactions.
Conclusions: Results cannot be directly generalized, but they could act as a basis for additional research on which to base a development of a structure for an approach to care that endorses coping processes in Lebanese parents with a child with cancer.

Nursing and medical staff need to be conscious of parent's coping strategies and its impact on the interaction process between the family and the health team and the family dynamics.

PUB-0006

NEGATIVE ASPECTS OF SUBCLAVIAN CATHETERS IN PEDIATRIC ONCOLOGY: SHOCKING ASIA.

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Purpose/Objective: Catheterization of subclavian vein - a common but dangerous procedure that requires the use of general anesthesia in children. Unfortunately, in Russia, it is the most popular way of chemotherapy.
Materials and Methods: From 2008 to 2013 we observed 1857 cancer patients aged 2 months to 17 years, who were installed 4428 subclavian catheters for the purpose of chemotherapy, that is, each patient had 2.3 catheterizations of subclavian vein
Results: The operating time of catheters ranged from 2 hours to 13 months. The minimum time is explained by frequent self-removal of a catheter by children - 348 cases (7.85%). From the first attempt we managed to puncture the subclavian vein in 3117 cases (70.4%), of which the successful catheterization rom the first attempt succeeded in 2650 patients (85.0%), from the second - 127 (4.0%), 340 (10.9%) required repeated puncture of the subclavian vein. In 543 cases (12.2%) we managed to perform catheterization of the subclavian vein only from the third attempt. In 32 cases (0.72%) catheterization of subclavian vein failed. In 613 cases (13.8%), there was migration of the distal end of the catheter to the internal jugular vein in 74 (1.67%) * to subclavian vein on the opposite side. Pneumothorax complicated catheterization in 29 cases (0.65%), the injury of the lung - in 7 (0.15%). Unintentional puncture of the subclavian artery was observed in 234 cases (5.28%). Catheter-related bloodstream infections developed in 316 (7.14%), catheter thrombosis - in 1832

(41.3%) that in 1213 cases (66.2%) required replacement. The destruction of the subclavian catheter outer part was noted in 43 cases (0.97%).
Conclusions: Taking into the account that chemotherapy usually lasts for at least 3 days with an interval of 21 days, using a subclavian catheter is not appropriate and is accompanied by many complications. In this case, the internal jugular vein catheterization is safer and easier done.

PUB-0007

LYMPHOPROLIFERATIVE DISORDERS AFTER INFANTILE RENAL TRANSPLANTATION

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Purpose/Objective: Despite the high frequency of liver transplantation in infants, there is data scarcity on the special characters of posttransplant lymphoproliferative disorders in liver transplant patients (LTPTLD). In the current study, we aimed to analyze special features and behavior of PTLD arising after infantile liver transplantation.
Materials and Methods: A comprehensive search of the literature was conducted for the available data on PTLD in infantile liver recipients (infLTPTLD) through Pubmed and Google scholar search. Infant was defined when a liver recipient was below 2 years of age at the time of transplantation. Overall 205 cases of LTPTLD (100 infLTPTLD) were found from 24 reports and were compared to pediatric and adult LTPTLD.
Results: Lesions in infLTPTLD patients were significantly more likely of polymorphic type while monomorphic lesions were more prevalent among patients of older age groups (Table 1). Remission rates, metastasis frequency and organ involvements were not different between the groups. Death at the end of follow up was significantly less among infLTPTLD patients ($p = 0.030$); although survival analysis did not show any significant difference ($p = 0.1$).

TABLE 1. Histopathological evaluations of the study groups.

Variable	Infant	Pediatric	Adult	Sig.
Histopathology				0.036
Early lesions	4 (8.3)	3 (5.6)	0	
Polymorphic	32 (66.7)	28 (51.9)	7 (35)	
Monomorphic	10 (20.8)	20 (37)	13 (65)	
Hodgkin's Dis.	2 (4.2)	3 (5.6)	0	

Conclusions: PTLD arising in infantile liver recipients are of more benign histopathological features, and may represent better outcome. Further studies with prospective approach are needed for confirming this data.

PUB-0008

DRUG-DRUG INTERACTION BETWEEN METHOTREXATE AND LEVETIRACETAM IN A CHILD TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: Seizures may occur in patients treated for acute leukemia (8*13%). However, an optimal anticonvulsant therapy regimen with respect to ongoing oncologic treatment has not yet been established. Levetiracetam could be used because of its low protein-binding affinity and the absence of an enzyme induction effect, but there are few reports of its use during chemotherapy. We report a case of methotrexate (MTX) intoxication, probably due to a drug interaction with levetiracetam.
Materials and Methods: A 15-year-old male was treated for a B-cell acute lymphoblastic leukemia according to the French FRALLE protocol. One day after the 7th intrathecal injection of MTX, generalized seizures occurred. Cerebral MRI and CSF were normal. Levetiracetam was started at 15 mg/kg/day b.i.d. At the end of the third MTX infusion (5 g/m2/24 hour), uncontrollable vomiting, renal failure, and high blood pressure occurred. Serum creatinine level and MTX serum levels increased. Neither hyperkalemia nor hepatic cytolysis was observed. Only ondansetron and metopimazine were concomitantly given to treat vomiting as in previous courses. Renal function was normal prior administration and there was no third-space fluid effusion.
Results: A rescue procedure was carried out and levetiracetam was switched to clonazepam. Because renal function did not improve, carboxypeptidase G2 was given on the 4th day, which resulted in a rapid decline in blood MTX level and progressive improvement in serum creatinine clearance. Renal function recovered entirely after 22 days. Due to this intoxication, MTX infusions were stopped.
Conclusions: We prescribed levetiracetam because of the lack of albumin binding and previously no reported significant pharmacokinetic interactions. Careful monitoring of MTX levels when several drugs are given concomitantly with MTX should be done, even if no interaction has previously been reported for those drugs. This case describes for the first time a potential drug*drug interaction between levetiracetam and MTX.

PUB-0009

OUTCOME OF ACUTE LYMPHOBLASTIC LEUKEMIA INTERCONTINENTAL BFM 2002 IN CHILDREN DIAGNOSED IN IRAN: RESULTS FROM A SINGLE CENTER

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Purpose/Objective: ALL IC-BFM 2002 is one of the most successful protocols for improving outcome of children with ALL. The trial evaluated the impact on outcome of intensified late re-induction in the context of newly developed risk stratification with some modifications.
Materials and Methods: From March 2007 to April 2012, 61 eligible patients aged 1-16 yrs with newly diagnosed B-precursor ALL were enrolled in this trial. Stratification into 3 risk groups was based on the protocol. After induction and consolidation phase, they were randomized into group A ($n = 32$) and B ($n = 29$). Standard and intermediate/high risk (HR) Group B patients were received protocol III two and three times, respectively. They received maintenance phase according to the protocol. Protocols II x 1/ x 2 were prescribed to standard/intermediate and high risk group A patients, respectively; then, conventional oral methotrexate/6-mercaptopurine maintenance therapy with vincristin/prednisolone (every 35 days) and intrathecal methotrexate (every 105 days) was used. Maintenance phase was continued 18 months for females and 24 months for males in this group.
Results: There was no significant difference between both groups for age distribution and median follow-up. Ten of all enrolled patients were HR (7 in group A and 3 in group B). With median follow-up 31.50 months (range 6-67), the estimated 4-yr Relapse free survival (RFS) was $86.10 \pm 7.60\%$ and estimated 4-yr Overall survival (OS) $98.30 \pm 1.70\%$ for all enrolled patients. There was no significant difference between OS of group A and B (100% vs. $96.40 \pm 3.5\%$, $p = 0.3$), but RFS of group A was significantly better than that of group B (100% vs. $62.8 \pm 19.60\%$, $p = 0.01$).
Conclusions: The IC-BFM 2002 protocol dramatically improved outcome of children with ALL. It appears that protocol II as late re-induction is significantly more effective than protocol III to improve outcome and decrease relapse.

PUB-0010

TRAJECTORY OF PSYCHOLOGICAL MORBIDITY FOR CHILDREN AND ADOLESCENTS WITH CANCER

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Purpose/Objective: To describe the psychological symptoms reported by cancer patients who were between 10 and 18 years of age.
Materials and Methods: 24 children (mean age, 14 ± 2.7 years; 63%, males) diagnosed with hematological malignancy (67%) and solid tumor (33%) were enrolled for analysis. Data were collected before commencement of chemotherapy (time 1), at 2 months from time 1 (T2), and at 4 months from time 1 (T3). Measuring instruments included the Memorial Symptom Assessment Scale Pediatric 10-18 (MSAS) and the Short-Form State Anxiety Scale for Children (SAI-C).
Results: 50%, 33%, 29% and 25% of the children reported feelings of sadness, feeling nervous, worrying and feelings irritable, respectively, at baseline. Feelings of sadness, feeling nervous and worrying decreased to 8%, 8% and 13%, separately, at T3. Feeling irritable was consistently common at T3 (21%). The median symptom scores ranged from 0.96 (IQR 0 * 1.8) for feelings of sadness to 0.61 (IQR 0 * 1.27) for feeling nervous at baseline, and in a descending pattern over time. The median scores for the MSAS Psychological (PSYCH) and Global Distress Index (GDI), and SAI-C were 0.65 (IQR 0.23 * 1.13) and 0.87 (IQR 0.40 * 1.17), and 14.5 (IQR 14 * 18), respectively. The PSYCH and GDI scores decreased significantly over time ($p < 0.05$). There were moderate correlations between feelings of sadness and feeling irritable at T1 ($r = 0.5$, $p < 0.01$), at T2 ($r = 0.6$, $p < 0.01$), and at T3 ($r = 0.6$, $p < 0.01$). Significant moderate to strong correlations were noted between PSYCH, GDI and SAI-C scores across the study time points ($r = 0.41 * 0.81$, $p < 0.05$)
Conclusions: Psychological symptoms are prevalent to children and adolescents after diagnosis with cancer but are in a descending pattern over time. These findings have implications for the continuous assessment of psychological symptoms and the need for psychological supportive care.

PUB-0011

A RARE CASE OF SECONDARY ACUTE MYELOID LEUKEMIA IN A CHILD WITH RETINOBLASTOMA

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Purpose/Objective: Secondary neoplasms in children with retinoblastoma are not uncommon. But, Acute Myeloid LEUKEMIA (AML) is infrequently reported second neoplasm, commonly after adjuvant therapy. We would like to report a case of AML occurring in a child with retinoblastoma who did not receive any adjuvant therapy either radiotherapy or chemotherapy.
Materials and Methods: A nine year girl presented with fever, pallor, skin bleeds of 2weeks. She was evaluated and found to have hemoglobin of 8gm%,total leukocyte count of 30,000 and platelets of 20,000. Bone marrow examination showed evidence of myeloid blasts,cytochemistry revealed MPO positive. Immunophenotyping showed AML M2. FISH for 11,22 translocation was positive. Parents gave a history of left eye enucleation at the age of 1year for a Tumor. She however did not receive any adjuvant chemo or radiotherapy. She wa well for 8years in between. She was started on induction with 7 + 3regime. She attained remission after day 25. She received consolidation with high dose cytarabine.
Results: Secondary AML is well known after chemotherapy. Secondary neoplasms after retinoblastoma are not uncommon. But to develop AML with any adjuvant therapy is unknown. A study from MD Andersons which looked into AML in children after retinoblastoma,all the 12 reported cases received adjuvant therapy. Our case is unique in not having any adjuvant therapy and developing AML after 8years of retinoblastoma.
Conclusions: Second neoplasms are not uncommon. Hereditary cancer predisposition syndromes like retinoblastoma can develop secondary AML even with out exposure to chemo or radiotherapy. Ours is a unique case of secondary AML in retinoblastoma without adjuvant therapy.

PUB-0012

MODELLING PARAMETERS OF POSTNATAL GROWTH OF EMBRYONIC TUMOR (MACROLEVEL ESTIMATION)

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Purpose/Objective: To modelling of the growth kinetics malignancies that manifest at the beginning of the organism's postnatal life
Materials and Methods: Sonographic data for primary malignancies in the group of 234 children both sexes aged from 1 to 2138 days with confirmed embryonic tumors: hepatoblastoma, neuroblastoma and nephroblastoma were estimated. The volume of tumor was calculated. We used the precedential data to define the parameters of the nonlinear regression model embrionic tumors such as tumor volume (TV in cm3), tumor doubling time (DT in days) and growth rate of DT (days per day).
Results: Were approximated the data at least for of the clinical phase of growth of the tumors (1/4 last part of time life of tumor). Nonlinear model for tumor volume depending on the child's age at the time of diagnosis was developed and used. Estimated parameters of the model for newborn were as follows: for TV - 23 (95% CI (13-59), for DT - 18,8 (95% CI (4,2-33,0), $p = 0{,}011$), for the growth rate of DT - 0,24 (95% CI (0,18-0,27), $p < 0{,}001$). Were shown that values of the kinetic parameters that are characteristic for childhood malignancies does not observed in adult. The estimating parameters our model were used to establish the age periods for planning the screening embrionic tumors beside infants.
Conclusions: The parameters of malignancies growth from infants based on sonographic data and with help of method nonlinear estimating were modelled. This is the tumor volume, doubling time and the instantaneous growth rate of embryonic tumors in the early neonatal period. This made possible to determine optimal age and periodicity for postnatal screening.

PUB-0013

ACUTE LYMPHOBLASTIC LEUKEMIA: A HOSPITAL BASED RETROSPECTIVE STUDY AT KANTI CHILDRENS' HOSPITAL, KATHMANDU, NEPAL

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Purpose/Objective: To study the clinical features and survival of children with ALL.
Materials and Methods: This was a retrospective study conducted at Kanti Children's Hospital, Kathmandu, Nepal from March 1998 to March 2011. The data was collected from hospital records. Bone marrow aspiration showing $\geq$25% blast cells was the criteria for diagnosis of acute lymphoblastic leukemia.
Results: A total of 624 childhood cancers were reported in this hospital during the study period. Of these 624 cases, ALL constituted 250 (40.1%) and among ALL cases, L1, L2 & L3 constituted 132 (52.8%), 113 (45.2%) and 5 (2.0%) respectively. The age of the children with ALL in this study ranged from 6 months to 14 years, with a mean age of 7.3 years. The majority of children (64.0%) with ALL fell into the age group of 2-9 years. There were 141 males and 109 females with a ratio of 1.3:1.

The most common presenting features were fever (89.2%) followed by splenomegaly (89.1%), hepatomegaly (69.2%), lymphadenopathy (58.4%) and ecchymosis (20.0%).

Of the 250 cases of ALL, 40 (16.0%) refused treatment and among the remaining 210 treated cases 56 (26.6%) died, 50 (23.0%) were lost to follow up, 49 (23.3%) went into remission for longer than 5 years and 55 (26.2%) were still on chemotherapy.
Conclusions: Despite limited resources, the survival rate is 23.3%. Efforts should be made to find out the reasons for loss to follow up and refusal of treatment.
Keywords: Acute lymphoblastic leukemia, Clinical features and survival

PUB-0014

DETERMINING PROGNOSIS OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA WITH THE AGE AT DIAGNOSIS 10 YEARS AND MORE WHO ADMITTED IN ALI-ASGHAR CHILDREN HOSPITAL

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Purpose/Objective: The prognosis of patients with acute lymphoblastic leukemia (ALL) is significantly associated with age. The more favorable prognosis is observed in children of 1-9 years. This study examined the prognosis of ALL patients of $\geq$10 years at diagnosis who were treated in Ali-Asghar Children Hospital.
Materials and Methods: In this study 80 patients with ALL by the age of 10 years or more who have been admitted in our department during the years 2001-2010 were evaluated. The variables in this study included: patients' age at diagnosis, gender, age at evaluation, morphology, immunophenotype, treatment protocols, occurrence of relapse, outcome. Data collected from patient records, were analyzed using SPSS 18 software.
Results: A total of 80 patients with ALL, with a male to female sex ratio of 1.2:1, the mean age at diagnosis 11.6 ± 1.3 (range 10 to 16 years). The morphology was L1 in 79.3%, L2 in 10.3%, L1-L2 2.5% and L3 2.5%. The result of flow cytometry was as follows: Pre B cell 70%, early pre B cell 7.5%, B cell 2.5%, and T cell 20%. Relapse was occurred in 40% of patients, which was mainly in bone marrow and then in the CNS. 32.5% of the patients died. Survival analysis revealed a 5-year survival in these patients equal to 60%.
Conclusions: According to this study, the outcome of ALL patients with age at diagnosis 10 and more is relatively favorable, and morphology, immunophenotype and occurrence of relapse are related to disease prognosis. L1 morphology and pre B cell ALL were associated with less mortality.

PUB-0015

EVALUATION OF LIVER STIFFNESS BY TRANSIENT ELASTOGRAPHY IN CHILDREN DURING AND AFTER MAINTENANCE THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA.

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Purpose/Objective: A range of the chemotherapeutic agents used in the treatment of childhood acute lymphoblastic leukemia (ALL) may cause hepatic damage. In particular 6-mercaptopurine (6MP) and methotrexate (MTX) are often implicated as hepatotoxic. Elevated liver-enzymes are frequently observed during treatment but will typically resolve after treatment cessation. FibroScan® is a novel non-invasive method of evaluating liver stiffness (LS) valuable for diagnosing liver fibrosis in patients with parenchymatous liver disease. The purpose of the present study was to evaluate LS during and after maintenance therapy with 6MP and MTX for childhood ALL.
Materials and Methods: A cross-sectional evaluation of patients in 1. remission, treated according to the regimens for standard and intermediate risk ALL at H.C. Andersen Children's Hospital, Odense University Hospital during 2005-2010. Liver stiffness was assessed by FibroScan®.
Results: Twenty-seven patients. Six in ongoing therapy with 6MP and MTX and 21 after completion of maintenance therapy was included. Patients had a median LS value of 4.10 kPa, range 2.8 * 9.0 kPa. Children receiving 6MP and MTX had higher LS values (median 6.05 kPa vs. 3.9 kPa). This did not reach statistical significance. However, by univariate regression LS was negatively associated with follow-up time from diagnosis. Elevated transaminases (ALAT, AST, GGT) was significantly associated with higher LS values for the group as a whole, and for children no longer receiving 6MP and MTX. Three children (1/6 in therapy and 2/21 after therapy) had LS values exceeding 7 kPa.
Conclusions: Patients receiving 6MP and MTX had higher LS values and there was a follow-up dependent decrease in LS suggesting a decline in LS after discontinuation of treatment. Elevated aminotransferases was associated with greater LS values after but not during maintenance therapy. Three children (11%) had LS values exceeding 7 kPa and thus possible fibrosis corresponding to findings in studies evaluating liver histopathology after ALL treatment.

PUB-0016

CARDIAC TRANSPLANTATION IN TWO PEDIATRIC CANCER PATIENTS WHO HAD DILATED CARDIOMYOPATHY

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Purpose/Objective: Cancer treatment occasionally causes dilated cardiomyopathy due to cardiotoxic agents. Cardiac transplantation is an effective treatment modality in cardiomyopathy. Here, we report two pediatric cancer patients who developed dilated cardiomyopathy and who were succesfully treated with cardiac transplantation
Materials and Methods: One patient with Wilms tumors, and one with Hodgkin lymphoma who developed dilated cardiomyopathy, and who were treated with cardiac transplantation were reported.
Results: Case 1: A four-year old patient with Wilms tumor had been admitted in 1997. The tumor was in right kidney, and she had stage III disease. After tumor resection, the patient was treated with vincristine + adriamycin + actinomycin-D for one year. She had recieved radiotherapy to the left renal area. Anthracycline cumulative dose was 420 mg/m^2, she did not get radiotherapy to cardiac region. One year after completing the treatment left ventricular ejection fraction was 47%. During the follow-up, ejection fraction decreased gradually while the patient received diuretics, digoxin, captopril, and carnitine. The patient had decompansated heart failure after 10 years, and was referred for cardiac transplantation in July 2007. She underwent a succesfull orthotopic cardiac tranplantation, and is fully active currently.

Case 2: 8- year old patient with Hodgkin lymphoma had been admitted in 2000. Disease was located in abdominal region and disease stage was II. He was treated with three cycles of adriamycin+ bleomycine+ dacarbazine+ vinblastine. Adriamycin cumulative dose was 150 mg/m^2. Radiotherapy has been applied to tumor area. While he has been followed in remission, he had developed dilated cardiomyopathy in 2006. The patient received diuretics, digoxin, captopril. In 2008 he had decompansated heart failure and was treated with orthotopic cardiac transplantation, and he is in good condition as the previous case.
Conclusions: Cardiac transplantation in pediatric cancer patients is the treatment of choice when dilated cardiomyopathy develops while the patient is in remission.

PUB-0017

URINARY NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) AS A BIOMARKER IN IFOSFAMIDE INDUCED CHRONIC RENAL FAILURE

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Purpose/Objective: The importance of NGAL in demonstrating chronic renal failure (CRF) was investigated in children surviving from cancer who were treated with ifosfamide.
Materials and Methods: Chronic renal failure and nephrotoxicity was investigated in 29 children treated with ifosfamide chemotherapy for various types of cancer after a remission time of a minimum of two months from the end of treatment. Complete blood count, blood gases, serum Na, K, Cl, urea, calcium, phosphorus, magnesium, creatinine, cystatin C, urine electrolytes and urea, creatinine, microprotein, microalbumin, urine β_2 microglobulin and neutrophil gelatinase associated lipocalin (NGAL) levels, spot urine pH, density, protein, glucose and creatinine clearance analyses were performed for evaluating renal functions.
Results: The cumulative dose of ifosfamide was 36 gr. Glomerular filtration rate was decreased in 41.4% and urine b_2 microglobulin levels and serum cystatin C levels were elevated in 31% of the patients. As the remission time increased, serum creatinine and cystatin C levels were also increased. The sensitivity for β_2 microglobulin, cystatin C and urinary magnesium in demonstrating CRF was 35.2%, 23%, and 100% and specificity was 33.2%, 50%, and 10%, respectively. Urinary magnesium and FeMg was elevated in 25% and 41.4% of the patients with CRF, respectively. 24-hour urine NGAL levels were measured to demonstrate the course of CRF. The cut-off value for NGAL was found to be 1.065 ng/mL/24 hours. The sensitivity and specificity for this cut-off value were 83% and 77%, respectively. NGAL levels were significantly higher in the study group as compared with the control group.
Conclusions: Although ifosfamide treatment was suggested to be safe with no complication of renal failure under a dose of 80 gr/m^2, CRF and deficits in glomerular and tubular function could be seen when the remission time increased. Elevated NGAL levels may be a good option in determining CRF.

PUB-0018

SINGLE CENTER ANALYSIS OF 983 CASES OF CHILDREN SOLID TUMORS INCIDENCE FROM 2009 TO 2011.

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Purpose/Objective: To investigate epidemiologic and clinical features of childhood solid tumor in our hospital from Jan. 2009 to Dec. 2011.
Materials and Methods: Clinical and pathological data, including patient gender, age, manifestations, imaging investigations, tumor histology, therapeutic measures and prognosis of childhood solid tumors confirmed by pathological biopsy, were retrospectively collected and analyzed. Tumor classification was performed according to WHO tumor classification and diagnostic criteria.
Results: Totally, 983 cases of childhood solid tumor were enrolled into the study, including 721 (73.35%)benign tumors and 262(26.65%) malignant tumors. There were 548 males and 435 females. Patient age ranged from 8 days to 14 years (median age of 4 years old). ?Sort by the original site:The top five benign tumors were skin and soft tissue tumors,craniofacial and neck tumors, bone tumors,abdominal tumors and thoracic tumors,while the top five malignant tumors were abdominal tumors,intracranial tumors,craniofacial and neck tumors,skin and soft tissue tumors and pelvic tumors; Sort by the pathological type: The top five benign tumors were vascular tumor, calcifying epithelioma, mature teratoma, chondroma and fibroma, while the top five malignant tumors were neuroblastoma, lymphoma, Wilm's tumor, germ cell tumor and hepatoblastoma. ?There was statistically significant differences in terms of age of onset distribution between benign and malignant tumor groups ($P < 0.05$). Benign tumors in gender distribution was not statistically significant($P = 0.396$),while malignant tumors was meaningful($P = 0.003$).?Solid tumors were much more prevalent in infants and toddlers,showing a characteristic single peak pattern($P = 0.003$). The different types of malignant tumor in different age stages were different distribution($P \leq 0.001$).?29/262 cases(11.1%)in infant were massive malignant tumor and 26 of them(89.7%)were from abdominal.
Conclusions: Benign tumor remains the primary type of solid tumor in children. Childhood malignant tumors commonly occur in the abdominal cavity with embryonic tumors as the predominant histological types. Neuroblastoma and Wilm's tumor are the primary tumor presenting with huge tumor mass in children under 4 years old.

PUB-0019

LOW PLATELET COUNTS AS A PROGNOSTIC MARKER IN ALL TREATMENT IN PLACE OF MRD IN COUNTRIES WITH LIMITED FINANCIAL RESOURCES

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Purpose/Objective: Aim: The aim of this study was to estimate prognostic and early response criteria for the patients treated by ALL.
Materials and Methods: There were 242 newly diagnosed non B-ALL patients who were admitted to Cerrahpasa Pediatric Hematology Department during January 1995 to 2012,
Results: The median age was 6,18y $\pm$ 3,75years (8 month- 17 years). CNS involvement: %7,7. T-cell immunophenotype: 11,8%. The OS of B cell-ALL: %81 3,1, (T-ALL: %62,2 12,4 (p:0.007)). The EFS of CNS involved cases were %47,6.

The OS and EFS of the whole group was 74,8 3,9 and 74 3,1, while EFS ratios for males 72% and females 80.5% (p:0.728). High risk patients were significantly associated with X3 relaps and X7 exitus (OS 22,7 9,1 and EFS 27,6 (p:0,0001). Having splenomegaly, hepatomegaly, t (9,22), CNS involvement (CNS leukemia increased exitus risk X4 times), higher Hb and WBC counts were related with poorer treatment results. (WBC $>$ 100.000 / mm^3 OS %53,7 12,8 (p:0.028); .Hb $>$ 8g/dl and T-ALL patients' OS 44,4 13,5 (p.0,01).

The platelet counts at diagnosis had no prognostic value, platelet count at 15 and 33th days $<$ 50.000/mm3 had higher risk for exitus (respectively X3 and X7), and had lower OS p:0,008, p:0,0001). Thrombocytopenia usually goes parallel with neutropenia and monocytopenia. If blasts were $>$ %5 at 15 and 33 day in bone marrow; OS 35,8 15,9 and 0%. The 13.3% of the group relapsed, generally in 3.5 years period after diagnosis, and 72% of the relapsed patients were succumbed in 5 months.
Conclusions: As a conclusion, platelet count $<$ 50.000/mm^3 at the 15 and 33th day of treatment, was associated with high mortality(p:0,0001) and this would be used just for a marker in countries with limited financial resources where MRD is not avaliable.

PUB-0020

ABSTRACT OF RETINOBLASTOMA MUTUAL SUPPORT GROUP ORGANIZED BY THE CHILDREN'S CANCER FOUNDATION IN HONG KONG

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Purpose/Objective: Aims of the 'Child's Vision' Mutual Support Group

(1) To develop an effective support group - organized by the Children's Cancer Foundation (CCF) * with the purpose of mutual sharing and providing support to the parents of newly diagnosed patients in the Hong Kong Eye Hospital.

(2) To organize programmes and activities for these families in order to create a support network and increase opportunities to share experiences within their own group.

(3) To design a booklet or a leaflet for public education in order to promote early detection of suspected RB and increase the recovery rate.

(4) To establish supporting networks within these families and encourage patients and parents to exchange information and experiences. To let them enjoy a better quality of life.

Materials and Methods: An interrelated triangular model was formulated to deliver services to patients and parents. This comprised of medical staff in the Hong Kong Eye Hospital, volunteer parents and CCF.

Results: The triangular model between medical staff, volunteer parents and CCF is an effective service model in helping RB patients and parents. With the facilitation of the CCF social worker, parents new to the disease gain support from experienced parents. As a result of enhanced communications patterns, this group of previously vulnerable parents become more cooperative with medical staff. And medical staff are able to focus on treatment as they are confident that parents of new cases are well-supported by an effective group of volunteer parents and CCF professional staff.

Conclusions: This successful experience in organizing a mutual support group has potential applications in other kinds of childhood cancer. With good cooperation between three parties, the enhanced outcome for RB patients and their parents is plain to see.

PUB-0021

CLINICAL STUDY OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDHOOD—REPORT ON TWO CASES AND LITERATURE REVIEW.

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Purpose/Objective: To review the clinical feature, diagnosis, treatment and prognosis of the reported children with post-HSCT-HLH. To enhance the understanding of them and improve the outcome.

Materials and Methods: Thirteen children with post-HSCT-HLH (include 2 cases from our hospital and eleven cases from MEDLINE search) were retrospectively analyzed.

Results: The median age of onset was 7.5 years (ranging from 2 to 16 years), The underlying conditions included infection (7/13); The majority presenting symptoms were fever (13/13), hepatosplenomegaly(5/6), engraftment failure, delayed engraftment or secondary engraftment failure after HSCT(13/13), histopathological evidence of haemophagocytosis(13/13), elevated ferritin(13/13), elevated serum lactate dehydrogenase(LDH) (8/9), hypertriglyceridaemia(5/5), hypofibrinogenaemia(4/5), elevated solube interleukin-2 receptor(CD25) (8/8) and decreased natural killer cell activity(2/2). To control infection, co-therapy with hormonal, gamma globulin, low-dose etoposide and second HSCT following graft rejection by HLH were effective for this disease. Of the 13 cases reviewed, 10 children survived, and the rest 3 cases died because their treatment caused too strong immunosuppression.

Conclusions: Post-HSCT-HLH is a rare and serious complication, and early reasonable therapy may improve the prognosis of children with this condition. If the treatment cause too strong immunosuppression, the chance of opportunistic infection and mortality will increase.

PUB-0022

COMPLEMENTARY ROLES OF 2-DEOXYGLUCOSE IN THE TREATMENT OF NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma (NB) is characterized by pleomorphic molecular characteristics, which may influence cellular metabolism as well as the use of glycolytic inhibitors in the treatment of NB.

Materials and Methods: We studied four NB cell lines, two without and two with *MYCN* amplification. Metabolic enzymes in the glycolytic pathway and pro-apoptotic and anti-apoptotic proteins in the BCL-2 family were studied by using Western blotting. Cell proliferation was studied with the use of WST-1 assay and cell apoptosis by PI staining.

Results: There were no unanimous metabolic characteristics among the four cell lines. The only common feature was a significantly higher HIF-1α expression level, which was associated with higher ATP content in the two NB cell lines with *MYCN* amplification compared to the two cell lines without *MYCN* amplification. Treatment of the *MYCN* amplified NB cells with glycolytic inhibitor 2-deoxyglucose (2DG) was associated with significantly greater inhibition of cellular proliferation and more apoptosis than those without. 2DG treatment increased the expression of the proapoptotic BH3-only protein Bad in both SK-N-AS (without *MYCN* amplification) and SK-N-DZ (with *MYCN* amplification) cells. 2DG complements the effects of cisplatin and the BH3-only mimetic ABT737 on suppression of NB cell proliferation. A low dose of 2DG (2 mM) was as effective as a high dose (20 mM) in NB cells that are sensitive to glycolytic inhibition. Furthermore, 2DG also complements the effect of polyinosinic:polycytidylic acid [poly(I:C)] in the treatment of NB.

Conclusions: Our data indicate that 2DG may be a useful adjuvant agent, which may complement the chemotherapeutic and immunotherapeutic drugs in future treatment of NB.

PUB-0023

SYNERGY OF CHURCH AND GOVERNMENT: A CHURCH ACTIVITY ADOPTED BY THE STATE

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Purpose/Objective: Until 2003, paediatric palliative care services for children with life-limiting diseases haven't existed in Russia. The term 'palliative care' as a legal concept was absent until November 2011. The costs of the palliative care, which was not associated with the treatment of the main disease, were not covered by insurance companies. Under these circumstances, the Russian Orthodox Church launched a charity project to improve situation of the affected families.

Materials and Methods: The 'Children's Hospice' Charity Fund (2003) and the Nonprofit Medical Institution 'Children's Hospice' (2006) were established. The charity-based Children's Hospice rendered comprehensive care to children and adolescents under the age of 18 years, suffering from terminal illnesses. The care included medical, psychological, emotional, social, and spiritual aid.

Children's Hospice succeeded in attracting attention of the medical society and the authorities. The City of St. Petersburg recognized that the paediatric palliative care for seriously ill and dying children was not provided within the national health system. In 2010, St. Petersburg State Autonomous Healthcare Institution 'Children's Hospice' was established. The team of the Nonprofit Medical Institution was offered to enter into the state institution. Thus, church activities have been recognized and adopted by the City Government.

The Federal Law 'Basis of health protection in the Russian Federation' was added by the article 'Palliative Care': palliative care may now be provided in outpatient and inpatient settings and be financed by the State.

Results: A church-based charity was able to improve situation with paediatric palliative care in the city. The St. Petersburg Children's Hospice has grown into the national leader of pediatric palliative care. Its experience will be multiplied in other regions of Russia.

Conclusions: Church structures are able to solve problems of national importance. The St. Petersburg Children's Hospice has become a model for establishing similar health and social care services in Russia.

PUB-0024

SUCCESSFUL DOSE-INTENSIVE TREATMENT OF DESMOPLASTIC SMALL ROUND CELL TUMOR IN THREE CHILDREN

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Purpose/Objective: Desmoplastic small round cell tumor (DSRCT) is a rare soft tissue tumor of primitive origin occurring primarily in children and young adults that has a poor outcome with current therapies. The response to conventional chemotherapy is unsatisfied.

Materials and Methods: We retrospectively reviewed three pediatric patients with DSRCT at Children's Hospital of chongqing medical university successfully treated with dose-intensive, multimodal therapy between July 2009 and December 2012. The diagnose was confirmed based on clinical presentation, radiologic staging, and pathologic review with immunohistochemical staining

Results: There were 1 female and 2 male patients. Age at diagnosis was range 2.5 -4years. In two patients, the primary tumor was retroperitoneal. The rest was origin from pleura and with tumor metastasis to bone marrow and pulmonary. All patients received a combined modality protocol including dose-intensive chemotherapy, second look surgery, and consolidative local irradiation. The chemotherapy regimen containing doxorubicin, vincristine, cyclophosphamide, cisplatin, etoposide and topotecan. The patients remain in continuous remission at 30, 20 and 10 months after diagnosis, respectively.

Conclusions: Our three patients were the youngest age group than any previously reported patients. Whereas the number of our series was limited and the benefit of combined modality protocol needs further confirmation, we conclude that prolonged event-free survival of DSRCT is possible with dose-intensive chemotherapy in combination with aggressive surgery and local radiation therapy.

PUB-0025

TREATMENT EXPERIENCE OF RARE RETROPERITONEAL KAPOSIFORM HEMANGIOENDOTHELIOMA(2 CASES REPORT)

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Purpose/Objective: Kaposiform hemangioendothelioma (KHE) is a locally aggressive vascular tumor that usually occurs in infants. It is commonly associated with Kasabach-Merritt phenomenon (KMP) and lymphangiomatosis. These tumors have been found in the neck, face, thorax and limbs, rarely, they happen in retroperitoneal site, with high mortality rate. This paper wants to analyze medical records of retroperitoneal kaposiform hemangioendothelioma (KHE) in our hospital, and to share experience and opinions in treatment of such kind of KHE.
Materials and Methods: 2 cases of retroperitoneal KHE with KMP were diagnosed and treated in Children's Hospital of Fudan University, their medical histories were reviewed.
Results: Huge retroperitoneal mass or hematochezia with thrombocytopenia in both cases were the main complains. They were misdiagnosed as retroperitoneal neuroblastoma or Necrotizing Enterocolitis(NEC) first, and were confirmed as retroperitoneal KHE after prudent multidisciplineary discussion. Predinisone was effective at the beginning of treatment, but symptoms rebounded shortly after medication withdrew. Vincristine(VCR) was especially effective on those 2 patients whose symptom were rapidly relieved after 2 dosages of VCR administration. The retroperitoneal masses disappeared finally during follow up in both cases.
Conclusions: Retroperitoneal KHE with KMP is very rare, and hard to be diagnosed. Understand such kind of disease and multidiscplineary discussion can prevent it from misdiagnosis. VCR is especially effective in patient who resist to predinisone. Standardized and personalize treatment is necessary in treatment of retroperitoneal KHE.

PUB-0026

CYTARABINE COULD ENHANCE THE SENSITIVITY OF K562 CELLS TO AD-TRAIL

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Purpose/Objective: To evaluate the effects of cytarabine on sensitivity of the human leukemia cell line K562 to tumor necrosis factor-related apoptosis inducing ligand (TRAIL)and to investigate the potential mechanism.
Materials and Methods: K562 cells were transfected with Ad-TRAIL and then exposed to cytarabine. The cell viability was monitored using the method of CCK-8. The cell apoptosis was analyzed by Hoechst staining and flow cytometry. RT-PCR was introduced to detect the apoptosis related genes, DR4, DR5, Caspase 3 and survivin. The apoptosis related proteins were measured by Western blot.
Results: The combination treatment of cytarabine and Ad-TRAIL could inhibit the proliferation of K562 cells significantly, which was chiefly attributed to the induction of obvious apoptosis. The enhancement of Ad-TRAIL by cytarabine was due to the up-regulation of DR5 and DR4 expression, and followed by the down-regulation of survivin and activation of Caspase 3.
Conclusions: Cytarabine could enhance the sensitivity of K562 cells to Ad- TRAIL.

PUB-0027

OCULAR KAPOSI'S SARCOMA AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A CHILD

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Purpose/Objective: To summarize the diagnostic and therapeutic experience of eye Kaposis' sarcoma (KS)
Materials and Methods: One 13 years-old child with acute lymphoblastic leukemia were reviewed retrospectively. He developed KS restricted in right conjunctiva, cornea and sclera after allo-geneic peripheral blood stem cell transplantation (PBSCT). Tumor clinical features, management and oncologic outcomes were analyzed.
Results: The Han nationality child received immunosuppressive treatment for PBSCT and had extensiveherpes zoster. Ocular KS manifested simply as blurred vision and progressed slowly to lump. Pathological examination confirmed KS with changes like capillary hemangioma and positive immunofluorescent result of HHV8 .He received excision of lump and transplantation of cornea and sclera .Antiviral therapy was given together with antiinfection, prevention of cornea rejection and biotherapy.
Conclusions: Ocular KS is rare, and there is no report in children with leukemia after PBSCT. Complete excision combined with biotherapy are safe and effective for single ocular lesions. Screening of HHV8 active infection in donor and receipient is valuable to prevent KS.

PUB-0028

PHOTOMEDICINE IN THE MANAGEMENT OF OROFACIAL COMPLICATIONS OF CANCER THERAPY USING LOW LEVEL LASER THERAPY

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Purpose/Objective: Management of orofacial complications from chemotherapy, radiation therapy (RT), a combination of both and haematopoietic stem cell transplantation (HSCT or SCT) is challenging while compromising the quality of life, cancer management, morbidity and even mortality. Photomedicine using low level laser therapy (LLLT) has been shown to be effective in reducing the severity of oral mucositis (OM) due to different cancer therapies since initial reports from the early nineties.
Materials and Methods: Meta-analysis involving 33 articles comprising nine reviews, six case studies and three animal studies with a final sample of 11 randomized placebo-controlled trials from 1997 until 2009 of head and neck cancers and other study results from chemotherapy, RT and SCT on LLLT.
Results: Common features of orofacial manifestations of cancer therapy including, chemotherapy, radiation therapy and stem cell transplantation (SCT) will be discussed along with an update on current knowledge on LLLT for RT-induced, chemotherapy-induced and SCT. Clinical aspects such as when where and how it should be administered in patients with orofacial complications will be covered. An update on intra-oral and extra-oral devices that could be used in orofacial complications with parameters to be considered when calibrating LLLT devices and the significance of clinical evaluation, trained clinicians will be discussed.
Conclusions: The mounting scientific evidence is promising and empirical to believe that photomedicine will soon become common practice in the preventative and therapeutic regimen of OM and others such as xerostomia, oral graft-versus host disease (GVHD), salivary gland dysfunction, cutaneous manifestations and trismus management.

PUB-0029

TREATMENT OUTCOME OF A MULTI-CENTRE CLINICAL STUDY OF HODGKIN LYMPHOMA: A REPORT BY HONG KONG PAEDIATRIC HAEMATOLOGY AND ONCOLOGY STUDY GROUP

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Purpose/Objective: Hodgkin's lymphoma is an uncommon childhood cancer. With proper treatment, it is highly curable.
Materials and Methods: The 5 regional hospitals in Hong Kong started to use a uniformed treatment protocol for children with Hodgkin's lymphoma from 1st February 2000. The clinical data were collected prospectively.
Results: Up till 31 December 2011, thirty six children were diagnosed to have Hodgkin's lymphoma. The median age was 13.8 (2.8 to 17.7). Male to female ratio was 1.1 to 1. The median follow up duration was 5.4 years (0.4 to 11.9). The clinical stages were 20% for stage 1 (n = 7), 47% for stage 2 (n = 17), 11% for stage 3 (n = 4), and 22% for stage 4 (n = 8). Seven patients (19%) had B symptoms. thirteen cases (36%) got bulk diseases. The histological subtypes were nodular sclerosis (n = 21; 58%), lymphocyte predominant (n = 6; 17%), mixed cellularity (n = 4; 11%), lymphocyte rich (n = 1; 3%), and unclassified (n = 4; 11%). The organs involved by the disease were combination of sites in 69% of patients (n = 25), 22% in head and neck regions (n = 8), and 9% in peripheral area (n = 3). COPP/ABV chemotherapy was given to the patients. Twelve patients had low-dose involved field radiotherapy. Thirty five patients had complete remission after treatment. Three patients had relapse of the disease. Autologous stem cell transplantation was performed in one patient with progressive disease and in two patients after relapse. The 5-years overall survival (OS) rate was 100% and event-free survival (EFS) rate was 91.3%.
Conclusions: The treatment outcome was good and the results were comparable to the published literature.

PUB-0030

PAPILLARY FIBROELASTOMA OF THE TRICUSPID VALVE IN A 4-YEAR-OLD CHILD

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Purpose/Objective: Cardiac papillary fibroelastomas (CPF) is an uncommon primary neoplasm. Among them,tricuspid valve papillary fibroelastoma is extremely rare. We report a pediatric case of tricuspid valve PFE, which was incidentally found by echocardiography and identified histologically.
Materials and Methods: A previously healthy 4-year-old girl was referred to our hospital due to a cardiac murmur. She had no recent fever, Chest pain, or cough. The patient had a grade II/6 diastolic ejection murmur over the left upper sternal border. The laboratory results were almost normal. The chest X-ray showed a normal lung field. Her echocardiography revealed a nearly 1.5cm in diameter mass, which was lobulated, pedunculated, mobile and arising from tricuspid valve.
Results: The mass was completely excited on cardiopulmonary bypass. The diagnosis was confirmed by the support of histological finding. The girl tolerated the procedure well and had an uncomplicated postoperative course.
Conclusions: Cardiac papillary fibroelastomas (CPF), the second most common primary cardiac tumors, usually small and predominantly affected the cardiac valves. CPF is extremely rare at the age of ten. Most CPF are asymptomatic and incidentally found by physical examination, echocardiography, cardiac catheterization, cardiac surgery or autopsy. The most common clinical presentations are embolism to the cerebral, systemic or coronary arterial circulations, followed by heart failure and sudden death. Differential diagnosis of CPF includes other heart tumors, thrombi and bacterial vegetations. Transthoracic echocardiography is a useful tool for diagnosis of CPF. Though CPF is benign and rarely causes valvular dysfunction, they can cause serious complications such as systemic or pulmonary embolism and death. CPF is avascular papillomas with a single layer of endocardial cells covering the papillary surface. Surgical treatment by simple complete resection is low risk and can achieve good results. The short- and long-term prognosis after surgical removal is excellent.

PUB-0031

TISSUE FACTOR EXPRESSION PREDICTS OUTCOME IN CHILDREN WITH NEUROBLASTOMA

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Purpose/Objective: In the last few years, it has become clear that the processes of tumor angiogenesis, metastasis and invasiveness are highly dependent on component of the blood coagulation cascade. One of the key proteins in coagulation is tissue factor(TF). In addition to its role in coagulation, accumulating evidence suggests that TF regulates intracellular signaling pathways that play a crucial role in angiogenesis and tumor development and metastasis as well.

To the best of our knowledge we report for the first time the detection of tissue factor expression by immunohistochemistry in neuroblastoma in pediatric and correlation with tumor pathology, stage and clinical outcomes.
Materials and Methods: A retrospective, immunohistochemical study was performed using materials obtained from 40 neuroblastoma cases treated at pediatric oncology unit, Zagazig University Hospitals, between 2005 and 2012. Pre-chemotherapy biopsy samples were stained for tissue factor and correlations between TF expression and clinical characteristics, stage, pathology and outcomes were evaluated.
Results: Positive TF expression was detected in 30 of tumor analysis (75%). TF expression was significantly related to patient outcome where 7 patients (70%) with negative TF survive while 24 patients (80%) with positive TF expression died. On the other hand, there was no statistically significant relationship between TF expression and age, gender, clinical characteristics as well as tumor stage and pathology
Conclusions: Tissue factor is expressed in neuroblastoma and its expression might be a promising prognostic factor for neuroblastoma outcome, but further studies are needed to verify our data in a larger cohort

PUB-0032

PEDIATRIC CNS EMBRYONAL TUMORS INCIDENCE AND TREATMENT RESULTS IN CHELYABINSK REGION

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Purpose/Objective: The purpose of this study was evaluating the incidence and outcome of pediatric CNS embryonal tumors in Chelyabinsk region. Also, the outcomes before (1995-2007) and after (2008-present time) regional multidisciplinary cooperative team work establishment were compared.
Materials and Methods: Since 1995 the data on pediatric cancer patients is entered in the regional pediatric cancer registry. The current study includes the registry data on children with embryonal CNS tumors. The age-standardized incidence rate (ASR) was calculated. Survival analysis was performed with R Project statistics software.
Results: A total of 43 patients with pediatric CNS embryonal tumors were registered during the studied period. They were diagnosed medulloblastoma (n = 40), atypical teratoid/rhabdoid tumor (AT/RT) (n = 2) and CNS primitive neuroectodermal tumor (n = 1). In patients with medulloblastoma the male to female ratio was 1.8:1, the mean age at diagnosis was 9.1 years. ASR in 1995-2007 was 0.28 per 100 000 children, in 2008-2011 the ASR was 0.61. All patients underwent neurosurgical intervention and HIT protocol-based chemotherapy. All children older, than 3 years, received craniospinal radiotherapy. In 1995-2007 (n = 27) OS in pediatric medulloblastoma patients was 40.4%, in consequent period (n = 13) it increased to 68.8% (p = 0.132). One of 2 patients with AT/RT died of disease progression 13 months after treatment initiation, the other is still alive 7 months after diagnosis.
Conclusions: Multidisciplinary efforts in our region lead to advances in pediatric CNS embryonal tumors patients treatment and allowed more efficient pediatric CNS tumors incidence and treatment results documentation. Although the mean follow-up period of the patients treated with effective multidisciplinary team is still small and the difference in survival is yet to obtain statistical significance, the trends currently observed inspire us for further work and cooperation.

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PUB-0033

LATE CARDITOXICITY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: To evaluate the late cardiac effects of anthracyclines in pediatric acute lymphoblastic leukemia and underline the importance of cardiologic follow-up
Materials and Methods: Forty patients without any cardiac pathology and completed ALL chemotherapy protocol at least 2 years ago in Pediatric Hematology & Oncology Unit of Istanbul Medical Faculty were included in Group 1. An age and sex matched control group (Group 2) served as control group. Echocardiographic and 24-hour electrocardiographic analysis were performed for 40 and 20 patients, respectively. Ejection fraction (EF) and shortenning fraction (SF) were analyzed as the measures of systolic functional capacity. Besides, diastolic dysfunction was determined by analyzing E/A ratio which is the ratio of early ventricular filling to filling by atrial contraction. The results below 65% for EF and 29% for SF was accepted as systolic dysfunction. The value below 1.5 for E/A pointed diastolic dysfunction.
Results: The cumulative dose of anthracycline was 250 mg/m^2 in 12 patients (30%) and 175 mg/m^2 in others. The drug was given as eight-hour-infusion in all patients. Acute cardiotoxicity - as sinusal tachycardia and bradycardia - was observed in 2 patients. The median duration after the last anthracycline infusion was 48 months (minimum: 24 months, maximum: 144 months). No difference was observed in EF values (p = 0.76) but an obvious difference was noticed in SF values ***(p < 0.05)*** between 2 groups. No diastolic dysfunction was noted in our patients. On the other hand; supraventricular and ventricular early beat was statistically greater in Group 1.
Conclusions: Late cardiotoxicity is an important side effect of anthracyclines. It is usually silent and may manifest as systolic and/or diastolic dysfunction and rythym anomalies. In this situation, echocardiographic evaluation alone is not sufficient and 24-hour electrocardiographic analysis is required for both early detection of cardiac dysfunction and rythym anomalies.

PUB-0034

SIGNIFICNCE OF SERUM NEURONE SPECIFIC ENOLASE LEVEL FOR DIAGNOSIS IN NEUROBLASTOMA

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Purpose/Objective: Neuroblastoma is the most common solid tumor in children. Various tumor markers have been used for diagnosis in this disease. However, vanillymandelic acid (VMA) and homovanillic acid (HAV) in urine are the tumor marker of choice in neuroblastoma but it is difficult to properly collect especially in young children. We evaluated the significance of serum neurone specific enolase (NSE) level for diagnosis in neuroblastoma.
Materials and Methods: Serum samples for NSE analysis from 1992 to 2008 were included. NSE level, clinical data and final diagnosis were recorded and analyzed for correlation between NSE level and diagnosis.
Results: One hundred and ninety five patients were enrolled. Sixty seven (34.4%) and 128 (65.6%) patients were diagnosed with neuroblastoma (NB) and non-neuroblastoma (NNB).

Mean NSE level for NB and NNB group were 278.5 and 41.15 ng/ml. The top three highest NSE level in NNB group were leukemia (209.64 ng/ml), Wilm's tumor (79.04 ng/ml) and gonadal germ cell tumor (47.43 ng/ml). For NB group, mean NSE for stage I, II, III, IV and IVs were 191.3, 60.15, 350.48, 653 and 137.5 ng/ml, respectively. If we used NSE level just above normal value ($>$ 15.2 ng/ml), the sensitivity, specificity, positive predictive value and negative predictive value were 98.5%, 27.34%,41.5% and 97.2%, respectively. However, we used NSE level $>$ 100, the sensitivity, specificity, positive predictive value and negative predictive value were 85.07%, 92.96%, 86.40% and 92.24%.
Conclusions: Serum NSE is a useful tumor marker for neuroblastoma. However, serum NSE can rise in many malignancies. The cut off NSE level $>$ 100 ng/ml can increase accuracy in diagnosis of neuroblastoma.

PUB-0035

OUTCOME OF CHILDREN WITH NEWLY DIAGNOSED HIGH GRADE GLIOMAS TREATED WITH ADJUVANT NIMOTUZUMAB® AND IRINOTECAN: A PRELIMINARY REPORT

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Purpose/Objective: The treatment for high grade gliomas (HGGs) is surgery and radiation. Adjuvant chemotherapy has not shown any effect on pediatric HGGs. Molecular studies have shown that there is the presence of epidermal growth factor receptor (EGFR) in 50 to 60% of patients. Therefore, this study aims to demonstrate the response of adjuvant EGFR inhibitor (Nimotuzumab®) in combination with irinotecan in pediatric HGGs.
Materials and Methods: Having received informed consent, new HGGs patients were enrolled. Two weeks after surgery, all patients received radiation (54-56 Gys) for 6 weeks. Nimotuzumab®, at 150 mg/m^2, was infused every week during radiation. After radiation, a 4-week cycle, consisting of Nimotuzumab®, at 150 mg/m^2, at week 1 and 3 and Irinotecan, at 125 mg/m^2, at week 1, 2 and 3, was given for a total of 1 year. MRI studies were done at pre and post-surgery, post radiation and every 3 months thereafter.
Results: Eleven patients (1 female, 10 males), mean $\pm$ SD for age of 7.7 $\pm$ 3.1 years, were involved in the study. The diagnoses included 6 glioblastoma multiforme patients, 3 anaplastic astrocytoma patients, and 1 anaplastic oligoastrocytoma patient. One patient was unable to have tissue diagnosis due to the tumor being located at brainstem. While 55% of the tumors were located in the infratentorial region, the remaining 45% were in the supratentorial region. Total tumor removal was performed in 3 patients, subtotal tumor removal in 2 patients and partial tumor removal in 2 patients. The remaining 3 patients had biopsies. EGFR was positive in 66% of the patients. The median follow-up time was 0.6 (0.2-2.5) years. From the three patients showing disease progression, one expired. The 1-year PFS was 60 $\pm$ 18%. No treatment-related complication was found.
Conclusions: This adjuvant regimen with Nimotuzumab® and irinotecan may have some efficacy and could be another option for the treatment of pediatric HGGs.

PUB-0036

THE CLINICAL STUDY OF THE DRUG-RELATED TOXICITY BY THE CCLG2008 PROTOCOL FOR CHILDHOOD LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: To evaluate the drug-related toxicity of CCLG2008 protocol by Chinese Children's Leukemia Group for childhood acute lymphoblastic leukemia (ALL) in single center.
Materials and Methods: 114 children with newly diagnosed ALL were enrolled in the study. The patients were diagnosed and treated with the CCLG-ALL2008 protocol. The drug-related toxicity were evaluated according to Common terminology criteria for adverse events version 4. The basic frame of the protocol including induction therapy with VDLD (phase A), early intensification therapy with CAM1 and/or CAM2 (phase B), high dose MTX, delayed intensification therapy with VALD (phase C) + CAM (phase D). χ^2 analysis was done by SPSS software for Windows
Results: For 114 patients with ALL, 473 courses of chemotherapy were carried out. The occurrence rate of hepatotoxicity was 85.1% in phase A, 29.3% in phase B, 17.8% in phase C, 21% in phase D. Significante differences were found between phase A and the other phases($P = 0.000$). The occurrence rate of dental ulcer was significantly higher in phase A (20.2%) than that in the other phases (4.1% in phase B, 4.8%, in phase D, $P = 0.000$). The occurrence rate of hyperglycemia was significantly higher in phase A (20.2%) than that in the other phases (0.7% in phase B,1.9% in phase D, $P = 0.000$, respectively). The occurrence of allergic reactions to L-Asp was 28% in phase C vs 7.9% in phase A ($P = 0.000$). The hypokalemia occoured in 21.1% of the patients with phase A vs 6.5% of the patients in phase C ($P = 0.002$). No significante differences were foud in terms of the incidence of digestive tract reaction, Cardiotoxicity and skin rash among different phases. Most of the drug-related toxicity is in grade 1 or grade 2. None of the patients were died of the Drug-related Toxicity.
Conclusions: The drug related toxicity of the CCLG2008 protocol for childhood ALL is limited in grade 1 and grade 2. No TRM occurred.

PUB-0037

CHRONIC MYELOID LEUKEMIA IN MOROCCAN CHILDREN. A SINGLE EXPERIENCE THROUGH 32 CHILDREN.

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Purpose/Objective: The objective is to analyse the clinical and demographic characteristics and outcome of children with chronic myeloid leukemia (CML) treated in the most important hematology center in Morocco.
Materials and Methods: Data of patients aged less than 20 years diagnosed with CML (according to CML diagnosis criteria of WHO 2008) from January 2002 to august 2012 were retrospectively collected. The treatment was by imatinib (240mg/m2/day) when the drug was available. Cytogenetic response was monitored and evaluated according to ELN 2009 revised criteria.
Results: Thirty- two patients were enrolled. The incidence of pediatric CML comprises 5% of newly diagnosed CML and 2.5% of pediatric haematological malignancies. The median age was 13 years (2 - 19). The H/F ratio was 1.13. The main symptoms were abdominal pain and B symptoms. All patients had splenomegaly with a median size of 13 cm. The median white blood cell and platelets were respectively 242 and 408 G/L. Only one patient had monosomy of 7 at diagnosis. Cytology showed chronic phase in 24 cases (75%) and blastic phase in 6 cases (19%). Imatinib was initiated in 23 patients (72%) after cytoreduction. Twenty three patients (72%) achieve complete hematologic response at 3 months. Ten patients (31%) have abandoned. A complete cytogenetic response was observed in 3 patients at 6 months. One patient achieves major molecular response and three patients transformed into acute leukemia, none had allogenic stem cell transplantation (ASCT). Grade 3 toxicity was seen in 3 patients. With a median follow up of 25 months (1*117) the estimated overall survival rate at 45 months was 90% and the progression free survival was 71%.
Conclusions: Low compliance and treatment abandonment are still difficulties in developing countries. ASCT just started in Morocco it could be interesting to perform randomized study between Imatinib and imatinib followed by ASCT in Moroccan pediatric CML.

PUB-0038

RISK FACTORS FOR COMPLICATED-VARICELLA INFECTION IN PEDIATRIC ONCOLOGY PATIENTS AT A TERTIARY HEALTH CARE FACILITY IN PAKISTAN

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Purpose/Objective: Varicella zoster infection (VZI) is well recognized as a potential cause of morbidity and mortality in immunocompromised oncology patients. The purpose of this study was to describe the clinical profile and risk factors for complications and the outcome of varicella in pediatric oncology patients treated with acyclovir.
Materials and Methods: Medical records of all pediatric oncology patients with discharge diagnosis of VZI over a period of 7 years (2005-2011) were retrieved, and reviewed by using hospital information management system. The demographic features, underlying malignancy, risk factors for varicella infection, complications and outcomes were recorded.
Results: During the 7 years period, 36 pediatric oncology patients with VZI were identified. Two secondary cases were excluded. Leukemia was the most commonly underlying malignancy ($n = 20$, 58.8%), followed by lymphoma ($n = 7$, 20.6%) and solid organ tumors ($n = 7$, 20.6%). Most (41%) cases were observed in children under 5 years of age. All patients were treated with acyclovir. Varicella-related complications developed in 10 (29%) patients. Most frequent complication was bloodstream infection ($n = 3$, 8.8%), followed by pneumonia ($n = 2$, 5.9%), skin infection ($n = 2$, 5.9%), hepatitis, renal failure and encephalitis. Independent risk factors associated with development of complications were age $<$ 5 years, weight for age $<$ 5th percentile, delay in seeking care ($>$ 7 days after onset of symptoms) and severe neutropenia (ANC $<$ 500/cm). One child died secondary to varicella encephalitis.
Conclusions: Our data suggests that young age, being underweight, poor health seeking behavior and severe neutropenia are the major risk factors for development of varicella-related complications in pediatric oncology patients in developing countries. These complications could be favorably modified through an active immunization of immunocompetent children.

PUB-0039

MALIGNANT MEDIASTINAL MASS IN CHILDREN: A SINGLE INSTITUTIONAL EXPERIENCE FROM A DEVELOPING COUNTRY

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Purpose/Objective: Children with malignant mediastinal mass (MMM) represent a potentially serious and at times life-threatening cardiorespiratory emergency.The Aim of this study was to review our institutional experience regarding clinical spectrum and management outcomes of these high-risk patients.
Materials and Methods: We retrospectively reviewed the medical records of all cases of mediastinal masses in children diagnosed and treated over a 7-year period.
Results: Out of 37 patients with mediastinal masses, malignancy was found in 32 (86%), among which 31 (97%) were hematologic in origin. The median age at diagnosis was 8.8 years. Twenty-two (69%) were males. According to their origins, Lymphoma (72%) was the most common diagnosis. Hodgkin lymphoma and Non-Hodgkin lymphoma were found in 41% and 31% cases, respectively. Leukemia was identified in 25% cases; all of them had T-cell leukemia. Only one patient had neuroblastoma. Common tumors of anterior, middle and posterior location was ALL, lymphoma and neuroblastoma, respectively. Eight (25%) patients were asymptomatic. Nonspecific symptoms such as fever (81%) cough (47%) and dyspnea (37%) constituted the most commonly presenting complaints. Lymphadenopathy observed in 69% cases, while visceromegaly were noticed in 44% cases. Airway compression (59%), superior vena caval compression (18%) and pericardial effusion (26%) was seen in children. Twenty-two patients underwent surgical procedures, local lymph node biopsy was performed in 5 cases, and CT/ultrasound-guided biopsy was done in two patients. Twenty-seven (84.4%) patients were admitted in PICU and assisted ventilation was required in 20 (62.5%) patients. Mean length of hospital stay was 9.3 days. None of our patient expired due to complication related to mediastinal mass or diagnostic procedure.
Conclusions: Although mortality rate were reduced significantly with refinements in surgical technique and anesthetic management, a high index of suspicion and a comprehensive multidisciplinary approach are crucial to further improve the outcomes.

PUB-0040

PAEDIATRIC MALIGNANCIES IN KANO, NORTHERN NIGERIA

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Purpose/Objective: With effective immunization control of several devastating childhood infections in the developing world, non-infectious diseases such as malignancies have become increasingly important causes of paediatric morbidity and mortality. Consequently, this 10-year retrospective study was undertaken to evaluate and document the pattern of childhood cancers in our locality.
Materials and Methods: We reviewed 438 childhood ($\leq$15 years) malignancies diagnosed at the histopathology and hematology laboratories of our teaching hospital over a period of 10 years (2001-2010).
Results: The 438 paediatric malignancies comprised 10.9% of all cancers. They most commonly occurred in early (0-4 years) and late childhood (5-9 years) respectively accounting for 46.1% and 34.7% of paediatric cancers. Retinoblastoma (30.6%), Burkitt lymphoma (19.9%) and acute leukemia (16.9%) were the most frequent childhood malignancies. Unlike most other parts of the world, acute myeloid leukemia was slightly more prevalent than acute lymphoblastic leukemia.
Conclusions: Although there were notable differences, our findings were in broad agreement with those of most other sub-Saharan African series, but differed markedly from the Western world and other high income countries. Further studies are required to identify the environmental factors for the high prevalence of non-familial retinoblastoma and possibly acute myeloid leukemia.

PUB-0041

TREATING CHILDHOOD RHABDOMYOSARCOMA: THE EXPERIENCE OF A START-UP PEDIATRIC ONCOLOGY UNIT

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Purpose/Objective: Introduction: Rhabdomyosarcoma (RMS) is the third most common extracranial solid tumour of childhood. It requires multimodality treatment that is intense and prolonged. We report our results in childhood RMS from a University hospital from Southern India.
Materials and Methods: Patients and Methods: There were 20 children with RMS registered between June 2009 to December 2012.
Results: Results: The age range was 1 to 21 years with the mean age of −− years. There were 9 males and 11 females. Of these, 18 patients were newly diagnosed and 2 patients had recurrent disease. Of 18 newly diagnosed patients, 2 had stage I, 1 had stage II, 6 had stage III and 6 had stage IV disease and in 3 patients staging could not be completed. Thirteen patients had embryonal RMS, 4 patients had alveolar RMS and 1 had a variant called rhabdomyofibrosarcoma. Of the 18 newly diagnosed patients, 5 refused any therapy and 1 patient with microcephaly was treated with metronomic therapy with palliative intent. Twelve patients were treated with intent to cure using the IRS V protocol. Of these, 7 achieved CR, of which 1 relapsed and died and 6 are alive. Of the 5 patients who failed to achieve CR, 4 died of progressive disease and 1 is alive with disease.
Conclusions: Conclusion: Childhood RMS is a difficult disease to treat even in tertiary care hospitals with multidisciplinary teams.

PUB-0042

DELAYED REFERRAL,TREATMENT REFUSAL AND ABANDONMENT, AND OUTCOME FOR HEPATOBLASTOMA IN BANGLADESH

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Purpose/Objective: The aim of this study was to describe the demographics, clinical presentation, treatment refusal, abandonment and outcome for hepatoblastoma at BSMMU Hospital, Dhaka (the largest referral centre) in Bangladesh.
Materials and Methods: A prospective study was performed between March, 2010 to December,2012 for all children with hepatoblastoma attending our department. Initial tumour staging included; detailed clinical history/examination, imaging with CXR, CT and ultrasonography. Patients were treated with either SIOPEL*3 (cisplatin/carboplatin/ doxorubicin) or COG protocol (cisplatin/vincristine/5*fluorouracil). Surgery was performed on most cases before or after chemotherapy depending on tumor stage and therapy response. .
Results: 35 cases of heaptoblastoma were seen, with a median age of 4.5 years (4 months -10 years). M:F ratio 4:1. Presentation was with an abdominal mass (100%), anorexia (35%),fever (30%), vomiting (20%), abdominal pain (10%) and diarrhea (3%). 55% patients had thrombocytosis and serum AFP raised in all cases. 45% had advanced stage (PRETEXT * IV), 10 (28.5%) had pulmonary metastasis at diagnosis. The families of 21 patients (60%) refused treatment at diagnosis because of affordability. Only 14 families (40%) opted for treatment. Among 14, only 6(5, SIOPEL*3 and 1, COG protocol) completed treatment, 2 (14.2%) dying during therapy, two families (14.2%) abandoned/ were lost to follow up. After completion of treatment 1 patient relapsed. 5 patients are well and alive without evidence of disease with a median follow- up of 8 months (range 1 to 21 months).
Conclusions: Hepatoblastoma is a common tumor in our centre (3.2% of all tumor). Most have advanced stage. Late diagnosis,treatment refusal, abandonment are all common. Nevertheless hepatoblastoma can be treated in Bangladesh with 5 out of 14 patients who received treatment alive (35%) albeit with a short follow up. 14% of overall survival rate can only be improved if we can reduce diagnostic delay, treatment refusal / abandonment and costs.

PUB-0043

THE IMPACT OF MPCCN ON THE NUMBER OF PEDIATRIC ONCOLOGY CASES SEEN AND PROCEDURES DONE AT DAVAO REGIONAL HOSPITAL SATELLITE FACILITY

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Purpose/Objective: The Mindanao Pediatric Cancer Care Network (MPCCN) is a system of healthcare facilities aimed to extend cancer care to areas at risk of poor access to existing specialist care. The objective of the study is to determine the number of pediatric oncology cases seen and procedures done at Davao Regional Hospital (DRH) before and after it became a satellite facility of MPCCN.
Materials and Methods: This is a cross sectional study of children diagnosed with cancer at DRH from October 2007- September 2011. Charts were reviewed for the demographic characteristics, diagnosis and procedures done as well as patient disposition on discharge and follow up. The aStat software and Chi square test were used for analysis.
Results: Forty-two pediatric patients with cancer were included in the study from October 2007-September 2009 (n = 15) before MPCCN and subsequently from October 2009-September 2011 (n = 27). Acute lymphoblastic leukemia (n = 9; 60%/n = 17; 63%) was the leading cancer in both groups. There were increases in blood transfusion 12/14 (80%); 25/25 (100%) (p = 0.0257), chemotherapy 1/15(7%); 14/26 (54%)(p = 0.0025) and discharged improved 3/15 (20%); 15/27 (56%) (p = 0.00257) among pediatric patients with cancer. There was a decrease among those discharged against medical advice 6/15 (40%); 2/27 (7%) (p = .0099).

Conclusions: There is a significant increase of pediatric oncology cases and procedures done at Davao Regional Hospital after MPCCN. More patients were discharged improved and there were fewer patients discharged against medical advice.

PUB-0044

COMIC STRIPS: VOLUME 1 RADIOTHERAPY / VOLUME 2 LONG-TERM FOLLOW-UP

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Purpose/Objective: creation and distribution of documents intended for the teenagers and the young adult (TYA) to explain them the radiotherapy (volume 1) and the interests of the long-term follow-up consultations in hematology-oncology (LTFU) (volume 2).
Materials and Methods: further to a survey in 2008 in the Integrated Center of Oncology-Gauducheau, Nantes, France, addressed to the TYA concerned by the radiotherapy, a working-group was created (1 radiotherapist, 1 psychologist-draftswoman and TYA treated by radiotherapy). A comic strips, *Tristan and Dr Radianeau*, was born and was validated (committee of patients, physicians and paramedical, parents, healthy and reached by cancers TYA, SFCE committee). The volume 2, *long-term follow-up, why not*, explaining the interests of the consultations LTFU was created in 2012, according to the same modalities.
Results: Regarding the volume 1: because of a first satisfactory local edition (2011), a second one (2012) was done and allowed its graceful distribution in all the French centers. At present, this comic strips is translated in English and in Spanish and will be soonly available. Regarding the volume 2, the model in course of validation will be available, in 2013, in all the French centers and could be either translated if whished.
Conclusions: according to the wishes of the TYA, 2 comic-strips were created. Tome 1 allows downplaying the radiotherapy and tome 2 explains why it is suggested to return in a center of oncology, sometimes several years after the treatment.

PUB-0045

EXPRESSION OF ICAM-1(CD54) IN PEDIATRIC TUMOR AND ACUTE LEUKEMIA AND THE CLINIC SIGNIFICANCE IN IMMUNOTHERAPY OF CYTOKINE-INDUCED KILLER CELL.

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Purpose/Objective: This study was aimed to investigate the expression of ICAM-1(CD54) in pediatric tumor and acute leukemia (AL).
Materials and Methods: The expression of ICAM-1 on 46 pediatric tumors were detected by immunohistochemistry, and on bone marrow cells of 60 pediatric acute leukemia patients were detected by flow cytometry. 46 pediatric tumor patients were including 10 lymphoma, 3 hepatoblastoma, 6 neuroblastoma, rhabdomyosarcoma, 6 Ewing's sarcomaofbone, 2 fibrosarcoma, 5 primitive neuroectodermal tumor, 11 nephroblastoma and 1 osteosarcoma. 60 AL pediatric patients were including 20 acute lymphocytic leukemia(ALL) patients,and 40 acute nonlymphocytic leukemia(ANLL) patients that contain 20 M1?M2?M3 patients and 20 M4?M5 patients.
Results: The results indicated that expression of ICAM-1 wasmore positive detected in all 3 hepatoblastoma cases, which represent a higher positive rate than in lymphoma, neuroblastoma, rhabdomyosarcoma, Ewing's sarcomaofbone and osteosarcoma. However, no expression of ICAM-1 was observed in fibrosarcoma, nephroblastoma and primitive neuroectodermal tumor patients. On the other hand, the expression rate of ICAM-1 was 55% in ALL, 64% in ANLL M1?M2?M3, and 50% in ANLL M4?M5.
Conclusions: In conclusion, the expression of ICAM-1 in pediatric tumor and acute leukemia had variability. The ICAM-1 positive expression was observed in hepatoblastoma and ANLL M1?M2?M3 patients, whereas it's undetectable in fibrosarcoma, nephroblastoma and primitive neuroectodermal tumor patients.

PUB-0046

EXPRESSION OF TRK IN NEUROBLASTOMA AND ITS CLINIC SIGNIFICANCE

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Purpose/Objective: This study was aimed to detect the expression of Trk family in the pathological specimens of various stages NB patients.
Materials and Methods: The 12 tumors in our hospital from 2005 to 2012 included the two clinical classes of NB: 3 stage 2 NB and 9 stage 4 NB. Each case take 4 biopsy.
Results: The results showed that three cases of stage 2 NB has 2 cases (66.7%) TrkA-positive, 2 cases (66.7%) TrkB-positive, and 2 cases (66.7%) TrkC-positive. Nine Stage 4 NB cases has 3 TrkA-positive cases (33.3%), nine TrkB-positive cases (100%),and two TrkC-positive cases (22.2%). TrkA-positive rate (66.7%) and TrkC-positive rate (66.7%)in stage 2 is higher than in stage 4 (33.3% and 22.2%), but TrkB-positive rate (100%) in stage 4 is higher than in stage 2 (66.7%), and has no statistically significant difference ($P > 0.05$). The distribution of each Trk gene vary among different stage of NB. TrkA and TrkC are expressed highly in stage 2 NB which have a good prognosis. All of the stage 4 NB which have a bad prognosis are TrkB positive.
Conclusions: It is concluded that the expression distribution of Trk family is interrelated with the prognosis of NB. The insignificantly different expression distribution of Trk gene in our experiment might be due to small amount of samples.

PUB-0047

THE EFFECT OF ARSENIC TRIOXIDE ON THE EXPRESSION OF TRK FAMILY IN NEUROBLASTOMA CELLS AND ITS CLINIC SIGNIFICANCE.

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Purpose/Objective: To confirm the Arsenic trioxide(As_2O_3) influence on cell cycle of SK-N-SH cells and gene expression of TrkA, TrkB and TrkC.
Materials and Methods: First culture cells to examine the cell cycle of SK-N-SH cells by flow cytometry analysis and gene expression of TrkA, TrkB and TrkC by Real-time RT PCR.
Results: The percentage of G2/M phase of experimental group is (30.93 ± 0.34)%, the percentage of G2/M phase of control group is (5.29 ± 0.23)%. After treated with As_2O_3, the cell number of G2/M phase is more than control group in SK-N-SH cells, this showed significant difference ($P < 0.01$). With the increase in concentration of As_2O_3, the expression levels of TrkA, TrkB and TrkC are all significantly upregulated, and it is more obvious at 48h than 24h, both of them have statistic difference compared to control group($P < 0.01$).
Conclusions: The result replay As_2O_3 can significantly arrest SK-N-SH cells in the G_2/M phase. It is indicated that to treat stage 1?stage 2 and stage 4S NB, which have a good prognosis and high expression of TrkA and Trk C, it should increase the drug concentration and extend treatment time when using As_2O_3; to treat stage 3 and stage 4NB, which have a bad prognosis and high expression of TrkB, it should use appropriate concentration and treating time when using As_2O_3.

PUB-0048

LONG-TERM OUTCOME IN PEDIATRIC RENAL TUMOR SURVIVORS: EXPERIENCE OF SIRIRAJ HOSPITAL IN THAILAND

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Purpose/Objective: The quality of life for renal tumor survivors depend on long-term outcome. We studied overall survival and renal outcome of Thai children with renal tumors whom treated at Siriraj hospital, Mahidol University, Bangkok, Thailand.
Materials and Methods: Medical records of patients younger than 15 years diagnosed with renal tumors at Siriraj Hospital during 1996-2007 were reviewed.
Results: 30 patients were included. Mean age was $36 +/- 24$ months; male to female ratio 1.7:1. Clinical manifestations included abdominal mass (96.7%), hypertension (40.0%), abdominal pain (36.7%), hematuria (26.7%), post renal obstruction (16.7%) and proteinuria (13.3%). 8 patients (26.7%) had Denys-Drash malformations, WAGR, Dandy-Walker malformation, or genitourinary anomalies. 27 patients (90%) had Wilms tumor and 3 patients had Rhabdoid tumor. 16 patients (59.3%) were stage 3 or more at diagnosis. 3 patients had bilateral diseases. All patients received chemotherapy and 13 patients had radiation therapy. Acute complications included febrile neutropenia (44.4%), hypokalemia (37.0%), hyponatremia (29.6%), Fanconi syndrome (11.1%), urinary tract infections (10.0%) and acute renal failure (7.4%). Mean follow-up time was 57.2 months (2.0-167.6 months). 10 patients (33.3%) died from progressive disease. Overall 5-year-survival was 69.7%. At last follow-up, 2 patients (7.4%) had chronic kidney disease. Both patients received Ifosfamide-Carboplatin-Etoposide protocol and abdominal radiation due to disease progression. Acute renal failure during treatment was noted. One of these had Denys-Drash malformations. Another received autologous peripheral blood stem cell transplantation after relapse of disease in the sacrum and also had proximal tubular acidosis. Antihypertensive medications were needed in 9 patients (30%) for a mean duration of 164 days (49-1,360 days). None had persistent proteinuria or hematuria. No difference was found among mean estimated GFR at diagnosis, one year after treatment and at last follow-up.
Conclusions: Renal impairment after treatment of renal tumors in children is not uncommon. Long-term follow-up of renal function in these patients is recommended.

PUB-0049

SIOP PODC: CONSENSUS CLINICAL GUIDELINES FOR THE MANAGEMENT OF CHILDREN WITH WILMS TUMOUR IN A LOW INCOME COUNTRY

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Purpose/Objective: In high income countries more than 85% of children with Wilms tumour survive. Reported survival in very resource limited settings ranges from 11% - 50%. Known challenges are late presentation with advanced disease, malnutrition, failure to complete treatment and poorer facilities both for the specific cancer treatment and for supportive care. Optimal management for these settings takes those challenges into account.
Materials and Methods: SIOP PODC is producing practical recommendations for the management of childhood cancers in low income countries. Levels of available facilities for the care of patients with Wilms tumour can be defined. Setting 1 is where the minimal requirements for treatment with curative intent are available. The recommendations for setting 1 are based on available published evidence and personal experiences (expert opinion) with consensus among members of the writing group if no higher level of evidence was available.
Results: Minimal requirements for treatment of children with Wilms tumour with curative intent are defined and include basic laboratory and radiologic facilities, chemotherapy and safe administration, surgical care, adequate supportive care and social support to enable parents to complete treatment. Practical recommendations for the general management include supportive care, social support and registration of patients. Recommendations specific for Wilms tumour care include the diagnostic procedures with emphasis on the role of adequate ultrasonography; the use of SIOP based preoperative chemotherapy with a reduced dosage for malnourished children and postoperative chemotherapy based on surgical staging. Surgery should be unhurried, follow a formal protocol and avoid resection of organs.
Conclusions: Multidisciplinary clinical guidelines that take local challenges into account will help to improve survival of children with Wilms tumour in very resource limited settings.

PUB-0050

DISTRIBUTION AND OUTCOMES OF PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS: A SINGLE CENTRE EXPERIENCE FROM INDIA

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Purpose/Objective: Central nervous system (CNS) tumors are the most common solid tumors in children. A multi disciplinary approach is paramount for good outcomes in this subset of patients. Due to lack of a centralized registry and financial constrains there is paucity of data on CNS tumors from India. Here we describe the spectrum of CNS tumors from a tertiary care centre in India focusing on distribution and outcomes.
Materials and Methods: Retrospective review of medical records of all pediatric oncology patients diagnosed at our centre between 2005 and 2012.
Results: Of 895 children diagnosed with cancer 87 (9.7%) had primary CNS tumors with a median age of 8.2y (9m-20y) and male: female ratio of 2.3:1. The distribution of these tumors at our centre was as follows: Medulloblastomas and Primitive Neuro-Ectodermal Tumors in 35.6% (n = 31), Astrocytomas in 27.6% (n = 24), Non-specified Gliomas and Brain-stem Gliomas in 9.2% (n = 8), Ependymomas in 8.1% (n = 7) and Craniopharyngiomas in 5.7% (n = 5). Twelve patients had other tumors. Six patients refused treatment upfront whereas 18 abandoned treatment. There were 17 patients who switched to another centre for further treatment. The major reason for refusal and abandonment (seen in 27%) was lack of finances and distance from the treating unit. There were 46 patients who took treatment or are presently on treatment at our centre and of these 12 have expired (26%).
Conclusions: Incidence of CNS cancers in the west is to the tune of 30% of all malignancies and mortality of approximately 5%. In India the reasons for their low incidence and poor outcomes are multifactorial. In a resource and awareness poor setting there is lack of adequate knowledge and referral. Refusal to treatment, abandonment and attrition rates are high. The lack of effective multi-modality approach, that is a key to effective management is also a major barrier in delivery of care.

PUB-0051

A DECADE OF CARING THROUGH MULTIDISCIPLINARY COLLABORATION AND EVIDENCE BASED PRACTICES AT THE CHILDREN'S CANCER CENTER OF LEBANON (CCCL)

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Purpose/Objective: The mission of the CCCL, established in 2002 is to improve the survival rates of children with cancer and provides the best possible treatment and care. This paper is to provide a brief overview of the multidisciplinary team efforts in fostering excellence in patient care and improving quality of life for children with cancer in Lebanon.
Materials and Methods: The CCCL is affiliated with St. Jude Children's Research Hospital in Memphis due to lack of specialized centers in Lebanon for treatment of malignancies. The cure rate was 40% much lower than what was reported in developed countries.Initially, there were 27 staff members and the number of admissions was limited to 50 per year. In collaboration with the Outreach Program at St. Jude, 13 staffs were sponsored to attend pediatric oncology workshops. The workshops covered a wide range of education and hands on experiences that are currently being implemented as ongoing processess in everyday utilization in clinical work. It was imperative for the team to strive making the center develop. Educational programs for patients and families in Arabic have been provided and evidence practice based policies and protocols for the treatment of cancer have been implemented and updated routinely based on current needs and published studies. A clinical research unit was initiated for generating new patient data, in addition to a Child Life depatment for social worker, psychlogical, volunteers and educational services.
Results: To Date ther are 76 staff members (33 staff nurses) and 880 patients. The cure rate for patients with ALL is now 88% (55% increase) a two fold increase since prior to 2002. 96 articles in peer review journals have been publihed and over 50 abstracts presented in national and international conferences.
Conclusions: The multidisciplinary team efforts at the CCCL are a success story which we proud of and eager to share

PUB-0052

MULTIDISCIPLINARY PROGRAM FOR THE USE OF MEDICAL CANNABIS IN ONCOLOGY PEDIATRIC PATIENTS

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Purpose/Objective: The medical use of cannabis is for the treatment of various symptoms and side effects such as pain, nausea and vomiting. Studies have been published regarding adults, but less research has been conducted on children with cancer. Although studies suggest the possible damage to the developing brain when used before the age of 16 years, cannabis use for improving of quality of life in patients with limited life expectancy is considered acceptable. The purpose of the project is to describe the multidisciplinary program of using medical cannabis, and to evaluate its role in symptoms relief.
Materials and Methods: A nurse led a multidisciplinary program that included a physician specialized in pain management and a social worker .The guidelines included identification of medical cannabis candidates, and education of parents and children regarding optimal use and side effect. Patients were interviewed about their expectations and a frequent follow-up was made by the multidisciplinary team.
Results: Seven patients, aged 2-25 years with various cancer diagnoses, most of them in their terminal stage of life, received cannabis. They all received the cannabis for pain relief, five for nausea and decrease in appetite, and two for the improvement of sleep. Five patients died during the first month of treatment, but four of the five families reported that the cannabis improved their child's last days. In those families we were not able to document a specific symptom relief due to the short time of use. The other two patients reported better pain control, appetite and well being. The only side effect was panic attack due to over- use above the prescribed dosage in two teenager patients.
Conclusions: Medical cannabis may provide a relief of major symptoms presented by the patients. Expansion of this modality for some patients along the continuum of the disease, presents a professional challenge for the future.

PUB-0053

NEUROBLASTOMA WITH INTRACTABLE DIARRHEA: A REPORT OF 6 CASES.

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Purpose/Objective: Neuroblastoma with intractable diarrhea is very rare, diagnosis is likely to be delayed, the treatment has something special also. So it needs to be summarized and discussed.
Materials and Methods: We'd like to report 6 cases of neuroblastoma with intractable diarrhea in our hospital, including the clinical features, electrolyte disturbance, pathological characteristics, treatment and prognosis.
Results: 6 cases of neuroblastoma with intractable diarrhea from 1996 to 2006.All of cases were male. The minimum age at diagnosis was 1 year, the maximum was 2 years old and a half. The minimum age when diarrhea occurred was 9 months old, the eldest was 2 years old, the minimum time of the diagnosis was 4 months, the longest was 1 year. Feces were Loose or watery, 3-8 times a day, routine examination were negative, drug was invalid. Ultrasound found abdominal tumor after diarrhea happened as the first symptom (5/6).2 diarrhea cases alleviated after preoperative chemotherapy, one case stopped. 3 cases received operation without chemotherapy, 2 of them stopped diarrhea after operation, while 1 case died. The other 1 case began with abdominal pain, during the preoperative chemotherapy, diarrhea became serious,the symptoms continued and the patient died at last mainly because electrolyte disorders. Tumor were located in the adrenal gland(4/6), retroperitoneal(1/6) and anterior sacral(1/6). Pathology were ganglioneuroblastoma and neuroblastoma. Clinical stage I-II(5/6), stage III(1/6).2 cases died, 4 cases survived. Blood vasoactive intestinal peptide (VIP)were not measured for some reason.
Conclusions: Intractable diarrhea and hypokalemia were the main feature of this kind of neuroblastoma, diarrhea often stopped after operation. Hypokalemia correcting preoperatively, serum potassium monitoring during the operation, cardiac arrest preventing are very important. The prognosis of neuroblastoma with intractable diarrhea is pretty good.

PUB-0054

NIMOTUZUMAB IN REFRACTORY BRAIN TUMORS

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Purpose/Objective: There is limited options for treatment of relapsed or progressive pediatric brain tumors. Nimotuzumab (epidermal growth factor receptor (EGFR) monoclonal antibody) has been used for adult advanced stage head and neck region tumors and high grade gliomas. Nimotuzumab has been used for pediatric high grade gliomas in phase 2 and 3 studies. The aim of this study is to evaluate the effect of nimotuzumab in refractory and relapsed brain tumors.
Materials and Methods: Between December 2010 and December 2012, 8 patients with refractory and relapsed brain tumors were included to the study. All received one or more systemic chemotherapy regimen before enrollment. Nimotuzumab was given 150 mg/m2 weekly for 6 weeks for induction, then two-weekly until clinical or radiological progression.
Results: One boy and 7 females aged between 2.5 and 17 years-old (median 7.5 years) were evaluated. Diagnoses were diffuse intrinsic pontine glioma (DIPG) in 3 patients, high grade glioma) in 3 patients, supratentorial primitive neuroectodermal tumor (sPNET) in 1 patient and embriyonal PNET in 1 patient. Median progression free survival time was 6.5 months (1.6-9.3 months). Two patients with objective responses were noted: complete response in the patient with sPNET and partial response in patient with DIPG. They are on treatment with nimotuzumab at 9 and 6 moths with aforementioned responses. Due to progressive disease nimotuzumab treatment was stopped in the rest of patients. Except one patient with resistant hyponatremia, there was not any major side effect related to Nimotuzumab.
Conclusions: In a small series of progressive pediatric brain tumor patients' two objective responses were observed. Interestingly the patient with sPNET responded very well for 9 months (still on therapy). Nimotuzumab might be an effective targeted therapy option with low-toxicity for pediatric brain tumors.

PUB-0055

COMPLETE RESPONSE WITH BRENTUXIMAB IN A PATIENT WITH PRIMARY REFRACTORY CD30 POSITIVE HODGKIN LYMPHOMA

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Purpose/Objective: The outcome of patients with primary refractory or early relapsed Hodgkin lymphoma (HL) after high-dose chemotherapy and autologous stem cell transplantation (HDCT-AuSCT) is poor. To improve the outcome of such patients the CD-30 targeted agent brentuximab vedotin has been used with impressive results in adult refractory HL.
Materials and Methods: Here we report the complete response of a 14.5-year-old boy with refractory HL
Results: Stage IIA nodular sclerosing HL with left anterior cervical primary was diagnosed in 13-year-old boy in 2010. Four cycle of ABVD regimen was given and radiotherapy was not planned due to complete metabolic response on PET-CT. At 2nd month off-therapy relapse was diagnosed on PET-CT with newly-developed mediastinal, right cervical lymph nodes and lung nodules on PET-CT. OEPA regimen was started. He underwent HDCT-AuSCT on his second complete response on PET-CT after 4 cycles at 12th month from diagnosis. Five months after HDCT-AuSCT (at 18th month from diagnosis) his second relapse with B symptoms, mediastinal, subdiaphragmatic lymph nodes, bone and lung involvement was diagnosed. Biopsy proved the relapse. Gemcitabine and vinorelbine was given but no response was noted. After Brentuximab vedotin was started as monotherapy at the dose of 1,8mg/kg three-weekly, fever resolved, sedimentation rate decreased, metabolic activity on PET-BT disappeared. Local radiotherapy (36 Gy) to involved fields was given after 4th cycle of targeted therapy. He has received 16 cycles of brentuximab monotherapy with no evidence of disease for 12 months. No major or minor adverse effect was noted.
Conclusions: Targeted therapy with anti-CD30 antibody has impressive results for treatment of relapsed/refractory CD30 positive lymphomas. Pediatric experience has been reported in a few patients mostly among adult series of patients. Brentuximab might be an effective treatment option as targeted therapy for such patients.

PUB-0056

INCIDENCE OF RETINOBLASTOMA IN CHILDREN CONCEIVED BY ASSISTED REPRODUCTIVE TECHNIQUES

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Purpose/Objective: Retinoblastoma is the most frequent eye tumor in children with an incidence of 1 in 15*20.000 live births. There are complicated results about RBL incidence born after assisted reproductive techniques (ART). We aimed to evaluate our patients with retinoblastoma conceived by ART.
Materials and Methods: Patients diagnosed with RB between 1993 and 2013 were retrospectively reviewed, five patients born after ART were evaluated.
Results: In a 20 years period, 3 females and 2 males among 302 retinoblastoma patients were born after ART (4 invitro fertilization and 1 ovarian stimulation). Maternal and paternal ages were between 29-39 years (median 35) and 33-51 years (median 36), respectively. Three mothers had their first pregnancy, one mother had previous abortion. Three mothers had hypertension, hypercholesterolemia and diabetes mellitus due to pregnancy. Median patient age at diagnosis was 11 month-old (ranged 0.5-18). 4 of 5 patients had unilateral tumor. Three patients were in remission after systemic chemotherapy, one patient with enucleation. Enucleation was performed for the fourth patients at diagnosis. He received systemic chemotherapy but died of central nervous system progression because of involvement of optic nerve. Fifth patient with bilateral tumor had additional congenital anomalies (polydactyly, clubfoot, mental motor retardation). Unilateral enucleation was performed for the progression after second line systemic chemotherapy. She is currently receiving radiotherapy. The other eye is in remission. One of the patients had triplet siblings; RBL did not develop the others. Birth weight and gestational ages were 1.740-3.900 gr (median 3420) and 35-39 weeks (median 38), respectively. None of the patients had history of retinoblastoma in their families.
Conclusions: There are conflicting results in the literature about various national perinatal surveys incidence of ART in retinoblastoma. The incidence of retinoblastoma in Turkey between 2002 and 2006 is 3.8%. It is difficult to interpret this result as increased incidence of retinoblastoma in reproductive techniques.

PUB-0057

EXPRESSION OF IMMATURE (NESTIN) AND MATURE (NEUROFILAMENT AND GLIAL FIBRILLARY ACIDIC PROTEIN) RETINAL CELL MARKERS IN RETINOBLASTOMA TO CLARIFY ITS ORIGIN.

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Purpose/Objective: To clarify which factors are expressed in retinoblastoma cells and to give insights into the cell origin of retinoblastomas
Materials and Methods: Eleven patients with retinoblastoma patients were diagnosed in Ocular Oncology Clinic, Ophthalmic Department, Ain Shams University; they were divided into five groups according to International Classification of Retinoblastoma. Sections were examined histopathologically and immunostained by mouse monoclonal antibodies against Nestin, glial fibrillary acidic protein (GFAP) and Neurofilament (NF) for identification of undifferentiated stem cells, mature glial cells and mature neurons.
Results: Histopathologic findings in the examined samples revealed that 6 cases were poorly differentiated and five cases were well differentiated. Both Nestin and GFAP expressions were detected in the stromal cells not in the tumor cells, possibly representing muller cells and reactive stromal astrocytes respectively, in contrast, in all samples neurofilaments were expressed in the cytoplasm of the most retinoblastoma cells.
Conclusions: The results of this study support that retinoblastomas are derived from mature neural cells and not originate from cancer stem cells.

PUB-0058

CURATIVE EFFECT OBSERVATION OF GAMMA GLOBULIN IN THE TREATMENT OF IMMUNE THROMBOCYTOPENIC PURPURA WITH ECZEMA AND HIGH IGE LEVEL

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Purpose/Objective: To observe the curative effect of gamma globulin in the treatment of immune thrombocytopenic purpura (ITP) in children with eczema and high IgE level
Materials and Methods: The clinical and laboratory records of 200 ITP cases from February 2005 to May 2010 were collected, which were divided into three groups: 69 cases in Group A(with no eczema and normal IgE level), 75 cases in Group B(with eczema and high IgE level) and 56 cases in Group C(with eczema and normal IgE level). The curative effect of the three groups was compared.
Results: ?The total gamma globulin effective rate of the 200 cases was 93.5% after three months. Effective rate of Group A, B, C was 97.1%, 90.7%, and 92.9%, respectively. The curative effect of Group A was much better than Group B and C($\chi^2_{AB} = 32.10$,$\chi^2_{AC} = 7.58$,$P < 0.017$).There was no significant difference between Group B and C($\chi^2 = 6.15$,$P > 0.017$)?After therapy, IgE levels of 62 cases were reduced with a total effective rate of 96.8%, and 16% of them had a platelet count of more than 100×109/L. While, IgE levels of 13 cases were not reduced with a total effective rate of 61.5% ($Z = -3.060$,$P < 0.05$). ?The response time of platelet of Group B was longest($P < 0.017$), the peak of platelet count of Group B was lowest($P < 0.017$), the hemorrhage control time of Group B was longest($P < 0.017$).?2 cases(2.9%) in Group A developed into chronic ITP while 23 cases in Group B(30.7%) and 6 cases in Group C(10.7%).There was significant difference between Group A and Group B as well as Group B and Group C($\chi^2_{AB} = 19.31$, $\chi^2_{BC} = 7.41$,$P < 0.017$).
Conclusions: The curative effect of ITP in children with eczema and high level IgE is poor, and they are prone to develop into chronic ITP.

PUB-0059

CROCIN EXHIBITS ANTI-TUMOR EFFECTS ON HUMAN LEUKEMIA HL-60 CELLS IN VITRO AND IN VIVO

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Purpose/Objective: Crocin is a carotenoid of the saffron extract that exhibits anti-tumor activity against many human tumors. However, the effects of crocin on HL-60 cells in vivo have not been evaluated. This study aimed to examine the effects of crocin on HL-60 cells in vitro and in vivo and investigate the underlying mechanisms.
Materials and Methods: HL-60 cells were treated by crocin, and cell proliferation, apoptosis and cell cycle profiles were examined by MTT assay, AO/EB staining and flow cytometry, respectively. Furthermore, HL-60 cells were xenografted into nude mice and treated by crocin, the tumor weight and size were calculated, and the expression of Bcl-2 and Bax in xenografts was detected by immunohistochemical staining.
Results: Crocin (0.625-5 mg/ml) inhibited HL-60 cell proliferation and induced apoptosis and cell cycle arrest at G0/G1 phase, in a concentration and time dependent manner. In addition, crocin (6.25, 25 mg/kg) inhibited the tumor weight and size of HL-60 xenografts in nude mice, and inhibited Bcl-2 expression and increased Bax expression in xenorafts.
Conclusions: Crocin inhibits the proliferation and tumorigenicity of HL-60 cells, which may be mediated by the induction of apoptosis and cell cycle arrest and the regulation of Bcl-2 and Bax expression.

PUB-0060

OUTCOME OF CHILDHOOD NON HODGKIN LYMPHOMA WITH INTENSIVE CHEMOTHERAPY IN BSMMU BANGLADESH.

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Purpose/Objective: a. To review feasibility of giving intensive chemotherapy in Non-Hodgkin lymphoma (NHL) at the BSMMU (largest referral centre) in Bangladesh.
b. To review patientsdemographics, disease stage,pattern, treatment refusal/abandonment, toxicities and outcome
Materials and Methods: A prospective study was conducted from January to December 2012 for all NHL patients referred. Details of patient's family status, parental education, immunization record, initial clinical presentation,diagnosis and treatment recorded were registered in POND database.Diagnostic,staging workup included histopathology or FNAC, serous fluid/CSF cytology (cytospin),bone marrow aspiration, biochemistry & imaging. Intensive chemotherapy given according to histological subtypes. Burkitt (BL) treated with LMB-96 and Lymphoblastic (LL) with BFM-95. Patients without definitive subtypes treated according to primary site of tumor. All patients were reviewed during & after each cycle of therapy.
Results: Out of 455 patients registered in 2012, NHL 51 (11.2%) was the second most common cancer after ALL. 80% started treatment but 20% families refused therapy. BL was the commonest type(75%), LL(25%). Median age 7 years, M:F 2.8:1. 11 were initially diagnosed & treated as TB elsewhere. 28 patients with BL received LMB-96, 3 discontinued treatment, 12 died, and 13(46%) are alive. Nine were treated with BFM-95 for LL; 2 discontinued, 2 expiredand 5(56%) are alive. 89% patients presented at advanced stage, mostly stage III; 89% of LL, 64% of BL and stage IV with involvement in CNS 8%, BM 10%, testicular 3%. Reasons for abandonment were cost of treatment (78%),disease progression (11%), excess toxicity (11%). Toxicities were commonly observed during COPADM 1&2, CYM/CYVE 1&2 in BL, induction & M phase in LL; including tumour lysis, mediastinal syndrome, febrile neutropenia/septicemia, mucositis, diarrhoea, vomiting, GI-bleeding, and hepatoxicity.
Conclusions: Delayed diagnosis, misdiagnosis, treatment refusal/abandonment, and excess toxicity must be reduced if we are to increase NHL survival rates.

PUB-0061

THE RELATIONSHIP BETWEEN CHFR MRNA EXPRESSION AND CLINIC-PATHOLOGICAL FEATURES IN B-CELL NON-HODGKIN'S LYMPHOMA

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Purpose/Objective: To investigate the CHFR(checkpoint with FHA and ring finger) expression in non-Hodgkin lymphoma(NHL), and the relationship between CHFR expression and clinic-pathological characteristics
Materials and Methods: The expression of CHFR mRNA were detected in the tissues of 81 patients with B-NHL as well as 38 reactive hyperplasia of lymph node (RH) by Real-time fluorescence quantitative PCR.
Results: ?CHFR mRNA was shown in the RH group, but the level of mRNA expression was significantly lower in 81 B-NHL examples, and the mRNA expression was loss in 2 patients, the discrepancy had statistical significance($P < 0.05$).?The expression was different between B-NHL patients in I + II group and III + IV group($P < 0.05$). B-NHL was divided into 0-1group and 2-5 group according to IPI score, the expression of CHFR mRNA in high score group was lower than that in the low score group ($P < 0.05$). However, the expression of CHFR mRNA had no correlation with clinicpathological characteristics,such as age, gender, B symptoms, serum LDH and ECOG.
Conclusions: The down-regulation of CHFR mRNA expression may contribute to the occurrence of B-NHL, and is associated with the malignancy and progress of B-NHL.

PUB-0062

ANALYSIS OF INFECTION PATHOGENS AND DRUG RESISTANCE IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES

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Purpose/Objective: To provide information for clinical anti-infection therapy by analyzing the distribution of pathogens and their resistance to antimicrobial drugs.
Materials and Methods: Retrospective analysis was used to study the characters of infection in 2655 children with malignant blood disease in department of children hematology in the Affiliated Hospital of Qingdao University Medical College from Aug.2010 to Aug.2012. The data was processed by the software SPSSl3.0.
Results: The detection rates of pathogens from ALL and AML were higher than solid tumor. 105 bacterial strains were isolated from 2655 cases. The percentages of Gram- negative bacterium, Gram- positive bacterium and fungus were52.38%,32.38%and15.24% respectively. The Gram-negative bacteria mainly consisted of Pseudomonas aeruginosa , Escherichia coli, pneumonia klebsiella ,Acinetobacter baumannii. The number of extended-spectrum beta-1actamages(ESBLs) was six, which accounted for 10.91% of all Gram-negative bacterium .The isolation rates of Escherichia coli and pneumonia klebsiella with positive extended-spectrum beta-1actamages(ESBLs) were 45.45% and 14.29% respectively. Resistance rates of Pseudomonas aeruginosa to ceftriaxon and ceftazidime were 61%and30.77% respectively. No Pseudomonas aeruginosa was resistance to imipenem, cefoperazone/sulbactam, piperacillin/tazobactam, gentamycin.One case was isolated from three Xanthomonas maltophilia which resisted to imipenem. The Gram-positive bacteria mainly consisted of coagulase negative Staphylococcus (CNS) and E. faecium. The detection rate of MRCNS was 20.58%,which accounted for 53.85% of all CNS. MSCNS were sensitive to the Second generation cephalosporin. MRSA were not founded. All Gram-positive bacterias were sensitive to vancomycin and teicoplanin except one E. faecium which was resistance to vancomycin. Fungus mainly consisted of Candida albicans, accounted for 73.33%.No Fungus was resistance to Flucytosin and Amphotericin .

Conclusions: Pathogens in children with malignant blood disease mainly consisted of Gram-negative bacteria and resistant organism had a high rate. The clinical practice should actively take bacteria culture and drug sensitivity test, use antibiotics properly, decrease the production of drug resistant stains.

PUB-0063

RETINOBLASTOMA: EXPERIENCE OF A SINGLE INSTITUTE IN NORTHERN PAKISTAN. (A DEVELOPING COUNTRY EXPERIENCE)

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Purpose/Objective: Purpose: To define characteristics, response to treatment, survival of children with retinoblastoma presenting to children's hospital during 2005-2012.
Aim: Our aim is to determine patient profile and outcome in northern region of Pakistan.
Materials and Methods: Method: Retrospective and ongoing study. All patients with the diagnosis of Retinoblastoma, visiting/ referred for evaluation or treatment from November 2005 to December 2012.
Results: Results: A total of 93 patients were registered, males 48(51%) and females 45(49%). Unilateral disease was seen in 74% and bilateral in 26%. Most were in stage II (51%) and stage III (18%). At present 70% are alive off treatment
Conclusions: Conclusion: Retinoblastoma is the commonest intraorbital tumor. It has good prognosis with timely treatment which includes enucleation, chemotherapy with or without radiotherapy.

PUB-0064

RESULTS OF TREATMENT OF PATIENTS WITH NEUROBLASTOMA STAGES 4S

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Purpose/Objective: OBJECTIVE: To review the clinical features and outcomes of treatment of all cases of stage 4S neuroblastoma
Materials and Methods: METHODS: from 2007 to 2012 years we had been observing 98 patients with morphologically confirmed neuroblastoma (low and intermediate risk group) at the mean age of 2.6 years (from 1 month till 15 years). There were 8 patients (8%) with IVS stage of the disease. Localization of primary tumor: adrenal glands - 4, retroperitoneal space - 4. Localization of metastases: combined metastasis to the liver and bone marrow * 3; liver and soft tissues - 2, bone marrow - 3. There were performed adrenalectomy or biopsy of liver or soft tissue component of the tumor for the purpose of diagnosis. All children received chemotherapy for intermediate risk group neuroblastoma according COG ?3961. Nobody received radiation therapy.
Results: RESULTS: Median follow up - 4 years (range 9 months - 5 years). One patient (age 1 month) with multiple liver metastases died from toxicity of chemotherapy. In 2 patients continues to be observed residual abdominal masses.
Conclusions: RESULTS: Median follow up - 4 years (range 9 months - 5 years). One patient (age 1 month) with multiple liver metastases died from toxicity of chemotherapy. In 2 patients continues to be observed residual abdominal masses.

PUB-0065

WILMS TUMOR IN TURKISH CHILDREN:EXPERIENCE OF A SINGLE CENTER

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Purpose/Objective: To evaluate the clinicopathologic features and treatment outcomes in Wilms tumor
Materials and Methods: We retrospectively evaluated clinicopathologic characteristics and treatment results of sixty-one patients, diagnosis of Wilms tumor, between February 1991-February 2012..
Results: Twenty nine of the cases(47.5%) were females and 32(52.5%) were males, ages ranged between 4 months-171 months(36 $\pm$ 27.62 months).The tumour was located in the right kidney in 26 cases(43%),left kidney in 28 cases(46%),and bilaterally in 7 cases(11%).Eleven patients(18%)were diagnosed with biopsy, 50 patients(82%) with total nephrectomy.The existence of anaplasia was determined in 5cases(8%).
There were 5 cases(8%)at stage I,22 cases(36%)at stageII,16 cases(26%)at stageIII,10 cases(17%)at stage IV and 8cases (13%)at stage V. All of the stageIV cases had lung metastasis.A treatment comprising of Vincristine + ActinomycinD $\pm$ Adriamycin $\pm$ Cyclophosphamide $\pm$ Radiotherapy was applied a period of 24-52 weeks depending on the stages.

During the 1-269(90 $\pm$ 10)month observation periods,the overall survival rate was found to be 81% and the event-free survival rate was 76% for 5 and 10 years. Overall survival rates according to stages were determined to be 100% in stageI, 86%in stageII, 81% in stageIII, 60%in stageIV, and 87.5%in stageV.It was observed that from the 11 patients that were lost, 6 died within the first 2 months following diagnosis and others died between the 12^{th} -20^{th} months. No significant differences were identified according to stage(p:0.367).Survival with the existence of anaplasia was also found to be lower in our patient group.While the EFS and OS were 60% and 60% in the group with anaplasia, they were 77.8% and 83%without anaplasia($p = 0.4$ and 0.23). Two of the 5 cases observed with the existence of anaplasia were lost, they were at stage IV. Secondary malignity did not develop in any of our patients.
Conclusions: Survival rates achieved with the application of combined treatment regimes increased by years. Minimizing the morbidities of surviving patients was aimed with the use of risk-oriented treatment regimes.

PUB-0066

ACUTE NEUROLOGIC COMPLICATIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: In recent years, 5 years event-free survival in children with acute lymphoblastic leukemia (ALL) has increased to 80% with the use of intensive chemotherapy protocols. It has been noted that the frequency of the side effects also increased. One of them is neurotoxicity reported in 3-13% of children with ALL. Aims: This study analyzed acute central nervous system (CNS) complications occurred during ALL treatment.
Materials and Methods: A total of 265 children diagnosed as ALL between 1995 and 2010 were enrolled into the study. They all completed the full courses of ALL-BFM-95 and ALL-BFM-2000 chemotherapy protocol. We retrospectively evaluated their clinical records and collected neurological events occurred during treatment. Patients with CNS leukemic infiltration and peripheral neuropathy at diagnosis and post-treatment late-onset encephalopathy or neurocognitive defects were excluded from the study. Neurological exam, cranial magnetic resonance imaging (MRI), electroencephalography (EEG), lumbar puncture (LP) and metabolic screening for differential diagnosis were performed. None of the patients had a history of neurological abnormalities prior to the onset of ALL.
Results: Twenty-three(5%) out of 265 children (F: 13,M:10) had developed CNS complication during therapy. Their median age at diagnosis was 4.8?}2.3 years (range, 1-17.5 years). None of them presented CNS leukemic involvement at diagnosis or at the time of the neurologic event. The events were convulsion(n:12), intracranial aspergillosis (n:4), PRES(n:3), sinus vein thrombosis (n:2), inadequate ADH syndrome (n:1) and transient ischemic attack (n:1). Ten children (43%) experienced neurologic events during the induction phase. In 8 cases (34%), the events occurred during reinduction and in 5 (21%), it occurred during the consolidation phase. Outcome of the 23 patients developed CNS complications, 14(60%) stayed healthy and 9 (39%) became epileptic. One (4%) died after the development of CNS complication.
Conclusions: CNS complications are frequent events during ALL therapy, and require rapid detection and prompt treatment to limit permanent damage.

PUB-0067

EFFECT OF THE DIFFERENT FUNGUS STIMULI ON THE EXPRESSION OF MEMBRANE RECEPTORS OF NATURAL KILLER CELLS

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Purpose/Objective: To explore the effect of the different stimuli and morphotypes of Aspergillus fumigatus and Candida albicans on the expression of membrane receptors of cytokine-induced natural killer (NK) cells derived from cord blood using Transwell non-contact cell culture system. Try to compare the differences between the antifungal activity and the tumor cytolysis performed by NK cells.
Materials and Methods: The experiments were divided into two groups: Transwell non-contact culture(indirect-contact groups) and mixture culture(direct-contact groups). The ratio of NK cells to fungus and K562 cells was 10:1. The expression of NKG2D?TLR2 and CD94/NKG2A on NK cells were evaluated by flow cytometry after 6h of co-culture.
Results: The expression of TLR2 on NK cells in fungus direct-contact group was significantly higher than those in control groups ($P < 0.05$). As to indirect-contact groups, TLR2 expression on the NK cells was not significantly different($P > 0.05$). There were no differences in the expression of NKG2D or CD94/NKG2A on NK cells in both direct-contact groups and indirect-contact ones($P > 0.05$). The expression of NKG2D on NK cells was significantly higher in K562 cell direct-contact groups than that in control($P < 0.05$), while

no differences of the expression of TLR2 or CD94/NKG2A on NK cells were found ($P > 0.05$).
Conclusions: Fungus can activate NK cells by up-regulating the expression of TLR2, which is different with tumor cells in activating NK cells. Either fungus or tumor cell stimuli have effect on the expression of CD94/NKG2A.

PUB-0068

KNOWLEDGE ABOUT CHILD HOOD CANCER IN ACCRA - GHANA

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Purpose/Objective: To determine the level of knowledge about childhood cancer among the general public in Accra.
Materials and Methods: Questionnaires were administered by nurses from the Paediatric Oncology Unit at Korle-Bu Teaching Hospital in three communities in Accra. Total number interviewed was 150. Informed consent was obtained.
Results: The respondents, 54% had tertiary education. Only 45% had good knowledge of what cancer was. 84% knew children could get cancer. Source of information was mainly from the media in 49% of respondents and others from friends in 30.3%. 59.7% had some idea about causes of cancer e.g. smoking, x-rays and chemicals. A high proportion 63.3% knew a child who had had cancer. About 50% knew some types of cancer and 64.3% knew signs of cancer. The majority 85.7% said childhood cancer could be treated and 97% that it should be treated. The main reason was treatment should be given to save their lives as they are future leaders. 75% stated hospital drugs should be used as treatment. Less than 25% stated spiritual, herbal and food for treatment. 92% knew that not all children die from cancer and 94.7% advocated for inclusion of cancer treatment in the National Health Insurance Scheme.
Conclusions: The general public in Accra is highly aware of the fact that cancers occur in children and can be treated successfully. There is still the need for further public education on childhood cancer, particularly the early warning signs. The media is an effective avenue and should be used to help disseminate information about childhood cancers in addition to other methods of awareness creation.

PUB-0069

PEDIATRIC ONCOLOGY: INCIDENCE AND SURVIVAL PROBLEMS IN EGYPT AS A MODEL OF DEVELOPING COUNTRY

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Purpose/Objective: The study aimed at reporting the incidence of different types of malignancy affecting the Egyptian children compared to other developing countries as well as western countries.

The survival of Egyptian children with cancer was also studied and compared to that of western countries
Materials and Methods: Children with different types of malignancy treated in Alexandria Main University Hospital,Egypt,over a period of 20 years were reported and analysed.Data were obtained from the Pediatric Surgery and Pediatric Oncology Departments as well as the Orthopedic and Neurosurgery Departments.

The overall survival incidence of these cancer children was reported and compared to that in the developed countries. The possible causes of low survival were studied.
Results: The total number of children with malignancy was 1277 over a period of 20 years.Leukaemia and brain tumors were of the same incidence compared to other developing and developed countries.However,there was a higher incidence of abdominal lymphoma and lower incidence of soft tissue tumors.The 5-years survival rate of all malignant tumors was reported to be 39.8%.This was much lower compared to that of Europe and USA (60-70%).

The main causes of this low incidence of survival were the delayed presentation and delayed diagnosis and thus the non-efficient therapy.These causes of delay were related to the side of the parents in one angle due to neglegence and low socioeconomic status and also related to the side of the pysicians in another angle due to lack of awareness.
Conclusions: *Several factors have their influence on the incidence of different types of pediatric cancer in developing countries.

*The survival rate of cancer children in Egypt as a model of developing countriy is much lower than that of developed countries.

*Among the possible causes of low survival rate are the delayed presentation,delayed diagnosis and lack of specialized peditric oncology centers.

PUB-0070

RESECTION OF LUNG NODULES IN PEDIATRIC ONCOLOGY PATIENTS

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Purpose/Objective: In children with solid malignancies, the most common site of distant metastasis is the lung. Pulmonary metastasectomy is part of the standard of care in adult malignancies, but its role in pediatric patients has been poorly characterized. The purpose of this study was to review our experiences with the resection of lung nodules to elucidate the indications for and optimal timing of metastasectomy.
Materials and Methods: A retrospective review of pediatric oncology patients who underwent lung nodule resection between 1998 and 2013 was performed. The benefits, outcomes according to the tumor histology, selection criteria, adjuvant therapies and the surgical techniques were retrospectively accessed.
Results: Eight pediatric oncology patients (hepatoblastoma 4, nephroblastoma 2, neuroblastoma 1, osteosarcoma 1) underwent eight thoracotomies and four thoracoscopies to resect lung nodules seen on computed tomographic scans after chemotherapy. They were recognized at the time of diagnosis in five cases, and developed as recurrent tumors in three cases. The number of resected tumors ranged from one to four (median; two). There were no perioperative complications. In two patients whose nodules were smaller than 5 mm, CT-guided localization was successfully performed before thorachoscopic resection. A histological examination revealed that the tumor was completely necrotic in three cases and viable tumor cells were detected in four cases, all of whom received additional chemotherapy after surgery. In one case, the pathological diagnosis was a mycobacterial infection, so that patient was treated with antibiotics. All eight cases achieved complete remission after surgery, and have been alive without disease for one to 11 years.
Conclusions: The resection of pulmonary nodules can help to achieve complete remission, and the pathological diagnosis of the resected nodules can help to determine the subsequent chemotherapy. The thorachoscopic resection after CT-guided localization of the tumor(s) was a safe and beneficial procedure to resect small nodules less than 5 mm in diameter.

PUB-0071

NARROWED AORTA AFTER PROTON BEAM THERAPY AT INFANCY: 30-YEAR FOLLOW UP IN ONE CASE.

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Purpose/Objective: We present clinical course of an infant with neuroblastoma who received proton beam therapy (PBT) in 1984.
Materials and Methods: The patient was diagnosed as stage 3 neuroblastoma in the neonatal period in 1982. The tumor was located at upper median retroperitoneum. Surgical resection was tried but tumor was unresectable because it encased the aorta and the inferior vena cava. Retrospective measurement of the mitosis-karyorrhexis index (MKI) of biopsied pathological samples showed a favorable histology consistent with International Neuroblastoma Pathology Committee (INPC) criteria (low MKI and $\leq$1 year old at diagnosis). The MYCN status was not measured. Chemotherapy with vincristine, cyclophosphamide and doxorubicin was effective to reduce the tumor size. PBT of 28.6 GyE in 13 fractions was tried at age of one in 1984.
Results: The disease was cured, and routine follow-up was once finished when she was 12 years-old. However, she visited our hospital due to unexplained occasional postprandial epigastric pain with loss of appetite during early pregnancy in 2010. Insufficient Weight-gain during pregnancy resulted in a premature delivery. A CT scan after the delivery showed vertebral growth insufficient growth of the vertebrae and the aorta including the celiac artery.
Conclusions: We experienced narrowed aorta resulting in abdominal pain after 28 years from PBT. This may lead to insufficient blood flow to gastrointestinal tract with increasing of blood flow relieved by cilostazol. The threshold dose for aorta was not established, therefore, it should be cared especially for female children not only in proton therapy but in photon radiotherapy. This is the first case of PBT to the infant in the world, but to the present knowledge, radiotherapy might not be necessary to the infant with unresectable neuroblastoma with favorable histology.

PUB-0072

THE PRELIMINARY ANALYSIS OF ABERRANT EXPRESSION OF PLASMA MIR-223 IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA WITH A DIRECT RT-PCR ASSAY

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China; [6]Beijing Children's HospitalCapital Medical University, Hematology Center Department of Ontology, Beijing, China

Purpose/Objective: To investigate the expression of plasma miR-223 in pediatric acute lymphoblastic leukemia (ALL) in different treatment time point.
Materials and Methods: A total of 64 pediatric ALL samples were selected from patients treated in Beijing Children's Hospital from May of 2005 to January of 2012, including 30 samples at preliminary diagnosis (PD), 30 samples at complete remission (CR) and 4 samples at relapse. Without RNA extraction, the levels of plasma miR-223 were detected directly by a reverse-transcription quantitative real-time PCR assay.
Results: The expression of plasma miR-223 in pediatric ALL was lower at preliminary diagnosis but elevated after complete remission. The expression of plasma miR-223 in relapse patients did not show significant difference probable due to a few cases of relapse. The levels of plasma miR-223 did not show significantly different between*TEL-AML1* positive and no fusion gene B lineage ALL patients either at preliminary diagnosis or complete remission.
Conclusions: The plasma miR-223 decreases in PD and increases in CR children with ALL. It could act as an anti-oncogene activity and a potential predictive biomarker for evaluating the therapeutic effect of leukemia.

PUB-0073

CANCER IN INFANTS: A 17 YEAR SINGLE CENTER EXPERIENCE

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Purpose/Objective: Cancer in infants is rare. The purpose of this study is to determine the epidemiology, treatment and outcome of the infants with cancer treated at our institution over a 17 year period.
Materials and Methods: Medical records of 100 consecutive infants with cancer treated at our Children«s Hospital during 1996-2012 were reviewed. Epidemiologic data, diagnosis, treatment, survival and outcome were extracted and analyzed.
Results: One hundred infants (52 males) were diagnosed with cancer over this period. Median age was 4 months (range, 1 day * 12 months). Hematological malignancies were diagnosed in 30% of the cases (16 ALL, 12 AML) and 70% had solid tumors (47% neuroblastomas, 16% CNS tumors, 11% LCH and HLH, 10% Wilms, 10% soft tissue sarcomas, 4% extracranial germ cell tumors). Among the solid tumors 21% were metastatic. Twenty-seven percent of all patients underwent a bone marrow transplant (52% autologous). For all infants, overall survival (OS) was 66 $\pm$ 5.7% and event free survival (EFS) was 63 $\pm$ 5.6% for a median follow up of 3.2 years. EFS of hematological malignancies and solid tumors were 34 $\pm$ 12.2% and 80 $\pm$ 5.1% respectively. Among those transplanted the EFS was 31 $\pm$ 11.7% compared with a 76 $\pm$ 5.2% EFS for those not receiving a bone marrow transplant. Thirty-one percent of the patients dying from a BMT died due to toxicity.
Conclusions: Neuroblastoma is the most frequent cancer in infants. The prognosis of infants with hematological malignancies is still poor, compared with a very good prognosis in those infants diagnosed with most of the solid tumors. Bone marrow transplant in infants have still a high rate of toxicity.

PUB-0074

ANALYSIS OF CLINICALLY RELEVANT SUBPOPULATIONS OF LYMPHOCYTES IN THE BONE MARROW IN CHILDREN WITH RHABDOMYOSARCOMA AND EWING SARCOMAS.

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Purpose/Objective: to study clinically relevant features of the subpopulation of lymphocytes in the bone morrow in children with rhabdomyosarcoma (RMS) and Ewing Sarcoma Family Tumours (ESFT).
Materials and Methods: The study included 49 children from 1 to 17 years. The 34 patients diagnosed with RMS or ESFT and 15 children without tumor (the comparison group). Bone marrow all pationts was studied by immunological.
Results: we identified to raise CD3 + CD8 + HLA-DR+ in children with rhabdomyosarcoma - 37,1% ? 12,2%, ? = 0,001; increasing γδT-cells -15.8% and 9.2%, p = 0.007 and decrease CD4 + T-cell (CD62L)-17.6% and 33.5%, p = 0.015. Subpopulations of the bone marrow in children with ESFT is difference from the comparison group, increased levels of mature T-cytotoxic cell -68.5% and 50.5%, p = 0.000 and reduction of CD4 + - 26.9% and 39.3%, p = 0.01. Reduction of the levels CD62L (Leu8) on T-cell in the bone marrow of patients with ESFT is difference from the comparison group - subpopulations of CD4 + CD62L + - 13.7 $\pm$ 2.4 and 30.5 $\pm$ 5.2; p = 0.005. On the basis of the analysis T-cell we found increasing populations CD3 + CD8 +- 68.5% and 50.5%, p = 0.001, and lower levels of TCRγδ -10.0% and 15.8%, p = 0.01 in children with ESFT. In the advance stages of rhabdomyosarcoma compared with localized tumors revealed increased levels of CD62L-positive lymphocytes mature T-cell 69.8% and 35.5%, p = 0.016, reducing NK-cells-18.6% and 6.9%, p = 0.039 and γδT-cells-18.5% and 11.0%, p = 0.019. ESFT showed a reduction in the number CD38 + T-cell -41.7% and 63.2%, p = 0.024 and γδT cells 7.6% and 12.9%, p = 0.016 in patients of high risk group
Conclusions: We found effector cells from bone marrow children with rhabdomyosarcoma and ESFT.

PUB-0075

NESTED EPITHELIAL-STROMAL TUMOUR OF LIVER: REPORT OF A UNIQUE AND RARE TUMOUR OF LIVER IN A NINE YEAR OLD MALE CHILD.

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Purpose/Objective: Nested epithelial stromal tumour of liver is a rare and unique childhood tumour of low aggressiveness. Histomorphology of this tumour poses diagnostic difficulty especially on a biopsy specimen. We report a case highlighting histopathology and Immunohistochemical profile along with discussion on differential diagnoses and therapeutic implications.
Materials and Methods: Histomorphology of biopsy and resected specimen of a liver tumour occurring in a nine year old male child were studied. He had complained of pain in abdomen of 2 years duration. CT-scan revealed, a well-defined, enhancing mass with calcification measuring 5×6 cm in segment 5 and 6 of liver.
Results: Biopsy from the liver mass posed considerable difficulty in diagnosis. DSRCT, heptoblastoma, synovial sarcoma were considered as differential diagnoses. Diagnosis of DSRCT was offered on the biopsy. However, upon excision of the tumour, characteristic morphology of nested epithelial stromal tumour consisting of nests of oval to spindle cells typically surrounded by biliary glandular structures was seen. Conspicuous calcification was present within the tumour. On immunohistochemistry, epithelial markers highlighted biliary structures and also spindle cells. Other markers supporting DSRCT were absent. There were no features suggestive of hepatoblastoma or synovial sarcoma.
Conclusions: Nested epithelial stromal tumour is a rare childhood liver tumour with unique histomorphology. Since it is a tumour of low aggressiveness, upfront surgery is the treatment of choice. Neo-adjuvant chemotherapy is not indicated. Differential diagnoses include DSRCT, hepatoblastoma and synovial sarcoma. Rarity of tumour can lead to low index of suspicion and misdiagnosis on biopsy as occurred in our case. Although histopathology of resection specimen revealed typical morphology, misdiagnosis on a biopsy specimen could have led to over-treatment with neo-adjuvent chemotherapy. Our case helps to re-enforce the existence of this rare tumour which needs to be considered by the pathologists within the spectrum of childhood liver tumours along with its therapeutic implications.

PUB-0076

FUSIFORM DILATION OF INTERNAL CAROTID ARTERY FOLLOWING CRANIOPHARYNGIOMA RESECTION

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Purpose/Objective: Fusiform dilation of internal carotid artery (FDCA) is rare after aggressive craniopharyngioma (CP) resection. Most FDCA were reported in pediatric population, and FDCA in adults is not well understood. Our cases indicate that: 1) Contrary to common beliefs, clinical outcome of FDCA in adult patients can be catastrophic. 2) Endovascular treatment can be used to treat FDCA, which is believed to be pseudoaneurysm in nature.
Materials and Methods: Two patients' clinical record were retrospectively reviewed and analyzed. Relevant cases in literature was also reviewed and discussed.
Results: Patient 1 was a 40-year old man who developed FDCA 6 months after CP excision. He had progressive headache, and an attempt to clip the aneurysm was aborted followed by coating of the dilated vessel. He died from a fatal subarachnoid hemorrhage (SAH) 1year later. Patient 2 was a 13-year old boy who had FDCA a years after CP resection. He was treated using stent assisted coiling of the dilated artery. Follow-up showed satisfactory outcome and disappearance of headache. Literature review demonstrated only 3 similar cases with age over 21 years. It seems that adult patients with FDCA tend to have progressive clinical course and relatively worse outcome.
Conclusions: FDCA can occur in adults with fatal outcome, and stent assisted coiling is a useful approach for FDCA following CP surgery.

PUB-0077

CO-ORDINATING FOLLOW-UP FOR ADULT SURVIVORS OF CHILDHOOD CANCER TREATED IN A TERTIARY CANCER CENTRE COVERING A LARGE GEOGRAPHIC REGION

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Purpose/Objective: To organize follow-up regarding late-effects for adults treated for childhood cancer.
Materials and Methods: The Swedish working group for long-term follow-up after childhood cancer (SALUB) has elaborated a protocol regarding required follow-up. Stipulated rules for echocardiography every fifth year is a cumulative doxorubicine dose $>210\,mg/m^2$ and/or an irradiation dose to at least part of the heart to >20 Gy. In case of irradiation, an exercise test should be added. Similar dose limits apply for kidneys, thyroid gland (any irradiation dose), mammary gland etc. In the Uppsala/. . .rebro health care region (1,7 million inhabitants), the Oncology department at the Uppsala University Hospital acts as the "spider in the web" for all persons treated in our region, irrespective of where they reside as grown-ups. The examinations are performed at and paid by their home counties. All patients are, at the age of 18, seen by a paediatric and an adult oncologist at a joint out-patient visit. The patients are given a survivor passport, where the future need for follow-up is stipulated. Referrals are sent out, when the time has come for the examinations.
Results: Since July 2006 a total of 92 patients with solid (except CNS) tumours have been seen at our hospital. Fifty-three of these (58%) needed some kind of follow-up (e.g. heart 38, kidneys 17, thyroid 6, mammary gland 5 patients). Twenty-two of the patients (24%) had undergone radiation therapy, of which xx (yy%) needed particular follow-up.
Conclusions: The majority of patients, who have undergone therapy for a childhood solid tumour, need some kind of special follow-up as grown-ups. Since the number of childhood cancer survivors increases, it is important to find a safe, but still easy-to-handle, organization. It is also important to have strict rules for the follow-up in order to convince the health authorities to pay for the examinations.

PUB-0078

TO RETROSPECTIVELY ANALYZE THE CLINICAL CHARACTERISTICS AND THE TREATMENT OUTCOMES OF OVER 10 YEARS OLD CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) MULTIMODALITY.

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Purpose/Objective: To retrospectively analyze the clinical characteristics and the treatment outcomes of over 10 years old children with acute lymphoblastic leukemia (ALL) multimodality.
Materials and Methods: Between March 2005 and September 2009, 115 patients newly diagnosed with ALL were included in the study. They were separated according to the risk, received ALL-2005 protocol, follow-up 0.4-92.6 months; the clinical characteristics, the event-free survival (EFS), the overall survival (OS) and the prognostic analysis were evaluated with SPSS 17.0 software.
Results: 103 cases were involved in analysis, including 62 males and 41 females with median age 12.3 years old. 90 cases were diagnosed as B-ALL (87.4%), 13 as T-ALL (12.6%). Abnormal chromosome structure and/or abnormal amount were 36.2%. 81 cases received reverse transcription polymerase chain reaction (RT-PCR) evidence or fluorescence in situ hybridization (FISH) tests and 16 cases showed positive. 4 patients were related to center nerve system leukemia (CNSL). 38 of 103 patients were divided into high risk group and 65 were medium risk group. 94.2% of patients attained complete remission (CR) after induction. 28 of 103 patients relapsed with median continuous CR period of 11.9 months. 3 cases received allogeneic hematopoietic stem cell transplantation and 38 cases died from any reasons. The total 5-year EFS and 5-year OS were $60.2 \pm 4.8\%$ and $64.1\% \pm 4.7\%$. Cox proportion hazard regression model analysis indicated that age, risk and BCR/ABL1 translocation or t(9,22) were independent risk prognostic factor in long-term survival
Conclusions: The incidence and prognosis in over 10 years old childhood ALL was related with age, risk and biological characteristics. BCR/ABL1 translocation or t(9,22) was the risk factors of prognosis and had the allogeneic hematopoietic stem cell transplantation indication. The usage of special doses of chemotherapy drugs in the ALL-2005 protocol might be one of the major factors to improve the treatment outcome. ALL in older children achieved beneficial effect in children's hospital.

PUB-0079

A DOSIMETRIC FEASIBILITY STUDY USING FORWARD PLANNING SEGMENTAL FIELD TECHNIQUE FOR STATIONARY CRANIOSPINAL AND SPINAL-SACRAL JUNCTIONS IN CRANIOSPINAL AXIS IRRADIATION (CSI)

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Purpose/Objective: Moving junctions, referred to as 'field feathering (FF),' are currently used in CSI to improve dose uniformity across the craniospinal (CS) or spinal-sacral (SS) junctions at match lines. This technique requires complex planning, time-consuming treatment verification and dose delivery. The purpose of this study is to incorporate forward planned segmented field (FPSF) technique to deliver homogenous dose at the proposed stationary CS and SS junctions, while simplifying CSI treatment planning, verification, and delivery.
Materials and Methods: Two pediatric and two young adult patients treated with FF CSI for medulloblastoma were retrospectively re-planned with a stationary single match line at CS and SS junctions. The two pediatric patients were treated in a supine position while the two adults were treated prone. A matched stationary junction was created at the CS junction where collimated opposed lateral cranial fields were matched or minimally overlapped with the superior border of the spinal PA field for all patients. Similarly, a matched stationary junction at the SS junction was created where the static spinal PA beam abutted or minimally overlapped with the superior border of the static PA sacral field in adult patients.
The dose homogeneity index (HI) for the length of the cord 3 cm above and below each junction was compared between FPSF and FF techniques.
Results: The average HI obtained with field feathering and FPSF techniques at the junctions were $6.38\% \pm 1.54\%$ and $6.97\% \pm 2.31\%$, respectively, without significant statistical difference ($p = 0.3$).
Conclusions: The results show that uniform dose distribution within junctions of a CSI plan can be achieved by FPSF technique without the need for feathering, creating gaps, or applying additional patch fields. FPSF technique offers efficiency in time required for planning, dose delivery, and daily or weekly port imaging. Daily Image guided radiotherapy and Mapcheck prior to initiation of treatment is recommended. FPSF technique should be further evaluated for CSI.

PUB-0080

A RANDOMIZED CONTROL TRIAL TO EVALUATE THE EFFICACY OF A GROUP SOCIAL SKILLS INTERVENTION FOR CHILDHOOD SURVIVORS OF BRAIN TUMOURS

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Purpose/Objective: Children who survive brain tumours often experience social competence deficits. Treatment for social competence deficits has received little attention. This multi-site randomized control trial (RCT) aims to test the efficacy of a previously developed and piloted manual for group social skills training intervention program for pediatric brain tumor survivors. We hypothesize that participants in the EG will improve their social skills, reported by parents, teachers, peers, and survivors, compared to the CG at the end of intervention and 6 months later.
Materials and Methods: Patients between 8 and 16 years of age in stable condition having been or being treated for a brain tumour and attending school regularly will be recruited to participate. After baseline assessment (T1), participants will be randomized to either the Experimental Group (EG) or an Attention Control Group (CG). 160 patients will be recruited from four pediatric cancer centres across Canada (Toronto, Calgary, Vancouver, London, ON). Both groups have 8 two-hour weekly group intervention sessions. The EG receives structured social skills training through games, and arts and crafts, based on the manual. The CG engages in similar activities without social skills training. The primary outcome measures are parent, teacher and self-rated Social Skills Rating System (SSRS) administered at the end of session 8 (T2) and 6 months later (T3), and peer's social ratings (Revised Class Play) obtained at T2.
Results: Study is actively accruing participants; 20 have completed T1 assessment, intervention, and T2 assessment; 8 have completed T3. The sample is expected to triple by the summer which will increase power for statistical test of hypothesis.
Conclusions: Rigorous testing of the efficacy of an intervention program is a critical step for validating evidence-based treatments. SSIP has the potential to maximize survivors' social competence and long-term social re-integration into their community.

PUB-0081

CLINICAL ANALYSIS OF 14 CHILDREN WITH EVI1 POSITIVE ACUTE MYELOID LEUKEMIA

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Purpose/Objective: To investigate clinical features and prognostic significance of EVI1 expression in children with acute myeloid leukemia (AML).

Materials and Methods: From 2010.07 to 2012.12, expression of EVI1 fusion gene was detected in 23 children suffered from AML by multiplex nested RT-PCR and PCR for EVI1 gene in Children's hospital of Chongqing, China. Clinical feather and treatment effect in 14 cases carried EVI1 fussion gene were studied.
Results: EVI1 expression is positive in 14 of 23 (60.9%) children with AML, including 1 case of AML-M0, 6 cases of AML-M2 and 5 cases of AML-M5. In these 14 cases with EVI1 expression, 6 patients presented with abnormal chromosome assay, and 4 children were also positive expression with other fusion gene. 10 patients received chemotherapy, but 2 of 3 patients relapsed in 3 mouth when they finished chemotherapy.
Conclusions: EVI1 fusion gene is common and may play an important role in pediatric AML, we think it an independed risk factor for pediatric AML.

PUB-0082

PARAVERTEBRAL PRIMITIVE NEUROECTODERMAL TUMORS IN CHILDREN: A CASE REPORT TREATED WITH CYTOKINE-INDUCED KILLER CELLS IMMUNOTHERAPY

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Purpose/Objective: We report a rare clinical case of pediatric subcutaneous peripheral paravertebral primitive neuroectodermal tumors (PNETs) in the paravertebral region and present a brief review of the literature of PNET. We apply autologous cytokine-induced killer (CIK) immunotherapy to treatment of PNET.
Materials and Methods: We diagnosed and treated a female patient with subcutaneous PNETs in the paravertebral region and found a small number of children cases around the vertebrae in the literature. Contrast-enhanced computed tomography of pelvis, T1- and T2-weighted magnetic resonance imaging and immunohistochemistry were performed and strongly supported the diagnosis of PNET. The patient received surgery with incomplete excision of the sacrococcygeal mass; local radiotherapy; combination chemotherapy with vincristine, adriamycin, ifosfamide, and actinomycin-D; and CIK immunotherapy twice after each chemotherapy, with 5×10^8 CIK cells intravenously transfused into the patient within 1 h of each treatment. There were no recurrence or distant metastases at 5 months after surgery.
Results: CIK immunotherapy was achieved in a rare case of PNET.
Conclusions: PNETs are malignant, small, and round cell tumors of soft tissues. It requires a multimodality treatment. The case exhibited obvious improvement and positive effects after receiving cytokine-induced killer cells as adoptive immunotherapy combined with conventional therapy. So, CIK immunotherapy could be a radical treatment.

PUB-0083

PERIPHERAL BLOOD STEM CELL COLLECTION IN CHILDREN OF WEIGHT UNDER 25KG: EXPERIENCE OF A SINGLE CENTRE

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Purpose/Objective: The pediatric apheresis requires complex process because there are no established principles of procedure and the apheresis equipment was designed for adults. To try establish the safe and effective pediatric apheresis, we analyzed our own experience of children weighing less than 25kg using Fenwal CS3000 Plus.
Materials and Methods: From October 2001 to June 2004, 18 children underwent peripheral blood stem cell collection. Stem cell mobilization was obtained by once-daily G-CSF(7.5μg/kg) after 5 days following chemotherapy(cyclophosphamide 2g/m^2, vincristine 1.5mg/m^2). Collection started during the hematological recovery phase, as soon as the next day of peripheral hematopoietic progenitor cells counts exceeded 5×10^6/L and was repeated until at least 10×10^6/kg CD34+ cells were obtained. During the procedure, patient maintained Hb over 10g/dl and platelet over 30,000/mm^3(brain tumors over 50,000/mm^3). A solution of 500ml ACD and 3000IU of heparin was infused at a whole blood to anticoagulant ratio of 20:1 for anticoagulation. Total processing volume was 3 fold of total blood volume and processing start rate was 20ml/min and was been increased not exceeding 15% of total blood volume between spillover and spillover steps. 30 minutes after collection, we evaluated electrolyte and complete blood count.
Results: The median weight was 14.6kg, median day at the time of apheresis was 10.4days after chemotherapy, median processing day for obtaining 10×10^6/kg CD34+ cells was 2.5days, processing volume was median 4130 ml, processing rate 43ml/min, total processing time a day was 144seconds and final products volume was 56.2ml. Transient discomforts like numbness, nausea and abdominal pain present 26%. Minimal electrolytic imbalances present 48%. But it was not require treatment and there are no symptoms.
Conclusions: Peripheral blood stem cell collection in children of weight under 25kg can be performed under safe and effective conditions even when systematic priming by blood is avoided. This procedure allows PBSC collection in small children without serious complication.

PUB-0084

HERBY: A PHASE II COMPARATIVE STUDY OF BEVACIZUMAB-BASED THERAPY IN CHILDREN WITH HIGH-GRADE GLIOMA

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Purpose/Objective: Despite therapeutic advances, pediatric high-grade glioma (HGG) outcomes remain poor. The phase I study (Glade-Bender et al., J Clin Oncol 2008) indicated that bevacizumab (Bv) is well tolerated in children with refractory solid tumors and supported further studies in children.
Materials and Methods: 120 evaluable patients (main cohort) aged ≥3*18 years with newly diagnosed histologically confirmed WHO grade III or IV HGG are randomized to standard therapy ± Bv. Treatment consists of 6 weeks of concomitant temozolomide (TMZ) and radiotherapy, followed by 4-week TMZ treatment break and 48 weeks of adjuvant TMZ + Bv every other week. Primary endpoint is event-free survival (EFS). Evaluation is based on Revised Assessment in Neuro-Oncology (RANO) criteria. Secondary endpoints are overall survival (OS), safety, feasibility, and tolerability. All Bv. patients will have PK sampling at cycles 1*4 of the adjuvant phase. Health-related quality of life, neurocognitive functions, MGMT methylation status, and functional tumor changes based on MR diffusion, perfusion imaging, spectroscopy, and correlation of biomarkers with clinical activity and adverse events are explored. In addition, a young patient cohort of 10 patients aged ≥ 6 months and < 3 years with recurrent or progressive localized or metastatic WHO grade III or IV HGG will be evaluated, and will receive TMZ and Bv for 12 cycles without radiotherapy. The exploratory objective is to assess safety, pharmacokinetics, and benefit of Bv (assessed by PFS). All children will be followed for ≥3 years. Endpoints for both cohorts will be analyzed after the 120 patients have been followed for 1 year. Multimodal imaging will aid development of new criteria for pediatric neuro-oncological treatment response. An updated OS and safety analysis will be performed 3 years after randomization of the last patient. The first patient was randomized in October 2011; study completion is expected in 2016.
Results: NA
Conclusions: NA

PUB-0085

HODGKIN'S LYMPHOMA IN CHILDREN: A REPORT FROM CHANG GUNG CHILDREN'S HOSPITAL, TAIWAN

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Purpose/Objective: The incidence of Hodgkin's lymphoma (HL) in Asia, including Taiwan, is much lower than that of western countries. The report about its clinical features and treatment outcome in Taiwanese children is rare.
Materials and Methods: All patients younger than 18 years old with HL diagnosed at Chang Gung Children's Hospital (CGCH) between 2000 and 2012 were included.The medical records were retrospectively reviewed.
Results: A total of 46 children with a median age of 14.9 years (range 4.0 * 17.8) were diagnosed and treated at CGCH. Thirty of 46 patients (80%) were aged above 10 years. There was a male predominance (male/female ratio: 2/1). Among the 46 patients, 23 (50%) presented with advanced stage (stages III and IV) disease, and 14 (30%) had B symptoms. The nodular sclerosis type was the most common histological subtypes (66%), followed by mixed cellularity (24%), lymphocyte predominant (4%), and lymphocyte depleted subtype (2%). Multiagent chemotherapy was applied to all patients as the mainstay of treatment. Twelve patients (26%) received involved field radiotherapy following chemotherapy. Five patients subsequently underwent hematopoietic stem cell transplantation (3 auto and 2 allo). Seven out of 46 patients (15%) had relapsed HL. One was in primary refractory status. One developed leiomyosarcoma at left neck in the field previously irradiated about 7.2 years after the initial diagnosis of HL. Five patients died after treatment of relapsed disease. The causes of death were sepsis in 3, transplant-related mortality in 1, and disease progression in 1. The 10-year overall survival and event-free survival rates were 85.6% and 75.1%, respectively.

Advanced stage disease and high LDH level (> 300 U/L) at diagnosis were poor prognostic factors.
Conclusions: This study demonstrated clinical features and treatment outcome in Taiwanese children with HL. Continued surveillance of long-term treatment-related morbidity is warranted.

PUB-0086

YOUNG ADULT CANCER SURVIVORS' (CS) FOLLOW-UP CARE EXPECTATIONS OF THEIR PRIMARY CARE PROVIDERS (PCPS) AND ONCOLOGISTS

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Purpose/Objective: The delivery of cancer survivorship care can be complicated by a lack of clarity surrounding physician roles during follow-up. Our aim was to characterize young CS' follow-up care expectations of their PCPs and oncologists.
Materials and Methods: A survey was mailed to all CS diagnosed with cancer from 2005 to 2009, aged 20 to 39 years at the time of diagnosis, evaluated at any 1 of 5 regional cancer centers, and lived beyond 2 years. The questionnaire focused on demographics, prior treatment, and CS attitudes regarding physician responsibilities during survivorship, specifically their views about their PCPs' and oncologists' roles. Descriptive statistics and regression analyses were used to summarize these expectations and to determine if they differed based on physician type.
Results: A total of 426 patients were included (response rate 59%): current median age was 40 years and 71% were women. Common tumor sites were breast (48%), testicular (27%), and gynecological (18%). Most patients (63 and 65%, respectively) expected PCPs to be responsible for following their most recent cancer and screening for future cancers. Nearly all (85 and 93%, respectively) indicated that PCPs should also provide preventive care and manage their co-morbidities. Conversely, a significant proportion (65%) felt that oncologists should remain responsible for addressing side effects of cancer treatments throughout survivorship. In terms of fertility discussions, half of patients viewed this as a role for oncologists whereas the remainder perceived this to be more suitable for PCPs. Interestingly, neither PCPs nor oncologists were seen to have any significant role in addressing social reintegration, interpersonal relationships, or sexual function, with < 30% of respondents expecting these to be discussed by either physician.
Conclusions: Young adult CS expect PCPs to be responsible for most aspects of their ongoing care. More clarity regarding physician roles is required with respect to specific survivorship issues, such as fertility, sexual function and psychosocial health.

PUB-0087

DISCUSSIONS REGARDING REPRODUCTIVE AND SEXUAL HEALTH AMONG YOUNG ADULT SURVIVORS OF CANCER

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Purpose/Objective: Infertility and sexual dysfunction can result from many cancer treatments and may become a source of significant distress for young adult cancer survivors. Our aims were to 1) characterize the frequency in which reproductive and sexual health discussions occur in a population-based cohort of young cancer patients and 2) identify clinical factors associated with such discussions.
Materials and Methods: Patients aged 20 to 39 years who were diagnosed with solid tumors from 2006 to 2008, evaluated at any 1 of 5 regional cancer centers, and alive at 2 or more years after their initial diagnosis were included. Demographics, tumor and treatment characteristics, and information on patient-physician conversations were analyzed. Using regression models, we explored the relationships between clinical factors and whether or not discussions had occurred.
Results: A total of 397 patients was identified: median age was 35 years, 28% were men, 88% had ECOG 0, and 73% reported being in a relationship. Tumor sites included breast (50%), testicular (27%), gynecological (17%), and colorectal (6%). A significant proportion of patients received chemotherapy and radiation that posed the potential risk of infertility or sexual dysfunction. However, only 56% and 6% of individuals had a discussion about reproductive and sexual health, respectively, within the first month of their diagnosis. At 6 months, an additional 6% and 4% of patients had discussed these concerns with their physicians. Age, gender, ECOG, relationship status, and type of chemotherapy and radiation were not correlated with whether or not discussions had occurred (all $p > 0.05$). In regression models, tumor site was associated with differences in reproductive and sexual health discussions between patients and physicians.
Conclusions: Among young adult survivors of cancer, fertility and particularly sexual function are inadequately addressed during discussions near the time of initial cancer diagnosis.

PUB-0088

LIFE EXPERIENCE OF CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: A phenomenological approach to describe the essence of life experiences of childhood cancer survivors
Materials and Methods: Settings: the pediatric hematology and oncology wards in medical centers.
Sample: 10 childhood cancer survivors at interview age between 13 and 20 years old were recruited from 2011 to 2012 in Taiwan.
Methods: Ten adolescents at aged 13 to 20 who had completed treatments were interviewed. Open-ended interviews were conducted in a quiet in-hospital setting. Interview data were transcribed and analyzed using Giorgi's four-step procedures.
Results: The essential structure of life experience contained four major themes: living shadows of relapse, I am different, searching forever health and normalization but still different.
Conclusions: Childhood cancer survivors perceived life was more different than before even they have completed treatments. They tried hard to get normal life and health. Survivors needed to be knowledge about the possible consequences of treatments, and health care system need to develop a long-term and follow-up care to help them to go back life.

PUB-0089

STUDY OF GLUCOCORTICOID RECEPTOR GENE POLYMORPHISM AND THE RELATIONSHIP BETWEEN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: By analyzing the gene polymorphism of glucocorticoid receptor(GR) in childhood acute lymphoblastic leukemia (ALL) cases, we studied the correction between the GR gene polymorphism and the clinical features and prognosis of childhood ALL.
Materials and Methods: All cases were diagnosed and treated from January 2004 to September 2010. The SNaPshot SNP genotyping was applied to detect GR gene polymorphism point Bcl I, rs4607376, N363S, ER22 and 9β single-nucleotide polymorphisms.
Results: The GR gene Bcl I loci was found three genotypes CC, CG and GG. The rs4607376 loci was found AA, AG and GG three genotypes. The N363S, ER22 and 9β were found AA, GG and AA genotypes. No statistical difference was found between the GR genotype groups and the clinical features in terms of the sex, immunophenotype, risk group, the initial white leukocyte counts.
Conclusions: There was no relationship between GR gene locus Bcl I, rs4607376 gene polymorphism and clinical features and outcomes of our ALL cases.

PUB-0090

RELIEF OF PAINFUL GANGLIONEUROMA BY SURGICAL EXCISION: A RARE SITUATION.

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Purpose/Objective: Ganglioneuroma are usually discovered following the observation of an indolent mass or incidentally. We report an unusual clinical presentation of painful ganglioneuroma diagnosed on abdominal pain that was fully relief by complete surgical excision.
Materials and Methods: 35 ganglioneuroma were operated among 270 patients managed in our single institution for neurogenic tumors since 12 years. Recently, we observed three female patients aged 9, 13 and 14 presenting with abdominal pain that revealed a ganglioneuroma.
Results: The younger patient was initially thought to have an abscess and was first treated by antibiotics without any efficiency. Tumor location was closed to the aortic bifurcation, in front of the left psoas muscle. For the two other females, locations were pelvic slightly lateralized to the left back of the rectum in the oldest girl and retroperitoneal extending from the liver to the iliac vessels, surrounding the upper part of the right kidney and its vascular pedicle and displacing forward the vena cava in the last case. Tumor volume was respectively 13, 113 and 115 cm^3. All three patients required preoperative analgesic medical treatment

associating morphine and neuropathic medication. Surgery decided because of incomplete relief after a mean delay of three months (1-5) was conducted by minimally invasive surgery in two and open approach in one. Pain was relieved immediately in the first case. Analgesic treatment was stopped within 6 months for the others. All are alive and free of disease with a follow up of 10, 12 and 12 months.
Conclusions: Although not classical, origin of pain was definitely related to the presence of the ganglioneuroma in our three patients, as symptoms disappeared after the surgical removal. Irritation of metameric or unknown nervous pathways may explain this unusual presentation. These observations support the surgical treatment of ganglioneuroma unusually revealed by pain.

PUB-0091

UP-REGULATION OF GABA-GABAAR SIGNALING SYSTEM IN LEUKEMIC CELLS OF CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA

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Purpose/Objective: Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the mammalian brain with growth regulatory properities. It has been reported that GABA and its receptors are expressed in the peripheral tissues and play important roles in the prolifiration, infiltration, and metastasis of tumor cells through specific signaling pathways. To date, there has been little research on the expression and clinical significance of endogenous GABAergic system in leukemic cells of childhood acute lymphocytic leukemia (ALL). The aim of this study was to examine if GABA-$GABA_AR$ signaling system is functionally expressed in leukemic cells of ALL children.
Materials and Methods: RT-PCR and Western Blot were carried out to examine the expression of mRNAs and proteins, respectively, of $GABA_AR$ subunits and the GABA synthetizing enzyme glutamic acid decarboxylase (GAD) isoforms GAD65 and GAD67 in leukemic cells from the bone marrow (BM) of ALL children before chemotherapy. Immunofluorescence staining was used to examine the cellular localization of GABAergic system.
Results: RT-PCR assays detected mRNAs encoding GAD65, GAD67, and several $GABA_AR$ subunits including $\alpha1$, $\alpha2$, $\beta2$, $\beta3$, δ, π, and θ in leukemic cells. In line with these results, Western Blot revealed the strong expressions of GAD65 and GAD67 (hereafter named as GAD65/67), and the $\beta2$ and $\beta3$ ($\beta2/3$) subunits of $GABA_ARs$ in leukemic cells. Immunofluorescence staining showed that GAD65/67 was expressed in the cytoplasma of leukemic cells. Remarkably, the expressions of $GABA_AR$ $\beta2/3$ subunits and GAD were significantly higher than those in BM mononuclear cells of age-paired normal children.
Conclusions: Our study shows that an autocrine GABA-$GABA_AR$ signaling system is expressed in leukemic cells in ALL children, and is up-regulated comparing to those in age-paired normal children. However, whether this GABAergic system plays a significant role in regulation of the proliferation and infiltration of leukemic cells in ALL remains to be further studied.

PUB-0092

BILATERAL BLINDNESS IN CHILDREN WITH NEUROBLASTOMA: REPORT OF 2 CASES

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Purpose/Objective: Ophthalmic manifestations are common in patients with metastatic neuroblastoma. Nevertheless bilateral blindness in these patients is very unusual. We report 2 cases of bilateral vision loss as initial manifestation of neuroblastoma.
Materials and Methods: Case histories of 77 patients with neuroblastoma treated in Federal Research Center of Pediatric Hematology, Oncology and Immunology during the period 01.2012-01.2013 were analyzed.
Results: Bilateral blindness was observed in 2 cases that represented 2,7% of all patients with neuroblastoma and 5,2% of stage 4 patients in this study. Case 1. Two year old boy presented with fever, fatigue and limping. Acute bilateral blindness was diagnosed one month after onset of symptoms. MRI of the brain showed solid mass involving sphenoid bone with optic nerve compression. Comprehensive work-up was consistent with undifferentiated neuroblastoma of the retroperitoneum with metastases to distant lymph nodes, bones and bone marrow. Ophthalmologic examination revealed bilateral optic disc atrophy. Patient received treatment according to high-risk group protocol without improvement of vision. Case 2. Two year old boy presented with bone pain, limping and fever. He initially was treated for two weeks for suspected osteomyelitis. Course of the disease was complicated by abdominal pain and right proptosis. Diagnostic work-up revealed neuroblastoma of the left adrenal gland with bone metastases to the right temporal bone, right orbit and sphenoid bone with bilateral optic nerve compression. He was referred to oncologist one month after onset of symptoms. Disc atrophy was confirmed by ophthalmologic examination. Permanent vision loss ensued despite intensive chemotherapy.
Conclusions: Bilateral blindness is a rare clinical presentation in patients with metastatic neuroblastoma. This symptom represents oncologic emergency. Timely referral to specialized cancer center for immediate treatment is crucial for vision preservation.

PUB-0093

EXCELLENT SURVIVAL OF CHILDREN WITH WILMS TUMOR IN KUWAIT: A STUDY FROM KUWAIT CANCER CONTROL CENTRE (KCCC)

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Purpose/Objective: The survival in children with wilms tumor has crossed 90% with in the past 3 decades due to multimodality therapy. KCCC is the only comprehensive cancer centre in Kuwait. This study was conducted to analyze the outcome of children who presented to pediatric oncology unit with wilms tumor.
Materials and Methods: This is a retrospective analysis of all the patients with diagnosis of wilms tumor who presented to our unit between January 1998 and December 2011. During the study period, a total of 56 children were referred with this diagnosis. However, one child each with CMN and bilateral nephroblastomatosis were excluded from analysis. Wilms tumor in our unit are treated according to the SIOP protocol, but some patients traveled to other centers and were treated according to NWTS protocol.
Results: The median age was 30 months (range: 3 months to 180 months). Hypertension was present in 5 patients at presentation, and equal number had various congenital anomalies. Bilateral tumor was present in 4 patients. Ten had metastasis at presentation. Post surgery, stage II was seen in 38%, stage I in 30%, while stage III was present in 23.5%. Radiotherapy was given to all stage III patients. Favourable histology was seen in 72%, while 20% had unfavourable histology. At end of therapy, 72% were alive with CR status, 4 died during treatment (3 PD, 1 due to septicemia). Six patients were lost to follow-up. During follow-up, 4 patients (8.8%) relapsed. One was salvaged with surgery and chemotherapy, one lost to follow-up, while 2 died due to progressive disease. At the last follow-up, 42 patients (75%) were alive with a median follow-up of 80 months.
Conclusions: The outcome of our patients with wilms tumor in quite encouraging. However high number of patients who were lost to follow-up even after remission caused lowering of survival percentage.

PUB-0094

EFFICACY OF SINGLE DOSE OF RASBURICASE IN TREATMENT OF HYPERURICEMIA IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: CASE SERIES WITH REVIEW OF LITERATURE

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Purpose/Objective: Tumor lysis syndrome (TLS) is a life-threatening disorder characterized by hyperuricemia and metabolic derangements. Hydration and allopurinol are the standard of care in the treatment and prevention of hyperuricemia. Rasburicase is a new alternative for the management of hyperuricemia. Rasburicase is currently approved at a dosage of 0.15-0.2 mg/kg once a day for 5 days in pediatric patients as recommended by the manufacturer.Information on rasburicase dosing in adults is available in literature, with some data on using rasburicase as a single dose instead of multiple daily doses. No similar data is available in pediatric patients.
Materials and Methods: We undertook a retrospective review of seven children treated in our institution with a single dose of rasburicase for hyperuricemia associated with acute lymphoblastic leukemia (ALL). All the patients were screened for G6PD before the administration of Rasburicase. The blood specimen for estimation of uric acid levels following administration of rasburicase was transported to the laboratory immediately in ice packs.
Results: Out of 7 children, 5 were males and 2 were females. Out of 7 children, 4 were CALLA positive ALL and 3 were T cell ALL. All seven had acute renal failure. Out of the 7, 4 required dialysis. Renal parameters normalized in 72 hours. One dose of rasburicase produced a rapid and sustained therapeutic effect of lowering the plasma uric acid levels in all seven patients. Uric acid levels remained below 4mg/dl throughout the adminstration of chemotherapy.
Conclusions: A single dose of rasburicase is highly effective and well tolerated in the treatment of hyperuricemia. It is cost effective too in developing countries.

PUB-0095

LANGERHANS CELL HISTIOCYTOSIS: ONE CENTER EXPERIENCE BETWEEN 1990-2012

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Purpose/Objective: Diagnosis and follow-up of Langerhans cell histiocytosis (LCH) patients at our center were evaluated in this study
Materials and Methods: Retrospectively the files of the LCH patients who were treated at our center were analyzed
Results: 80 patients (56 males and 24 females) were diagnosed with LCH. The patients were evaluated at 4 different groups; One system one organ involvement (n:28), one system multifocal involvement (n: 15), multisystem low risk (n:21), multisystem high risk (n: 16). The mostly involved area was bone; (one system one organ involvement n:22, one system multifocal involvement n: 14, multisystem low risk n:14). Fourteen patients with one system one organ involvement and 4 patients with one system multifocal involvement were treated with curretage-excision of the tumour. Only one of these patients had a local relapse and treated succesfully with re-excision of the tumour. Three patients received systemic chemotherapy after curretage because lesion could not be removed completely. Five of the patients with one bone involvement received radiotherapy to the involved side; and 3 of these patients relapsed. Remission was achieved at patients with soft tissue involvement with local intralesionel steroid thereapy (n:4.) Twenty seven of the patients with systemic involvement received prednisolone + vinblastine, 13 received prednisolone + vinblastine + etoposide and 3 patients received prednisolone + vinblastine + methotraxate. Respectively 7, 4 and 1 of these patients had reccurence. Twelve of patients had (17%) had relapse. One of these patients died after the second relapse. The rest 11 patients are in remission. Four patients with multi system involvement died during treatment due to progression of the disease. These patients were not in remission and died with an avarage of two months after the diagnosis.
Conclusions: LCH can be curable either with systemic or local treatment, but 20-25% of patients might have relapses.

PUB-0096

A PEDIATRIC CASE SUFFERING FROM LHERMITTE-DUCLOS DISEASE WHO DEVELOPED ANAPLASTIC OLIGOASTROCYTOMA

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Purpose/Objective: Dysplastic gangliocytoma, known as Lhermitte-Duclos Disease (LDD) is a rare cerebellar slowly growing hamartamatous lesion of unknown origin.
Materials and Methods: We herein report a 10-year-old boy presenting with progressive headache and LDD confirmed by its characteristic magnetic resonance imaging (MRI) findings.
Results: In view of his progressive symptoms, a computed tomography scan of the brain showed a hypodense lesion in the right cerebellar hemisphere with no compression or distortion. MRI revealed a nonhomogenous $50 \times 40 \times 33$mm lesion in superior right cerebellar hemisphere compressing 4th ventricle mildly, hypointense in T1 and hyperintense in T2 weighted sections with cortical striations; its parenchyma was not contrast-enhanced. The diagnosis of LDD was made on its unique MRI findings. He was under control by repeated MRI.

4 years after the diagnosis of LDD, he complained severe headaches with nausea and vomiting. On MRI, his lesion's size was the same; however, cystic component enlarged with round contrast enhancement. On computerized tomography, there was a hypodense 16×11 mm lesion in right cerebellar hemisphere compressing 4th ventricle with vasogenic edema. It was excised subtotally. Histopathological diagnosis verified anaplastic oligoastrocytoma (WHO grade III) with cerebellar dysplastic gangliocytoma. His post-op MRI showed residual tumoral lesion.

External radiotherapy totally 54 Gy was given with 75 mg/m2/day temozolomide. After radiotherapy, 150 mg/m2/day temozolomide was planned for six sessions. Control MRI scans four months after surgery and five cures of temozolamide showed complete regression.
Conclusions: The diagnosis of LDD is frequently based on MR imaging. This advance has markedly improved the diagnosis, prognosis and follow-up for the disease. LDD is often asymptomatic in the beginning. Because of its benign nature, conservative treatment can be preferred. Wide excision is essential because of the risk of recurrence. In addition, all patients with LDD should be evaluated and followed for systemic cancers associated with Cowden Disease.

PUB-0097

OUTCOME OF LOCALLY ADVANCED NASOPHARYNGEAL CARCINOMA: USING CHEMOTHERAPY AND RADIOTHERAPY

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Purpose/Objective: Background: Nasopharyngeal carcinoma (NPC) is extremely rare in pediatric patients; it account less than 1% of all pediatric cancer. Survival of patient with T1 and T2 lesion is excellent with local control rate in excess of 75-80%. The prognosis of patients with T3 and T4 lesion is worse, with survival estimates in the 30-40% range.
Objectives: To review registered children and adolescent treated at our center to find out age, sex, pathology, stage, type of chemotherapy, concomitant chemo-radiotherapy, and outcome
Materials and Methods: From jan.2002-December 2010 nine patients less than 20 year with locally advanced NPC were registered. Three treated by pediatric oncology regimens and 6 treated by radiation oncology regimen. Tumors were classified according to WHO and AJCC (TNM) staging system. Pediatric ($n = 3$) received cisplatinum, 5-flurouracil (5-FU) for 3-6 courses followed by local radiotherapy and interferon-b (IFN-b). Adolescent ($n = 6$), treated with Docetaxel, cisplatinum and 5-FU for 3 courses. Both groups received concomitant chemo-radiotherapy as cisplatinum and carboplatinum.
Results: Age range 7-20 year, median 16, male 6, female 3 (ratio 2:1). Pediatric cases $n = 3$ all stage 4A, adolescent $n = 6$ showed stage IVA 2, stage IVB2, and stage III 2. All registered cases in both group survived with one pediatric developed local recurrence which responded to salvage therapy included Gemcitabine and taxotere. Concomitant chemo-radiotherapy given in 2/3 and 4/6 respectively. Median follow up 66 month, event free survival 88% and overall survival 100%.
Conclusions: NPC in advanced local stages in children and adolescents could have favorable survival with concomitant chemotherapy and radiotherapy. Adolescent used regimen is more tolerable. Further future uses of such trial in children with less number of courses and less toxicities need larger studies. Gemcitabine with taxotere could be used for recurrence NPC.

PUB-0098

CLINICAL FEATURES AND TREATMENT OUTCOME OF PEDIATRIC LANGERHANS CELL HISTIOCYTOSIS IN HONG KONG

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Purpose/Objective: To review the clinical features and outcome of pediatric patients with Langerhans cell histiocytosis who have been treated with two prospective protocols at consecutive periods in Hong Kong
Materials and Methods: We reviewed the clinical data of patients with LCH treated at 5 pediatirc oncology units in Hong Kong from 2000 to 2011 (12 years' period).
Results: Fifty-five children were diagnosed with LCH (range: 37 days * 15.4 yr, median 3.0 yr) with male predominance (38/55). The annual incidence ranged from 1 to 9 cases with median of 5. Forty patients had single system involvement (SS-LCH) and 15 had multi-system involvement (MS-LCH). Patients with MS-LCH were younger (range: 0.3 yr - 10.2 yr, median 1.0 yr) than the single system LCH (range: 37 days - 15.4 yr, median 4.6 yr). Majority of the SS-LCH had bone (33/40) lesions except 4 with skin, 2 with pituitary and 1 with lymph gland involvement. Eleven patients had multi-focal bone lesions. The patients in MS-LCH group had diverse manifestations and the most frequent symptoms were bone pain, fever, skin lesions and lymph node involvement. Diabetes insipidus was present in 4 of the MS-LCH patients. The patients were treated prospectively according to LCH II protocol before 2008 and thereafter with modified LCH III protocol. The MS-LCH patients were classified into low-risk group ($n = 3$) and risk group ($n = 12$). Three patients had reactivation of the disease after chemotherapy and two of them responded to alternative chemotherapy. Three patients had complication of sclerosing cholangitis. One patient died of refractory LCH.
Conclusions: Pediatric LCH is rare in Hong Kong with diverse clinical manifestations and favorable outcome. The best treatment option for relapse or refractory LCH remains to be determined.

PUB-0099

THE VALUE OF CT SCAN IN THE DIAGNOSIS FOR OVARIAN NEOPLASMS IN CHILDREN

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Purpose/Objective: To analyse multi-slice spiral CT characteristics of ovarian neoplasms in Children.
Materials and Methods: 27 females of ovarian neoplasms were confirmed by surgery and pathology with a total of 34 tumors. The age was11.7 ± 5.1(1.1 to 18.0) years. The studies were performed by a PHILIPS Brilliance 6 multi-slice spiral CT with routine and enhanced scan. 1 case with tumor torsion was only performed with un-enchanced CT.
Results: In CT finding, 11 tumors (11/34, account for 32.35%) were simple cystic tumors; 9 tumors (9/34,account for 26.47%)were solid masses; 17 tumors(17/34,account for 50.0%) were mixed cystic and solid masses. After enhanced-CT scan, ovarian vascular pedicle sign(OVPS) were viewed in 29 ovarian neoplasms,account for 87.88%. Ascite were viewed in 12 cases. peritoneal implantation metastasis were viewed in 4 cases. The enlargement of lymph nodes were viewed in 9 cases. The distant metastasis of liver or lung were viewed in 5 cases. Calcification was viewed in 15 tumors. Among the 13 ovarian teratomas, calcification was viewed in all, both calcification and fat were viewed in 11. Certain fat weren't viewed in 2.
Conclusions: CT imaging can easly disply the sign of ovarian vein and the component of the tumor (including cystic, solid, calcification, fat), which also play an impotant part in locating, qualitation and assisted staging of ovarian neoplasms in children.

PUB-0100

PREOPERATIVE INTERVENTIONAL THERAPY FOR CHILDHOOD UNDIFFERENTIATED EMBRYONAL LIVER SARCOMA:RETROSPECTIVE 2 CASES IN A SINGLE CENTER

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Purpose/Objective: Undifferentiated embryonal liver sarcoma (UELS) is an uncommon tumor. It accounts for only 9% to 15% of all malignant liver tumors in children. Typically, UELS occurs in old children and presents abdominal mass. Most UELSs are unresectable because of later diagnosis. The outcome of UELS is very poor with a 5-year overall survival of $< 37.5\%$. Transarterial chemoembolization (TACE) was reported to be an effective modality for unresectable liver tumors. To investigate the effects of TACE on UELS in children, we present 2 cases of UELS who underwent TACE/chemotherphy and surgical resection in our center within the past 10 years.
Materials and Methods: Two children with UELS were treated by TACE with cisplatin, doxorubicin and iodized oil. The size of the tumors was measured before and after TACE using ultrasonography. Routine chemotherphy was also adopted before and after surgical resection. Side effects were recorded. Both patients were followed up.
Results: After interventional therapy, both patients presented vomiting, fever, and transient liver dysfunction, without cardiac and renal dysfunction. One patient had bone marrow depression. The size of the tumors was reduced by 22.5% to 30.5% after TACE. Tumors were completely removed by surgical procedures in both patients. Both patients survived with free of disease for 1 and 9 years.
Conclusions: TACE presented satisfied effects on unresectable UELS in children with lower dosage of chemotherapy and less side effects. It may be applied as a preoperative therapy method to the unresectable UELS in children.

PUB-0101

CLINICO-DEMOGRAPHICS AND OUTCOME OF CNS RELAPSED CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN BANGLADESH.

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Purpose/Objective: The aim of this study was to describe the clinico-demographics and treatment outcome of CNS relapse in Acute Lymphoblastic Leukaemia (ALL) from paediatric haematology oncology department of BSMMU Bangladesh.
Materials and Methods: A prospective observational study was done between January 2012 to January 2013 in patients of ALL who developed CNS relapse during therapy . All the patients were initially treated with MRC-XII or modified UKALL-2003 protocol. Initial clinical presentation, diagnosis including CSF for malignant cell, treatment and subsequent clinical events with related investigation profile were recorded in POND database. Patients with CNS involvement at presentation were excluded. Enrolled patients were categorized as early ($< 8^{th}$ month of therapy), intermediate ($> 8^{th}$ to $< 18^{th}$ month of therapy) and late relapse ($> 18^{th}$ month of therapy) respectively according to time of relapse and treated with CNS phase of modified UKALL-2003 regimen B plus cranial irradiation(1800Gy).
Results: Out of 264 registered ALL patients 113 received treatment. 14(12%) developed CNS relapsed were enrolled. Median age 6.5 years (1-16 years), M:F 8:1. 2 patients with CNS involvements at presentation were excluded. Most patients presented with fever (85%), pallor (64%), bleeding (36%), hepatosplenomegaly (88%), lymphadenopathy (37%), headache (27%). Initial WBC $> 50 \times 10^9$/L in 75% cases and thrombocytopenia in 100% cases. 9 patients received MRC-XII, 5 patients received UKALL-2003 modified regimen-A. Most of patients (70%) had intermediate, 3 (21%) had early and 1 (9%) had late relapse. Most patients were asymptomatic during relapse, only 2 headache and 1 with 7^{th} cranial nerve involvement. All patients were followed by CSF (cytospin) with every visit of intrathecal therapy. 78% are in remission, 2 patients (17%) discontinued and 1 patient (9%) died.
Conclusions: CNS involvements were 6 times more during treatment than at presentation. Despite high treatment refusal and abandonment patients with CNS relapse were salvaged successfully with CNS directed therapy of modified UKALL2003 protocol.

PUB-0102

EFFECT OF THE DIFFERENT FUNGUS STIMULI ON THE EXPRESSION OF ENDOCELLULAR CYTOKINES IN NATURAL KILLER CELLS CELLS

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Purpose/Objective: This study was purposed to explore the effect of K562 cells and the different morphotypes of Aspergillus fumigatus and Candida albicans on the expression of endocellular cytokines(IFN-r?IL-4)in cytokine-induced natural killer (NK) cells derived from cord blood using Transwell non-contact cell culture system. Try to compare the differences between the antifungal activity and the tumor cytolysis performed by NK cells.
Materials and Methods: The experiments were divided into two groups: Transwell non-contact culture(indirect-contact groups) and mixture culture(direct-contact groups). The ratio of NK cells to fungus and K562 cells was 10:1. The expression of IFN-r and IL-4 in NK cells were evaluated by flow cytometry after co-culture 6h.
Results: The endocellular IFN-r expression was significantly higher in NK cells contacting with A.fumigatus hyphae?the different morphotypes of C.albicans for 6h,which were (20.12 ± 0.53)%? (21.40 ± 0.53)%?(20.69 ± 0.34)%?(20.57 ± 1.09)%?(20.83 ± 0.37)%?(20.20 ± 0.51)%($P < 0.05$), which were not significantly different in the A.fumigatus spores groups, which were (14.33 ± 0.98)%?(14.97 ± 1.53)%($P > 0.05$). The endocellular IFN-r expression was significantly lower in NK cells contacting directly with K562 cells for 6h,which were (5.88 ± 0.76)%?(6.30 ± 1.02)%($P < 0.05$). The endocellular IL-4 expression was no significant difference in NK cells contacting directly or indirectly with the different morphotypes of A.fumigatus? C.albicans or K562 cells for 6h,which were (1.25 ± 0.06)%?(1.21 ± 0.06)%?(1.21 ± 0.03)%?(1.25 ± 0.04)%?(1.22 ± 0.46)% ?(1.27 ± 0.03)%?(1.26 ± 0.11)%?(1.26 ± 0.10)%?(1.12 ± 0.42)%?(1.18 ± 0.11)% ($P > 0.05$).
Conclusions: It indicated that A.fumigatus hyphae can significantly reduce the secretion of IFN-r, but A.spergillus spores can't activate NK cells,indicating an immune escaping mechanism depending on the morphotypes. The different morphotypes of C.albicans C.albicans can significantly reduce the secretion of IFN-γ, which is not related with the contact modes. The different fungus stimuli all can reduce the secretion of IFN-r in NK cells, which is opposite with tumor cells stimuli. Both of fungus and tumor cells can't effect the expression of IL-4 in NK cells.

PUB-0103

BRAF V600E MUTATIONS IN PLEOMORPHIC XANTHOASTROCYTOMA: THERAPEUTIC IMPLICATION WITH VEMURAFENIB

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Purpose/Objective: Pleomorphic xanthoastrocytoma (PXA) is glial neoplasm principally affecting children and young adults. Upon recurrence, patients receive radiation therapy and conventional chemotherapeutics designed for high-grade gliomas. Genetic changes that can be targeted by selective therapeutics have not been extensively evaluated in PXA. The high mutation frequencies in pleomorphic xanthoastrocytomas, gangliogliomas and extra-cerebellar pilocytic astrocytomas implicate BRAF (V600E) mutation.
Materials and Methods: Here we are describing a 14 year old girl who six years ago was diagnosed with Temporal lobe brain tumor type Pleomorphic xanthoastrocytoma (PXA). She was treated with several therapy:3 neurosurgeries with radio therapy including radio surgery and different chemo therapy s. Unfortunately recurrent disease was observed as the tumor became unrespectable and more aggressive in behavior. Recently Braf-V600E was found positive on specimen of the tumor and Vemurafenib is BRAF inhibitor the in dose of 700 mg 2 x day was added to the metronomic therapy that she was on including: Etoposide ,Avastin and Celecoxib.
Results: Following 2 months of therapy, significant reduction of tumor size was observed on the MRI for the first time. She is currently 9 months on therapy with stable disease.
In our knowledge it is the first time that a patient with brain tumor other then melanoma was treated with Vemurafenib
Conclusions: Further studies are needed to access Vemurafenib,this medication in tumors displaying BRAF V600E mutation.

PUB-0104

FC? RECEPTOR IIIA POLYMORPHISMS IN HEALTHY CHILDREN OR THOSE WITH HEMATOLOGICAL MALIGNANCY

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Purpose/Objective: Fcγ receptor IIIa(FcγRIIIa) polymorphisms was considered to influence clinical response to therapeutic monoclonal antibody(mAb) in cancer, which is suggested to affect mAb binding, and mAb-dependent NK cell-mediated cytotoxicity.The purpose of this study is to examine the FcγRIIIa gene polymorphisms in healthy children or those with hematological malignancy, and speculate possible effect to mAb in children with hematological malignancy.
Materials and Methods: In this study, 43 healthy children and 20 pediatric patients with hematological malignancy consented to participate. DNA was isolated from peripheral blood, and then nest-polymerase chain reaction-restriction fragment length polymorphism (nest-PCR and PCR-RFLP) was performed to determine the FcγRIIIa-158 genotypes in each groups of subject, digested fragments were subjected to electrophoresis on 15%PAGE.
Results: The results showed that there was a higher frequency of FcγRIIIa-158V/F (72.1% and 75.0% in healthy and hematological malignancy group, respectively), the frequency of FcγRIIIa-158V/V was 27.9% and 25.0% in healthy and hematological malignancy group, respectively, but there was no FcγRIIIa-158F/F in the two groups. No significant difference in distribution of the FcγRIIIa-158 genotype was found between healthy and hematological malignancy groups ($p > 0.05$).
Conclusions: It is concluded that FcγRIIIa-158V/F is frequent, while FcγRIIIa-158V/V less, but FcγRIIIa-158F/F is very rare in healthy and hematological malignancy groups. No significant difference of FcγRIIIa polymorphism distribution is found between healthy and hematological malignancy groups.

PUB-0105

HIGH-DOSE CHEMOTHERAPY FOLLOWED BY AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION FOR RECURRENT MALIGNANT MEDIASTINAL GERM CELL TUMOR: A CASE REPORT

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Purpose/Objective: Despite the recent advances in the treatment of germ cell tumors (GCTs), adolescents with malignant mediastinal GCTs constitute the most prognostically unfavorable subgroup, with an overall survival of less than 50%. Thus, a more intensive approach is required in these patients.
Materials and Methods: Review of medical records
Results: We report a 15-year-old boy who presented with an anterior mediastinal mass; multiple lung metastases; and obstruction of the left brachiocephalic vein, superior vena cava, and subclavian vein. Percutaneous CT-guided biopsy revealed a yolk sac tumor. Five courses of BEP (bleomycin 15 mg/m^2 [day 1], etoposide 100 mg/m^2 [days 1-5], cisplatin 20 mg/m^2 [days 1-5]) were administered, resulting in a significant reduction of the anterior mediastinal mass and complete disappearance of the lung metastases. Surgical removal of the anterior mediastinal mass was performed. The patient was treated with ICE (ifosfamide 1.5 g/m^2 [days 1-4], carboplatin 600 mg/m^2[day 1], etoposide 100 mg/m^2 [days 1-4]), and TIP (paclitaxel 175 mg/m^2 [day 1], ifosfamide 1.2 g/m^2 [days 2-6], cisplatin 20 mg/m^2 [days 2-6]), resulting in normalization of his AFP concentration. However, elevated AFP levels and abnormal accumulation in the right upper lung were detected by diffusion-weighted MRI a few months after the end of treatment. Surgical removal of the lung metastasis was successful. Subsequently, 2 courses of TI (paclitaxel 200 mg/m^2 [day 1], ifosfamide 2.0 g/m^2 [days 2-4]) and 2 courses of high-dose chemotherapy (carboplatin AUC of 7 [days 1-3], etoposide 400 mg/m^2 [days 1-3]) were administered followed by autologous peripheral blood stem cell transplantation (auto-PBSCT-HDCT). The patient has not experienced a relapse for more than 1 year even though his condition was complicated by auditory disorder and subclinical renal dysfunction.
Conclusions: Although auto-PBSCT-HDCT is considered an effective treatment for adolescents with recurrent malignant mediastinal GCTs, a treatment strategy that avoids late complications is warranted.

PUB-0106

A SIMPLE MRD MONITORING METHOD IN ACUTE LYMPHOBLASTIC LEUKEMIA FOR DEVELOPING COUNTRIES: DETECTING CLONAL IGH AND TCRG REARRANGEMENTS BY MULTIPLEX PCR AND AUTOMATED FRAGMENT ANALYSIS

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Purpose/Objective: Multiparameter flow cytometry and real-time quantitative polymerase chain reaction (RQ-PCR) analysis have been successfully used to detect minimal residual disease (MRD) in acute lymphoblastic leukemia (ALL), however, they are not easy to be carried out in many developing countries. Although classical qualitative PCR followed by agarose gel electrophoresis analysis may be a simple and low-cost technique to detect IgH/TCRγ rearrangement, it is difficult to distinguish between clonal and non-clonal IgH/TCRγ amplification products and yields a high rate of false-positive results in MRD monitoring. A simple and cost-effective approach to detect MRD in developing countries is required.
Materials and Methods: Four children with very early bone marrow relapsed non-high risk ALL (relapse group) and 12 with non-high risk ALL without relapse (control group) were enrolled. The patients were treated with ALLIC BFM2002 protocol. Bone marrow samples were collected at four time points: initial diagnosis (TP1), the end of VDLD induction therapy (TP2), the beginning of VALD reinduction therapy (TP3) and the third month of maintenace treatment (TP4). Clonal IgH and TCRγ gene rearrangements were detected by multiplex PCR and automated fragment analysis for evaluation of the PCR products using GENEMAPPERID software. A 1:3 matched case-control study design was used.
Results: The frequencies of detection of clonal IgH and TCRγ in all of the 16 patients were 100% and 56% at TP1 respectively. In relapse group and control group, the positive rates of IgH and/or TCRγ were 50% and 42% at TP2 ($P > 0.05$), 75% and 0% at TP3 ($P < 0.01$), and 75% and 8.3% at TP4 ($P < 0.05$), respectively.
Conclusions: Our preliminary results suggest that multiplex PCR followed by automated fragment analysis is a simple, low-cost and useful method for detection of monoclonal IgH and TCRγ gene rearrangements. It could be used in developing countries for MRD monitoring in ALL and therefore warrants further study.

PUB-0107

RESULTS OF TREATMENT OF LYMPHOBLASTIC LYMPHOMA IN CHILDREN AND ADOLESCENTS OF HONG KONG

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Purpose/Objective: Lymphoblastic lymphoma is one of the major subtypes of childhood non-Hodgkin lymphoma. We aim to review the treatment results of T cell and B cell lymphoblastic lymphoma in children and adolescents of Hong Kong.
Materials and Methods: The five hospitals forming the Hong Kong Paediatric Haematology and Oncology Study Group (HKPHOSG) treated children and adolescents with lymphoblastic lymphoma using successive treatment protocols for acute lymphoblastic leukaemia from 1995-2008 and a protocol based on EURO-LB02 study from 2008. The clinical data of all cases diagnosed between 1-Mar-1995 and 31-Dec-2011 were reviewed up to the date of 31-Dec-2012.
Results: During the study period, a total of 42 patients including 34 T cell (T-LBL) and 8 B cell (B-LBL) cases were diagnosed. Thirty-one (74%) were males. The median age was 10.4 years (range, 3.0 to 17.7 years). The median follow up duration was 7.0 years (range, 0.08 to 17.5 years). The Murphy stages consisted of 7% stage 1 ($n = 3$), 10% stage 2 ($n = 4$), 43% stage 3 ($n = 18$) and 40% stage 4 ($n = 17$). The 5-year event-free survival (EFS) and overall survival (S) were 66.3% and 76.7%, with those for T-LBL 60.3% and 73.7% and for B-LBL 87.5% and 87.5%, respectively. The 5-year EFS and S for stage 1 and 2 cases were both 100% whilst those for stage 3 were 76.9% and 72.3% and for stage 4 47.1% and 70.6%, respectively ($p = 0.038$ for stage 4 v stage 1-2). All 3 cases with primary refractory disease died. Only 3 of 9 cases with relapsed disease could be salvaged with second line chemotherapy followed by allogeneic stem cell transplantation.
Conclusions: Although survival of LBL with contemporary treatment reaches $> 70\%$, stage 3 or 4 lymphoblastic lymphoma which is refractory to treatment or relapses has very poor prognosis.

PUB-0108

ANALYSIS OF EFFECTS AND MECHANISM OF MISTLETOE ON LEUKEMIC CELL LINE

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Purpose/Objective: Mistletoe (Abnoba viscum®) extracted from Viscum album L. have mistletoe lectins and viscotoxins which have been known to have cytotoxic and

immunomodulatory effects. This study was performed to evaluate the cytotoxicity and the mechanism of Abnoba viscum® in myeloid leukemic cell line, U937.
Materials and Methods: Cytotoxicity of Abnoba viscum® was measured with MTT assay and the mechanism of apoptosis was investigated with the expressions of pro-/anti-apoptotic controlling proteins and the generation of reactive oxygen species (ROS) with FACS and Western blot.
Results: Cytotoxicities of the drugs were dose-dependent, and LD50 values of adriamycin, cytarabine, and Abnoba viscum® were 1.39 ng/mL, 22.24 ng/mL, and 1742.14 ng/mL, respectively. Cells in sub-G1 phase and fragmentations of PLC-γ1, substrate of caspase, showed increased activity with dose- and time-dependent patterns in various concentrations and exposure durations of Abnoba viscum®, while caspase-3 showed decreased activity. Among pro-/anti-apoptotic controlling proteins, there were no changes of expressions, except Mcl-1, which was decreased, with higher concentration and longer duration of Abnoba viscum® exposure. Apoptosis and fragmentation of PLC-γ1 by Abnoba viscum® were inhibited by pre-exposure with caspase inhibitor, z-VAD-fmk. Apoptosis by Abnoba viscum® was inhibited by pre-exposures with anti-oxidants.
Conclusions: In conclusion, Abnoba viscum® showed cytotoxicity and caspase-dependent apoptosis by ROS generation in myeloid leukemic cell line U937. The prospective studies for clinical effects and therapeutic mechanism of Abnoba viscum® including the expression of Mcl-1 and whether Abnoba viscum® could be used in leukemic patients as supportive and maintenance therapeutic agents in pediatric leukemic patients seem to be warranted in near future.

PUB-0109

IMMUNOPHENOTYPING AND CYTOGENETICS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A TERTIARY CARE EXPERIENCE FROM INDIA

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Purpose/Objective: To collect immunophenotype and cytogenetics data in all patients with childhood ALL and correlate with their outcome.
Materials and Methods: Data of children with ALL in the age group of 1 to 18 years treated at our center was collected. All patients received treatment as per a uniform protocol.
Results: The data of 114 patients was analyzed with mean and the median age of 7.2 ($\pm$ 4.1) and 6.5 yrs respectively (1.5-15.8 yrs). 85 (74.6%) patients were below 10 years. The TLC was $>$ 50000 in 23.7% patients. The analysis revealed Pre B ALL in 88.6%, B cell ALL in 1.7% and T cell ALL in 9.7% patients. Karyotyping data was available in 63 of which normal karyotype was seen in 54, hypodiploidy in 6 and hyperdiploidy in 3. FISH for TEL AML, MLL, BCR-ABL gene rearrangement analysis was positive in 8(33.3%), 2(9.1%), 3(9.7%) patients respectively. 62 (55.85%) patients were high risk and the remaining 49(44.14%) patients were standard risk. The bone marrow status at day 28 revealed M1 marrow in 109 patients and there were 2 induction deaths. Out of 111 patients there were 96 survivors. At a median of 4 years from diagnosis, 99 (86.8%), are alive free of disease. The OFS and EFS of the standard risk and high risk patients was not statistically different (p = 0.896). Among the 15 nonsurvivors, 10 patients relapsed and died, 4 patients died due to treatment related toxicity out of which 2 were induction deaths and 1 patient died in an accident.
Conclusions: The prevalence of adverse prognostic factors in the urban setting is comparable to the data reported from the west. With appropriately risk stratified treatment the outcomes of standard and high risk groups are equivalent and comparable to the best reported outcomes to date.

PUB-0110

IMPROVED SURVIVAL RATE OF CHILDREN WITH HEPATOBLASTOMA TREATED WITH PREOPERATIVE CHEMOTHERAPY AND SURGERY

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Purpose/Objective: Hepatoblastoma (HB) is the most common primary malignant tumor of the liver in children. Surgery is the mainstay of the treatment for HB. However, less than half of HBs are resectable at the time of diagnosis and preoperative cisplatin-based chemotherapy was introduced to make unresectable tumor to become resectable mass and improve the cure rate
Materials and Methods: From Jan. 2000 to Dec. 2010, a total of 45 patients were enrolled. Medical record was reviewed retrospectively
Results: Male to female was 25 and 20 and median age at diagnosis was 10.3 months. Most common histological subtype was epithelial type (27) and next was mixed epithelial and mesenchymal type (13) and 5 patients had no applicable data. Metastasis at diagnosis was observed in 7 patients. Complete surgical resection was performed initially in 5 patients (11%) and biopsy only was done in other 40 patients (88.9%), which was followed by preoperative chemotherapy. After pre operative chemotherapy, 30 patients had partial response (PR), 9 had stable disease (SD), and 1 had progressive disease (PD). Among 10 patients with SD or PD 8 had relapse or progression, but eventually 6 patients are alive without disease and 4 patients died of disease. Thirty four patients (74%) had complete surgical resection with clear resection margin. Median follow-up time from diagnosis was 124 months (range, 24-128 months) and 5-year overall survival rate and relapse-free survival rate was 89.1% $\pm$ 5.5% and 67.4% $\pm$ 7.2%, respectively. Relapse-free survival was statistically significant according to chemo-responsibility (PR vs SD; 80% $\pm$ 7.8%, vs 22.2% $\pm$ 13.9%, $P = 0.001$), complete surgical respectability (79.4% $\pm$ 7.6% vs 25% $\pm$ 15.3%, $P = 0.003$), and metastasis at diagnosis (78.4% $\pm$ 7.4% vs 28.6% $\pm$ 17%, $P = 0.001$).
Conclusions: Cisplatin-based chemotherapy made unresectable tumor to become resectable and increased the cure rate up to 80-90%. However, patients with poor chemo-responsibility or metastasis at diagnosis had poor survival outcome. This is the reason for development of new treatment modalities adjusted by pathology and pathophysiology.

PUB-0111

MANAGEMENT AND OUTCOME OF PATIENTS WITH HEPATOBLASTOMA TREATED AT KING HUSSEIN CANCER CENTER

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Purpose/Objective: Hepatoblastoma is the commonest malignant liver tumor in children. Increase in survival is reported with better risk stratification coupled with improvement in surgical techniques and supportive care. In this study we report our experience in children with hepatoblastoma treated at King Hussein Cancer Center (KHCC).
Materials and Methods: We conducted a retrospective analysis of children ($<$ 18 years) with hepatoblastoma who presented from February 2003 until December 2012. Patients' characteristics, treatment modalities and outcome were analyzed. High risk disease was defined as having PRETEXT IV and/or extra-hepatic involvement.
Results: We identified 22 patients (11 females) who presented with hepatoblastoma to our center. The median age at diagnosis was 12.5 months (range 3 to 142). Diagnostic biopsy was done in 13 patients and resulted in no major complications. Ten patients had high risk disease for the following reasons: PRETEXT IV (N = 3) and extra-hepatic involvement (N = 7). Cisplatin alone was used in 5 patients while other regimens were used in the rest of the patients including 2 patients who were enrolled on SIOPEL 4 protocol and remain disease-free. Only one patient died within 30 days after surgery for an unclear etiology. After a median follow up of 3.6 years, 18 patients remained free of disease while 3 had recurrence and 1 died of another reason. The 3-year EFS was 76% +/− 9.5%.
Conclusions: Results of treatment of hepatoblastoma at KHCC are acceptable. We avoided doing a biopsy in many patients. We recommend less intensive treatment (Cisplatin monotherapy) for standard risk patients, while intensification of treatment of high risk patients can be of value with proper support. Multidisciplinary care with well-equipped PICU and trained surgeons are essential in achieving good results.

PUB-0112

OUTCOME OF PATIENTS WITH LYMPHOBLASTIC LYMPHOMA TREATED AT KING HUSSEIN CANCER CENTER

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Purpose/Objective: Lymphoblastic lymphoma is a high grade non-Hodgkin lymphoma. Good outcome was reported by many study groups especially the BFM. In this study we report our experience in children with lymphoblastic lymphoma treated at King Hussein Cancer Center (KHCC).
Materials and Methods: We conducted a retrospective analysis of children ($<$ 18 years) with Lymphoblastic lymphoma who presented from April 2004 until December 2012.The protocol which is adopted at KHCC is based on BFM 95. Patients characteristics and outcome were analyzed.
Results: We identified 33 patients (6 females) who presented with Lymphoblastic lymphoma to our center. The median age at diagnosis was 9.5 years (range 2 to 17). Diagnostic biopsy was done in all patients. Three patients had stage lV disease due to involvement of the bone marrow with less than 25%. Twenty seven children (80%) had T cell immunophenotype. After a median follow up time 24 months (range 3-101), the estimated 5 years OS and EFS were 86% +/ − 9.4% and 82% +/− 9.7% respectively. Two patients had CNS relapse one is still alive in CR, the other patient died of disease. One child had a brain tumor and developed lymphoblastic lymphoma later and died of his brain tumor.
Conclusions: Our results in treatment of lymphoblastic lymphoma at KHCC is comparable to that reported by the BFM. Adopting intensive treatment protocol with the appropriate supportive care in a developing country can be applicable.

PUB-0113

TRANSMANUBRIAL OSTEOMUSCULAR-SPARING APPROACH FOR CERVICOTHORACIC TUMORS IN CHILDREN: LONG-TERM RESULTS

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Purpose/Objective: Cervico-thoracic tumors consisting mainly of neurogenic tumors in childhood, represent a challenging location because of the proximity of important vessels and nerves and the possible extension in the spinal canal. We had shown that the transmanubrial osteomuscular-sparing approach (TOSA) permits an optimal resection of neurogenic tumors in children, while allowing a perfect control of the supra-aortic vessels and nerves. We report here a larger series of patients, including non neurogenic tumors, and long-term results of this original surgical approach.
Materials and Methods: Patients with cervico-thoracic tumors operated through TOSA in a single institution from January 2000 to November 2012 were retrospectively reviewed in a long-term follow-up.
Results: Thirteen patients were collected, 7 males and 6females. Median age at surgery was 72 months (4- 188). There were 6 neuroblastoma, 3 ganglioneuroblastoma, one rhabdoid tumor, one melanocytic schwannoma, one chordoma and one malignant peripheral nerve sheath tumor (MPNST) in a patient with a type 1 neurofibromatosis. Median duration of intervention was 220 minutes (110-315). Two children presented a chylothorax that spontaneously resolved. Post-operative course was uneventful in 11 patients (85%). The median duration of hospitalization was 7 days (4-22).Two patients died: one stage Ms neuroblastoma from treatment toxicity and one rhabdoid tumor from rapid local and metastatic progression respectively 6 and 3 months after surgery. All other patients are free of disease with a median follow-up of 39 months (2-159). Morbidity consisted in homolateral Claude Bernard and upper limb vasomotor dysfunction in all patients due to the mandatory resection of the stellar ganglia. No osteomuscular morbidity was noted.
Conclusions: The TOSA is a good option for excision of neuroectodermic tumors but also for other cervico-thoracic tumors. Long-term follow-up demonstrate a low morbidity allowing considering this approach for any tumor involving the thoracic inlet.

PUB-0114

EARLY PREB-ACUTE LYMPHOBLASTIC LEUKAEMIA (CALL): IMPROVED SURVIVAL OVER 3 DECADES IN DIFFERENT ETHNIC GROUPS WITH RISK ADAPTED TREATMENT

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Purpose/Objective: Two previous cohorts (1980-1989/1992-2000) of early preB Acute Lymphoblastic Leukaemia (cALL) have shown an inferior survival rate in the Black African patient (White versus Black = 70%/80% versus 30%/60%, p = 0.025). In 2002 the protocol used was changed to a modified BFM ALL 95 protocol, using the triple FISH test and prednisone response to try and improve survival rate with risk adapted treatment.
Materials and Methods: A retrospective analysis was performed on all patients diagnosed with ALL at the CMAJH between 2002 and 2010.
Results: 153 patients with ALL were diagnosed. There were 117(76.4%) patients with cALL Male to female ratio was 1.4:1. 72% Black African patients and 75% white patients had cALL. The mean age at diagnosis was older in the black patient at 6.5years versus 4.94 years in the white patient. The mean white cell count at diagnosis was $19.3.3 \times 10^9$/l in the white patient versus 36.2×10^9/l in the black patient. 7 patients were t(9;22)(bcr-abl) positive. 17/42(40%) white patients were hyperdiploid versus 11/57(19%) black patients. 18 patients (5 white,12black & 1 Indian) received High Risk(HR) blocks for Prednisone poor response, poor prognostic cytogenetics and no remission Day 33. Significant good prognostic factors were hyperdiploidy ($p = 0.004$), and female gender ($p = 0.02$). Significant poor prognostic factors were a white cell count $> 50 \times 10^9$/l ($p = 0.004$), and age over 10yrs ($p = 0.09$).The overall survival rate was 76%. Of note was that the survival of Black patients with cALL improved to 72.5%, and ethnic group is no longer a significant prognostic feature($p = 0.23$).
Conclusions: Improved laboratory data and steroid response rate has better delineated poor prognostic ALL. This has allowed intensification of treatment with HR blocks of the BFM ALL 95 protocol. This cohort of patients has demonstrated an improved survival rate in the black patients with cALL despite more poor prognostic criteria, but with considerable morbidity, increased cost and period of hospitalization.

PUB-0115

MUSCULOSKELETAL SEQUELAE OF BONE AND SOFT TISSUE SARCOMAS IN CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY

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Purpose/Objective: recommendations for screening, prevention, and management of survivors
Materials and Methods: Childhood Ewing,s sarcoma family tumours (ESFT), osteosarcoma (OS) and soft tissue sarcoma survivors are known to be at risk for serious musculoskeletal late effects that may result in disability. 48 children and adolescents at the mean age of 14,0 years (28 males, 20 females) with ESFT and OS were treated between 1987 and 2011 years, followup of 2 to 26 years. Histologically, 17 patients had OS, 26 - ESFT, 5 * STS. The most often affected area was lower extremity - 29 cases, pelvis was affected in 5 cases, ribs * 5 cases, upper extremity - 3 cases, clavicula * 2, axis * 4 case. 15 patients had distant metastases: 7 patients had distant metastases at lungs, bones were involvement in 2 cases, lymph nodes - in 4 cases, pleura - 2. 8 patients had solitary metastases, 7 *multiple. Treatment consisted of neoadjuvant chemotherapy, the radiotherapy of the initial tumor and metastasis left after the induction (unless cases of OS), oncologic surgery and adjuvant chemotherapy, 7 patients with unresectable or metastatic ESFT underwent high-dose chemotherapy with peripheral blood stem cells transplantation
Results: The most common late effects we had observed were: muscular hypoplasia * in 19 cases and osteopenia * in 14 cases, limb-length discrepancy in spite of usage of growing endoprosthesis - in 26 cases, scoliosis - in 40 cases, deformation of chest wall - in 5 cases. Pathological fractures were described in 3 cases, poor joint movement in 26 cases. Neurological disturbance - in 8 cases and lymphedema were in 5 cases, deforming osteoarthrosis - in 2 cases
Conclusions: Long-term survival is possible, even for patients with metastatic disease. All long-term survivors of childhood cancer therapy should attend a specialized late effects clinic yearly

PUB-0116

HIGH RISK AND RELAPSED NEUROBASTOMA OF CHILDREN: RESULTS OF TREATMENT

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Purpose/Objective: the evaluation of treatment of children with high risk and relapsed neuroblastoma
Materials and Methods: from 2011 to 2012 years we had been observing 17 patients with morphologically confirmed neuroblastoma at the mean age of 5,1 years (from 14 days till 16 years). There were 13 patients with IV stage of the disease and 4 patients had relapse. All patients received therapy according NB 2004 protocols after *thoroughly evaluation* (imaging, MIBG, bone marrow morphology, molecular studies, immunohistochemistry). Surgery treatment was performed after chemotherapy. Stage by INSS and group of the risk were established after histological examination. The patients with MNA, stage IV and with recurrence of the disease received intensive chemotherapy, consisting of doxorubicin, etoposide, cisplatin, vincristine, dacarbazine, ifosfamide and RT
Results: 9 (52,9%) patients (from 17) were alive without disease with a followup of 5 to 12 months. One patient is alive with the disease
Conclusions: these results support further investigations. Intensification of the chemotherapy increases the survival of the patients with the high risk and relapsed neuroblastoma. Our data confirm that survival is possible, even for patients with high risk and relapsed disease

PUB-0117

THE GASTROINTESTINAL MUCOUS MEMBRANE BARRIER FUNCTION DETERMINATION AND ITS SIGNIFICANCE IN CHILDREN WITH TUMORS AFTER CHEMOTHERAPY

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Purpose/Objective: To discuss the influence of the intestinal mucosal barrier function and the role of Diamine oxidase(DAO) and Intestinal fatty acid binding protein (I-FABP) in evaluating the function of gastrointestinal mucous membrane barrier,by measuring the levels of DAO and I-FABP and the changes of intestinal flora.
Materials and Methods: Choose 30 cases of tumour children, which were divided into three groups (mild group,n1 = 10;moderate group,n2 = 10;height group n3 = 10),according to the different vomit strength of chemotherapy drugs.Collecting the venous blood before chemotherapy was given and at three and seven days after chemotherapy.Measured the level of DAO and I-FABP,recorded the vomiting times during chemotherapy and collected daily fresh specimen of bowels,calculate bacillus/number of bacteria.
Results: 1.Before chemotherapy was given, the level of DAO(mild = 13.75 ± 1.02;moderate = 14.04 ± 1.06;height = 14.01 ± 0.98)and I-FABP (mild = 1024.75 ± 72.10; moderate = 968.60 ± 90.74;height = 998.86 ± 115.47)among different strength groups have no significant difference ($P > 0.05$).3 days and 7 days after

chemotherapy, the level of DAO (mild3 = 28.31 ± 1.84;moderate3 = 32.49 ± 1.63;height3 = 37.643 ± 1.76;mild7 = 20.71 ± 1.68;moderate7 = 20.75 ± 1.33;height7 = 22.82 ± 1.67) and I-FABP(mild3 = 1838.93 ± 100.14;moderate3 = 2085.47 ± 63.74;height3 = 4097.04 ± 119.57;mild7 = 1402.73 ± 60.51;moderate7 = 1577.57 ± 71.10;height7 = 2135.98 ± 110.11) has significant difference($P < 0.05$) between any two groups, the height group was significantly higher than the others.The level of DAO and I - FABP after chemotherapy was significantly higher than that before,and the three days was higher than that of the seven days after.2.The vomiting times and the level of DAO and I-FABP has positive correlation, ($r_{DAO} = 0.744$, $P < 0.05$;$r_{I\text{-}FABP} = 0.889$, $P < 0.05$);The bacteria/total bacterial count ratio and the level of DAO and I - FABP has negative correlation ($r_{DAO} = -0.180$, $P < 0.05$; $r_{I\text{-}FABP} = -0.222$, $P < 0.05$).
Conclusions: The level of DAO and I-FABP can reflect the injury state of the gastrointestinal mucous membrane barrier after chemotherapy and its degree. The detection of the two index, can be used as a quantitative and sensitive method to reflect gastrointestinal barrier function of pediatric after chemotherapy.

PUB-0118

CRANIAL RADIOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA: FAVORABLE OUTCOME WITHOUT ITS USE

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Purpose/Objective: To analyze the incidence of CNS relapse between the standard risk (SR) and high risk(HR) patients with ALL.
Materials and Methods: We analyzed data analysis of all children with ALL aged 1 to 18 years treated at our center between 2003-2012 regarding CNS disease status at diagnosis, treatment given for CNS prophylaxis, treatment for CNS positive cases and outcomes.
Results: Data of 163 patients revealed the mean and the median age to be 8.2 and 7.1 years respectively. CNS disease at diagnosis was seen in only 5(3.08%) patients all of whom received CRT. In addition 2 more patients received CRT because of inability to come for regular follow up while all others received intrathecal chemotherapy. Out of 156 patients, 76 (48%) were SR and 80(52%) were HR. There were a total of 12 relapses, 8 bone marrow, 1 testicular, 1 bone marrow with CNS and 2 extramedullary relapse. Among the relapses 7 (58.3%) were SR and 5(41.7%) were HR. The only CNS relapse was in the SR group. Of the 7 patients who received CRT, 3 patients had CNS relapse. At a median of four years from diagnosis, 145 (88.9%) are alive, free of disease.
Conclusions: Optimal outcomes can be achieved in patients with high risk ALL even without use of cranial radiotherapy.

PUB-0119

MALIGNANT MELANOMA WITH LI-FRAUMENI LIKE SYNDROME

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Purpose/Objective: Malignant melanoma is a very uncommon tumor in children particularly in Indian population. Clinical presentation of childhood melanoma can be atypical leading to delayed diagnosis. Prognosis of tumours diagnosed early is excellent. However, cure rate of metastatic tumours is extremely poor. Treatment involves multimodality approach. We present a case of lower extremity malignant melanoma in a child who is now free of recurrence over 9 yrs following treatment.
Materials and Methods: An 8 yrs old female child presented with ulceroproliferative growth over right 2nd toe about 1.5 × 1.5 cm in size for more than a year. She had been treated elsewhere with ATT for five months with no response. On examination, a hard lymph node mass was felt in right inguinal region. Biopsy of the local region and FNAC of inguinal lymphnodes revealed morphology and immunohistochemistry consistent with malignant spindle cell melanoma
Results: Patient underwent ray amputation of the involved digit and right ilioinguinal block lymph node dissection. Subsequently she was given 6 cycles of dacarbazine. Immunotherapy was not feasible. She continues to be free of disease 9 years from diagnosis.
During her follow up her grandmother, has been detected to have carcinoma breast and her father has been recently diagnosed to have Glioblastoma Multiforme. By Birch's criteria, on clinical grounds, this family fulfills the criteria for Li-Fraumeni like syndrome.
Conclusions: Malignant Melanoma in childhood can sometimes present atypically. It is imperative to be aware of this rare entity in children presenting with skin lesions that are new or unusual in appearance. Aggressive surgical treatment along with adjuvant chemotherapy can achieve long term survival even with locoregional spread.

PUB-0120

SIDE EFFECTS OF HIGH-DOSE METHOTREXATE TREATMENT TO CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: To study the side effects of high-dose methotrexate (HD-MTX) treatment to children with acute lymphoblastic leukemia (ALL), and to explore the practicality of different HD-MTX protocals in different guidelines (or recommendations) of children ALL.
Materials and Methods: 100 children cases with ALL had received HD-MTX treatment from February 1, 2004 to October 30, 2010. 20 cases received MTX 3g/m^2,80 cases received MTX 5g/m^2. 6-mercaptopurinum(6-MP) 50mg/m^2 were given orally 7 days in both groups. Side effects were recorded and statistically analyzed by SPSS 13.0.
Results: Bone marrow suppression, mucosal damage, gastrointestinal discomfort, liver function damage, and erythra were the most common side effects in HD-MTX treatment.The incidence of bone marrow suppression in both groups were 100 percents,and there was no significantly difference in bone marrow depression period in MTX 3g/m^2 group and MTX 5g/m^{2}group(18.95d ± 5.74d vs.19.17d ± 6.04d, $P > 0.05$). There was significantly difference in incidence of gastrointestinal discomfort in MTX 3g/m^2 group compared to MTX 5g/m^2 group(10% vs.40%,$P < 0.05$). There were no significantly differences in incidence of mucosal damage (10% vs 15%,$P > 0.05$),liver function damage and erythra (10% vs.7.5%,$P > 0.05$).
Conclusions: Except for high incidence rate of gastrointestinal discomfort,high dose MTX 5g/m^2 was relativly safe to treat ALL in children.In order to shorten the period of bone marrow supression of HD-MTX plus 6-MP treatment, it is might be suggested to reduce the dosage of 6-MP in HD-MTX plus 6-MP protocal in children ALL.

PUB-0121

EFFECT OF FLAG REGIMEN IN TREATMENT OF CHILDREN WITH ACUTE REFRACTORY AND RELAPSED LEUKEMIA

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Purpose/Objective: Purpose. The purpose of this study was to evaluate the effect of FLAG regimen in the treatment of children with acute refractory or relapsed leukemia.
Materials and Methods: Methods. From June 2010 to Octber 2012, 11 children with refractory or relapsed leukemia were treated with FLAG regimen. Of the 11 children, 9 were AML and 2 were ALL. The FLAG regimen were consisted of Fludarabine 30mg/m^2/d on days 1-5 and Ara-C 2g/m^2/d on days 1-5,and granlocyte colony-stimulating factor 200μg/m^2/d on days 0-5. The response rate,toxicity,and overall survival were evaluated.
Results: Results. 7 (63.7%) AML patients achieved complete remission (CR) after 1 course, 1 AML patient achieved partial response and subsequently CR after 2 courses, 1 AML patients and 2 ALL patients were non-responders. The overall response rate was 72.7%. The median duration for ANC > 500/μL was 17 (13-27) days and platelet > 20/μL was 15 (10-23) days. The main toxicity of this regimen were gastrointestinal side effects, myelosupression and neutropenia, All patient developed fever during neutropenia period and resolved after potential anti-bacterial therapy. No treatment-associated mortality occurred. 5 CR patients received allogeneic stem cell transplantation(SCT) and all survived during a follow-up period of 15 (6-27) months, 1 CR patient relapsed 3 months after refusing to receive further treatment. The other 2 CR AML patient continue to receive consolidation chemotherapy and wait for SCT.
Conclusions: Conclusions. The FLAG regimen showed high responsive rate in children with refractory/relapsed AML but poor effect on ALL and the side effect was tollerable.

PUB-0122

THREE PEDIATRIC CASES OF HIGH-DOSE CHEMOTHERAPY FOR ATYPICAL TERATOID/ RHABDOID TUMOR OF THE CENTRAL NERVOUS SYSTEM.

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Purpose/Objective: Atypical teratoid/ rhabdoid tumor (AT/RT) is a rare and highly aggressive brain tumor in children. The survival rate is still miserable in spite of active multimodal therapy. The present study evaluated the role of high-dose chemotherapy (HDC) followed by autologous stem cell rescue in treatment for AT/RT.
Materials and Methods: We retrospectively analyzed clinical courses and prognoses of three consecutive cases of AT/RT treated with multimodal therapy including HDC in our hospital from 2004 to 2012.
Results: Case1: 2-year-old female, cervical spine AT/RT. Case2: 2-year-old male, periventricular AT/RT. Case3: 5-year-old male, frontal lobe AT/RT. In 2 (Case1 and 2) of 3, tumors were completely resected. After surgery, all 3 cases received ICE

(Ifosfamide + Cisplatin + Etoposide) and/or rhabdomyosarcoma*targeting chemotherapy (Vincristine + Cyclophosphamide + Doxorubicin + Cisplatin + Etoposide) for adjuvant therapy. Intrathecal injections were added to these systemic chemotherapies. Radiation therapy was performed in an interval of chemotherapy in Case 3; however, for 2 younger cases, it was postponed until they reached 3 years of age (just after HDC). HDC regimens were Thiotepa+ Etoposide + Carboplatin or Melphalan + Etoposide + Carboplatin, followed by autologous stem cell transplantaion (2 BM, 1 PBSCT). No serious regimen-related toxicity was experienced. To date, Case1 and 2 have survived more than 5 years with acceptable growth and development. Case3 died from disease only 1 month after HDC.
Conclusions: For cases under 3 years of age, HDC can gain time of complete remission, and allows them to wait for radiation therapy. However, HDC itself seem to be insufficient salvation for cases with partial remission. Control of disease before HDC, and full-dose radiation with an adequate margin may be more important factors that improve the survival rate.

PUB-0123

ABERRANT DNA METHYLATION OF THE RIZ1 GENE IN CHINESE CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA

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Purpose/Objective: To investigate the role of retinoblastoma protein-interacting zinc finger gene 1 (RIZ1) in pediatric acute lymphoblastic leukemia (ALL).
Materials and Methods: Quantitative real-time polymerase chain reaction and methylation-specific polymerase chain reaction were used to examine the expression level and promoter methylation status of RIZ1 gene in childhood ALL.
Results: The expression of RIZ1 was significantly decreased in ALL group than control group. RIZ1 expression in high risk group statistically decreased by 88.73-fold than control group. Promoter hypermethylation of RIZ1 was detected in 28.13% of patients with ALL, but in none of control group. Compared with unmethylated samples, RIZ1 expression was significantly decreased by approximately 10-fold in methylated cases.
Conclusions: Down-regulated expression of RIZ1 gene may participate in leukemogenesis of pediatric ALL, and is a potential prognostic indicator of ALL. In addition, hypermethylation of RIZ1 promoter partially contributes to decreased RIZ1 expression in childhood ALL, whereas other mechanisms should be involved.

PUB-0124

TWO CASES REPORT OF PEDIATRIC ATYPICAL NEUROBLASTOMA

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Purpose/Objective: To show the clinical characteristics of atypical neuroblastoma in two Chinese pediatric patients.
Materials and Methods: Retrospective analysis was made of two cases of atypical neuroblastoma.
Results: Atypical neuoblastoma refers to the primary onset of neuroblastoma without a detectable mass in common sites, but in bone marrow or/and other metastasis parts, is an infrequent occurrence. We present two unusual cases of Chinese atypical neuroblastoma that the extramedullary substantial mass not be found. Moreover, the two cases both presented with typical neuroblastoma cells that forming Homer-Wright rosettes in bone marrow smear. The diagnosis of neuroblastoma was further established by markedly elevated of vanillylmandelic acid (VMA) in urine,serum neuron-specific enolase (NSE) and neuroblastoma MRD level in peripheral blood, amplifications of bone marrow N-myc were both absent. Noteworthy, the first case showed no other parts of the tumor infiltration in addition to bone marrow, while in the second case the involvement of neurobalstoma both in bone marrow and bone. In the first case, imaging examinations consisting of the whole body bone scan, abdominal ultrasound and chest X-ray did not reveal additional tumor involvement. The two patients were treated with nine courses of induction chemotherapy as high-risk neuroblastoma protocol, which includes CAV (Cyclophosphamide + Pirarubicin+ Vincristine), PVP (Cisplatinum+ Etoposide) and CT (Cyclophosphamide + Topotecan). Although the first patient achived complete remission, the child is not free of recurrence at a follow-up of half a year due to lack of consolidation chemotherapy. In the second case, by contrast, complete remission was not obtained, and then he abandoned further treatment for economic reason.
Conclusions: In case of atypical neuroblastoma, chemotherapy might be the only effective firstline treatment for the absense of visible solid mass. In our limited experience, it seems that the patients of atypical neuroblastoma have unfavorable prognosis after conventional intensive chemotherapy, especially in the presence of bone involvement.

PUB-0125

PET SCAN BASED RESPONSE ASSESSMENT TO REDUCE USE OF RADIOTHERAPY IN PEDIATRIC HODGKIN LYMPHOMA: A STUDY FROM KUWAIT

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Purpose/Objective: Use of radiation therapy (RT) can cause various long term side effects in children in terms of growth retardation, hormonal disturbances and second malignancies. Efforts are on to limit the use of RT in pediatric Hodgkin Lymphoma (HD). FDG *PET based response evaluation after initial 2 cycles of chemotherapy is now standard practice in many European countries. This policy was adopted in our centre from 2008 after installation of PET scan. Use of radiotherapy has really come down after adopting this protocol.
Materials and Methods: This is a retrospective analysis of all children with HD, who were treated between January 2008 and December 2011. The PET scan was done at the initial presentation and after 2 cycles of chemotherapy. Children who were PET negative were not given any RT. Chemotherapy was given according to risk category.
Results: During the study period, a total of 30 children were registered with diagnosis of classical HD, but only 25 were eligible for analysis.. The median age was 13.5 years (range: 3.5 * 15 years). Nodular sclerosis was predominant pathology (60%), followed by mixed cellularity (40%). Forty four percent had stage 2, while 24% had stage 4 disease. PET scan was positive only in 4 patients after 2 cycles of OEPA chemotherapy, and all these patients received radiation therapy. There were no significant hematological toxicity. At the end of therapy, 24 patients (96%) were in CR, while one had progressive disease (PD). Subsequently 2 patients relapsed (at one and 8 months). At last follow-up, 24 patients (96%), were in CR, while one is undergoing salvage therapy, including high dose with autologous stem cell. The median EFS was 22 months (range: 0- 53 months), while median survival was 32 months (Range: 10 * 53 months).
Conclusions: By adopting this protocol, RT was avoided in 84% of patients, without compromising the survival.

PUB-0126

NOVEL MUTATIONS IN THE UNC13D GENE CARRIED BY A CHINESE NEONATE WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Purpose/Objective: Hemophagocytic lymphohistiocytosis (HLH) in different ethnicities has been described in the literature, but few cases in patients of Chinese descent have been reported. Here, we describe the case of a Chinese neonate presenting with HLH.
Materials and Methods: Peripheral blood samples from the HLH patient, his parents, and 50 normal children were obtained; FHL-related gene analysis using genomic DNA sequency, functional tests with resting NK cells and CTL cells, including perforin detection and degranulation assay quantifying CD107a surface expression with flow cytometry, and Th1/Th2 cytokine levels during the course of HLH using a BD™ CBA Human Th1/Th2 Cytokine Kit II (BD Biosciences, San Jose, CA, USA), were performed.
Results: The patient had novel, compound heterozygous mutations of the UNC13D gene, including [c.2295_2298delGCAG, p.Glu765Aspfs*27] in exon23, c.-250C > T, c.1 + 30G > A, c.279C > T, c.888G > C, c.18 + 36A > G, c.20-48T > C, c.1977C > T, c.2296C > T, c.24-46C > T, c.26-9_−26-8insC, c.2599A > G, c.28 + 48C > T and c.3198A > G. No mutation was found in PRF1, STX11, and STXBP2 genes of this patient and his parents, except for one synonymous change in PRF1 gene [c.900C > T, p.His300His]. Th1/Th2 cytokine monitoring by CBA technique showed that during the acute phase of HLH without complicating bacterial infection for this patient, both IFN-g and IL-10 levels increased, while IL-6 remained normal or only slightly elevated; When the HLH patient entered remission, the levels of IFN-γ and IL-10 both declined, usually with IFN-γ declining faster than IL-10; When IFN-γ,IL-10 and IL-6 levels returned to normal or close to normal, the HLH related conditions of the patient were controlled.
Conclusions: We described the case of a Chinese male neonate who presented with HLH and had novel, heterozygous mutations in the UNC13D gene, some of which have not been reported in the literature. Cytokine profile monitoring may be helpful in differentiating various clinical phases of HLH.

PUB-0127

EPIDEMIOLOGICAL PROFILE OF CANCERS IN ADOLESCENT AND YOUNG ADULTS: A TERTIARY CENTRE EXPERIENCE FROM INDIA

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Purpose/Objective: To study the profile of cancers in adolescent and young adults(AYA) presenting to MNJ IO RCC, a tertiary care centre in India during the year 2012
Materials and Methods: All the patients registered at MNJ IO RCC from 1st January 2012 to 31 December 2012 between the ages of 15 to 29 years were included in the study. The epidemiological data was grabbed from th registration, case sheets and department of pathology. Cancer was diagnosed after a histological proof. Non malignant cases were excluded.
Results: The institute had a total registrations of 8322 patients during the above period. Adolescent and young adults were 870(10.4%). Malignancy was confirmed in 611(70.2%). Benign and nonmalignant states were noted in 259(30%). There were 266 (43.5%) women and 345(56.5%) men. Hematolcogical malignancy was noted in 236 (38.6%). Solid tumors were seen in 375(61.4%). Acute leukemia,lymphomas and chronic myeloid Leukemias were seen in 135(57%),70(30%) and 31(13%) respectively. Bone and soft tissue tumors were noted in 75(21.5%). Head and neck cancers in 55(15%) of cases. Other malignancies noted include thyroid,female genital tract and male genital tract malignancies in their order.
Conclusions: Cancers are not uncommon in AYA. They form a special group with different supportive needs. Hematological malignancies are common. Bone and soft tissue tumors I are more common amongst the solid tumors in this age.

Many of them can be prevented by lifestyle modification.

PUB-0128

PROFESSIONALS HEALTH OF THE WEST, NORTHWEST AND SOUTHWEST OF PARANÁ, BRAZIL ARE TRAINED TO SUSPECT THE EARLY DIAGNOSIS OF CANCER FOR CHILDREN AND YOUTH.

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Purpose/Objective: Introduction: The juvenile cancer is a rare but is the second leading cause of death in the range 5 to 19 years. Moreover, the cure rate reaches 70% if diagnosed early. The Cancer Hospital of Cascavel - UOPECCAN in partnership with the Ronald McDonald Institute through the Early Diagnosis of Cancer Children and Youth Program, train professionals of Health and Pediatrics of the municipalities in the west, northwest and southwest of Parana on suspicion cancer in children and youth. Objetivo: Train professionals of health program and pediatricians to recognize the main signs and symptoms of juvenile cancer, and forward early the suspected case, reducing the time between the onset of signs and diagnosis of disease.
Materials and Methods: Methodology: We trained professionals in the municipalities of the twelve cities of West, Northwest and Southwest of Paran‡, Brazil, from April / 2008 to dez/ 2012.These professionals received basic information regarding various topics (National Policy Oncology, Cancer Epidemiology Children and Youth; Signs and symptoms of suspicion; The Importance of Family Health in the context of juvenile cancer; care needed for the attention to children and adolescents with the organization of the reference system and cross-reference). The groups were formed with 40 professionals in various areas. 20 hours / course / class for non-physicians and 24hs for physicians.
Results: Results: We trained: 786 professionals, 52 doctors, 91 nurses, 126 technicians / Nursing assistants, 360 Community Health Agents, 75 upper level and 74 medium-level professionals or auxiliary.
Conclusions: Comments: The training of these professionals with basic information on the recognition of major signs and symptoms of cancer in children and adolescents is a strong ally in programs for Early Diagnosis of Cancer Children and Youth. Shortening the time between the suspicion of cancer and early diagnosis and treatment, will certainly contribute to the increasing expectations of cure in developing countries.

PUB-0129

CHARACTERISTICS OF CANCER IN CHILDREN WEST PARANA- BRASIL

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Purpose/Objective: INTRODUCTION- The Cancer Hospital of Cascavel - UOPECCAN (West Union Paranaense and Study Against Cancer) was founded in June 1991 in order to meet cancer patients. From January 2000 we started the service the child with cancer and become a reference center for the diagnosis and treatment of cancer Children and Youth. OBJECTIVE - To analyze the distribution of cancer juvenile under 19 treated from January 2007 to December 2012 from the West of Paran‡.
Materials and Methods: MATERIALS AND METHODS-The study used data registered in the medical records and analyzed according to the International Classification of Childhood Cancer
Results: RESULTS: 232 cases were recorded, distributed in the following groups: Group I - Leukemias in 67(28.88%) cases; II Lymphomas and other malignancies reticulo-endothelial 33(14.22%)cases; III Central Nervous System Tumor 39(16.81%) cases; IV Sympathetic Nervous System Tumor 8(3.45%) cases; V Retinoblastoma 2(0.86%)cases; VI Renal tumors 13 cases (5.6%); VII Hepatic tumors 3(1.29%) cases; VIII Malignant bone tumors 13(5.6%) cases; IX Sarcoma soft 23(9.91%) cases; X Germ cell neoplasms 13(5.60%) cases; XI Carcinoma and other epithelial malignancies 10 cases (4.31%); XII Other and unspecified malignant tumors 8 cases (3.45%).There were 74 (31.90%) under 5 years, 60 (18.58%) of 5 to 10 years, 34 (14.66%) of 10 to 14 years and 64 (14.66%) between 14-19 years. Were 129 (55.6%) male and 103 (44.4%) female.
Conclusions: Conclusion- In the west of Paran‡, the distribution of Childhood cancer is similar to data published in the international literature, except for the increase in frequency in group XI, represented by the increase in cases of adrenal carcinoma, collaborating with international reports of increased incidence of this tumor in southern Brazil.

PUB-0130

CENTRAL NERVOUS SYSTEM TUMOR IN CHILDREN IN THE WEST OF PARANA- BRAZIL

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Purpose/Objective: Introduction: The central nervous system tumor (CNS) is the second most common cancer in children < 18 years, surpassed only by leukemia. They account for proximately 25% of all cancers diagnosed in children below 15 years.
Objective: Analyze cases of central nervous system tumors in patients younger than 19 years treated from January 2007 to December 2012 in Western Paran‡, Brazil.
Materials and Methods: The data were collected directly of the Handbook Medical of the Cancer Hospital of Cascavel.
Results: 39 cases were registered, 20 (51.2%) were male and 19 (48.7%) were female with mean age at diagnosis of 7 years (range 10 months to 17 years). The clinical manifestations were vomiting and headache in 20 (51.3%), strabismus 9 (23.1%), weakness in 4 (10.26%), irritability in 4 (10.3%), aggression in 3 (7.7%), change on march in 3 (7.7%), change in vision in 4 (10.3%), and others as weight loss, difficulty speaking, seizures, abdominal pain and regression in motor skills found in 20.5% of cases, more than one complaint was reported by the patient. The most common were medulloblastoma 10 (25.6%), followed by astrocytoma 7 (17.9%) and gliomas 6 (15.4%). The least frequent were: ependymoma 2 (5.1%), choroid plexus carcinoma 2 (5.1%), pineoblastoma 1 (2.6%), primitive neuroectodermal tumor (PNET) 3 (7.7%), glioblastoma 3 (7.7%), rhabdoid tumor 1(2.6%), craniopharyngioma 1(32.6%), and other 3 (7.7%). The time from onset of symptoms until diagnosis was less than 30 days in 16 (41.0%) cases and over 180 days in 17 (43.6%) cases. Of the 39 patients 27 (69.2%) remain alive in monitoring the institution.
Conclusions: The medulloblastoma tumor is the most common central nervous system in children and adolescents in western Parana, Brazil. Although it is the second most common tumor in childhood, there is delay in diagnosis, reducing the chance of cure in these patients.

PUB-0131

ADMINISTRATION OF PEGYLATED ASPARAGINASE RESULTS IN HIGHER ASPARAGINASE ACTIVITY AT THE END OF INDUCTION AS COMPARED TO UNMODIFIED ASPARAGINASE IN ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: The principle of asparaginase therapy is the enzymatic cleavage of the amino acid asparagine into aspartic acid and ammonia, with consequent depletion of asparagine levels. Serum asparaginase activity can be used as a surrogate parameter for asparagine depletion. The aim of the study was to evaluate if administration of pegylated asparaginase (PEG-ASP) or unmodified Escherichia coli asparaginase (ASP) results in higher asparaginase activity at the end of induction in children with ALL.
Materials and Methods: The large majority of children with ALL in the unit receive ASP. Option of PEG-ASP was offered to patients whose parents could purchase the expensive medication. Patients with ALL-B lineage received 3-drug induction with dexamethasone, vincristine and ASP or PEG-ASP, besides intrathecal methotrexate. Patients with ALL-T lineage received Daunorubicin in addition. ASP was administered as 6000 IU/m^2 x 9 doses, IM and PEG-ASP as 1000 IU/m^2, IM x 2 doses. Serum asparaginase activity was measured by medac-Asparaginase-Aktivit*ts-Test (MAAT) (medac-Hamburg-Germany) assay at the end of induction. Study was approved by Institute ethics committee and funded by Dept. of Science and Technology, Chandigarh. Unpaired t-test was utilized to assess significance.
Results: 25 patients received ASP and 9 PEG-ASP. Mean age of patients in the ASP and PEG-ASP group was 6.1 $\pm$ 3.2 and 7.3 $\pm$ 2.3 years, respectively ($p = 0.3$). Number of patient with T-lineage ALL in the ASP and PEG-ASP group were 6 (24%) and 1 (11%), respectively ($p = 0.66$).

Mean serum asparaginase activity at the end of induction in the ASP and PEG-ASP groups was 18.5 $\pm$ 42.7 and 193.7 $\pm$ 273.7 U/L, respectively ($p = 0.0033$). The corresponding median serum asparaginase activity was 1.92 and 65 U/L, respectively. This indirectly

indicates greater asparagine depletion in the PEG-ASP group. Effect on long-term survival cannot be commented from the study. Small sample size is a limitation.
Conclusions: Administration of PEG-ASP resulted in higher asparaginase activity at the end of induction as compared to ASP in children with ALL.

PUB-0132

PILOT PROJECT IN CHR-LIEGE: INVITING SIBLINGS OF CHILDREN WITH CANCER TO A CREATIVE AND EXPRESSIVE WEEK-END WITH PSYCHOLOGISTS AND ONCOLOGIST.

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Purpose/Objective: To evaluate the siblings and their parents interest in a week-end presented as an opportunity
- to feel the consideration of the psycho-medical team for their distress
- to develop friendly relations and possible exchange of views with children in the same situation and concerned adults
- to spend a recreational time in a nature soothing spot were no usual (due to treatments) restrictions are requested

Materials and Methods: -Were invited: 18 siblings (age: 5-11; 7 males/11 females) of 11 patients (age: 2-14; 7 males/4 females; 5 Acute Lymphoblastic leukemia, 1 Acute Myeloblastic leukemia, 2 Medulloblastoma, 1 Wilms tumor, 1 Ewing tumor and 1 Ependymoma)

Exclusion criteria for the siblings: age < 5, diagnosis delay of the sick child < 1 month, sick child out of any treatment
- Schedule: saturday 9 AM to sunday 4 PM
- Transport: assured by the parents who were invited with the sick child for teatime
- Place: an old house with animals in the countryside by a river
- Proposed activities: walks in nature, games, moments to express themselves through artistic creations
- Accompanying persons: 3 psychologists and 1 oncologist concerned by the siblings

Results: None of the 18 siblings refused the invitation

12/18 participated to the w-e (3 were abroad, 2 were moving, and 1 finally prefered another option)

This 12 (age: 5-11; 8 females/4males) were the siblings of 8 /11 patients

All children were fully enthusiastic

They found moments to discuss and express their suffering

The parents supported the project and joined us for teatime on sunday with 7 of the 8 sick children

Conclusions: The siblings week end with the psycho-medical team was highly successful

It opens another way to improve the care of the siblings

Questionnary forms should be developped in the future to evaluate the real psychological impact

Acknowledgements: to the children and their family, the ceramist who welcomed us, the Liege pediatric team in Montreal and Quebec.

PUB-0133

HEALTH STATUS OF SURVIVORS TREATED FOR HODGKIN'S LYMPHOMA IN CHILDHOOD

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Purpose/Objective: The study aimed at estimation of health status of patients in first remission after Hodgkin's Lymphoma (HL) therapy treated in single center.
Materials and Methods: The study group consisted of 93 patients (66 males and 27 females) aged 3.7-41.7 years, 0.1-28.8 years (mean 9,8 years) after completing HL therapy. Body Mass Index (BMI) was calculated at initial diagnosis, and in four subgroups: I - 0.1-5.0, II- 5.1-10.0, III- 10.1- 15.0, IV * over 15.1 years after completing therapy (B-DOPA, MVPP, radiotherapy). The detailed socio-demographic data were obtained on interview. The subgroups were compared with statistical threshold set at p (α)$\leq$0.05. Spearman rank correlation coefficient was calculated to assess correlation of parameters.
Results: Significant increase of BMI after therapy ($p < 0.001$) was observed. This correlated significantly with time from therapy cessation in the whole group ($R_S = 0.4522$; $p < 0.001$), in subgroup IV ($R_S = 0.5130$; $p = 0.01$), with age at diagnosis * in the whole group ($R_S = 0.2027$; $p < 0.01$), in subgroup I ($R_S = 0.5955$; $p < 0.001$), and III ($R_S = 0.4041$; $p = 0.01$), and with number of MVPP cycles (whole group: $R_S = 0.3750$; $p < 0.001$, subgroup I: $R_S = 0.3464$; $p < 0.05$), B-DOPA (whole group: $R_S = 0.2343$; $p < 0.01$, subgroup I: $R_S = 0.3521$; $p < 0.05$), and radiotherapy dose on lymph nodes in cervico-supraclavicular region ($R_S = 0.2178$; $p < 0.01$). Some health-related problems were reported by 39 individuals. A total of 26 patients aged < 19 were during their education period, while 53 persons were professionally active, and 3 were on disability pension. Menstrual disorders were reported by 4 females, infertility by 1 female and 4 males. A total 34 persons were married, and 18 patients (10 females and 8 males) had offsprings (11 daughters, 16 sons). Neurophysical development of offsprings was normal.
Conclusions: Individuals treated for HL in childhood experience decrease in quality of life with time. Health problems, psychological problems and obesity positively correlate with intensity of chemotherapy and age at HL onset.

PUB-0134

THE BODY COMPOSITION OF CHILDHOOD CANCER SURVIVORS

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Purpose/Objective: Nutritional late effects in childhood cancer survivors are important to understand because they can potentially contribute to the development of other later health problems such as cardiovascular disease and diabetes. The aim of this study was to examine the body composition of childhood cancer survivors, a key determinant of nutritional status.
Materials and Methods: This study involved 47 childhood cancer survivors ($n = 31$ leukeamia) who were attending the After Cancer Care Clinic, Queensland Children's Cancer Centre, Australia. This cross-sectional study measured height, weight, body cell mass via measures of total body potassium, and percent fat via measures of air displacement plethysmography. Subjects were compared to 47 age and sex matched healthy controls using independent t-tests.
Results: The population had a mean age of 14.2 ± 3.7 years and a mean time since active treatment of 9.2 ± 2.9 years. There was no significant difference in the height, weight and body mass index between the childhood cancer survivors and healthy controls. However, the study group had significantly higher percent fat (mean $= 25.6 \pm 9.1\%$; $p = 0.001$) and significantly lower body cell mass (mean $= 18.0 \pm 6.5$kg; $p = 0.0004$) than the healthy controls (mean percent fat $= 20.0 \pm 8.5$; mean body cell mass $= 23.1 \pm 7.8$). There was no significant correlation between length of time since active treatment and body composition.
Conclusions: This study demonstrates that childhood cancer survivors have similar body sizes to their healthy peers but that their body composition is altered with increased fat and decreased body cell mass. The implication of this finding is that poor nutritional status may go undetected and untreated when only height and weight are used to define nutritional status. Childhood cancer survivors should undergo comprehensive nutritional screening and would benefit from a program aimed to improve body composition through physical activity and a balanced diet.

PUB-0135

STUDY OF THE REGULATORY REGIONS OF THE WWOX GENE METHYLATION IN LEUKEMIA CELL LINES OF HL-60 AND K562

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Purpose/Objective: To detect and analyze the level of the regulatory regions(promoter and exon 1) of the WW domain-containing oxidoreductase (WWOX) Gene methylation in leukemia cell lines of HL-60 and K562;To investigate the relationship between the regulatory regions of the WWOX Gene methylation and its mRNA expression.
Materials and Methods: HL-60 and K562 were chosen as the object of the study. DNA was extracted from each of the two cell lines and then it was bisulfite-modified using the EZ DNA Methylation -Gold^{TM} Kit. Methylation of the WWOX promoter and exon 1 were WWOX Gene methylation and its mRNA expression.
Results: 1. There were unmethylated bands of the WWOX promoter and exon 1,and methylated bands is negative of HL-60 by MSP; The bisulfite sequencing showed that WWOX promoter have no methylated CpG sites.

2. The positive bands were amplified by the methylated primer and the amplification of unmethylated primer were negative in the WWOX promoter of K562, and all above were detected by MSP; The bisulfite sequencing showed that *WWOX* promoter have 28(82.4%) CpG sites.

3. The mRNA expression of WWOX in K562 (0.53?0.12) is lower than in HL-60 (1.25?0.14), and the difference was significant(*P*
Conclusions: 1.There were different level of methylation in K562 and HL-60. There was no methylated CpG site in the regulatory regions of the WWOX Gene in HL-60,but were methylated CpG site in K562.

2.WWOX mRNA expression was significantly reduced in the region of methylated WWOX promoter of K562 when compared with that in HL-60 with no methylated CpG sites. It points out methylation of WWOX promoter maybe is an important reason led to low expression of mRNA.

PUB-0136

A RETROSPECTIVE INSTITUTIONAL REVIEW OF INFANT NEUROBLASTOMA CASES WHO UNDERWENTPATIENTS HAVE A LESS FAVORABLE PROGNOSIS WITH NEUROBLASTOMAMUTILMODAL THERAPIES

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Purpose/Objective: In general, the prognosis outcome for infants with neuroblastoma in infants is much more favorable than in older children. But we sometimes experienced life life-threatening cases in infants, and they who need to multimodality therapy. However, it revealed that their life prognosis is good.
Materials and Methods: We performed reviewed a retrospectively review of 104 patients diagnosed at younger than 12 months referred toin our institution between 1991 and 2012. Among them, There are 9 cases, included children from between 1-month old to and 7-month old, they were looked like to be difficult to treat at first. Factors evaluated in tests of association and survival analyses were as follows: MYCN gene amplification, urine VMA, HVA, neuron specific enolase(NSE), lactic dehydrogenase(LDH) and ferritin.
Results: INSS stages 1, 2, 3, 4 I-IV were 2, 1, 3 and 3 cases, respectively. Primary tumor location are were 6 are nonadrenal extraadrenal primary and 3 are adrenal primary lesions. Of the 9 patients with fully known biologic features, 8 cases had neuroblastoma and 1 had ganglioneuroblastoma. No case showed MYCN amplification. Median VMA, HVA, NSE, LDH and ferritin are 80.1, 78.8, 51, 659 and 104.8. 4 of 9 patients had chemotherapy and 2 of 4 had neoadjuvant chemotherapy. They all required surgical intervention. Except for 2 cases who had neoajuvant chemotherapy, 6 patients had tumor resection as much as possible and 1 had only biopsy at first. Mean follow-up period is 9 years and 7 months. Overall survival rate is 100%. LDH level is considered effect on the MYCN gene expression.
Conclusions: In this study, in spite of the high LDH level, no case showed MYCN amplification. And life prognosis is good. It is suspected that MYCN amplification strongly correlates with the overall survival ratio.

PUB-0137

HSP27 IN PEDIATRIC AML-M4/M5

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Purpose/Objective: Heat shock protein 27 (Hsp27), a member of heat shock protein (Hsp) family, is important in the regulation of cancer development, progression and chemotherapy resistance. However, the roles of Hsp27 in mediating chemoresistance in leukemia are poorly understood.
Materials and Methods: We evaluated the expression level of Hsp27 in bone marrow samples from 7 children with newly diagnosed acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) and 5 leukemia cell lines. Additionally, we transfected a target-specific siRNA duplex against Hsp27 into leukemia cells, and examined the chemosensitivity,cell apoptosis and autophagy on the response to antitumor drugs.
Results: we showed that Hsp27 was expressed abundantly in acute myelomonocytic leukemia (M4), acute monoblastic leukemia (M5), THP-1 and K562 leukemia cell lines. And its expression was positively correlated with the clinical status in childhood M4/M5 subtypes. We reported that autophagy was involved in Hsp27-mediated resistance to anti-cancer drugs. Knockdown of Hsp27 expression by RNA interference inhibited the anti-cancer drugs-induced autophagy, resulting in increased chemotherapeutic drugs cytotoxicity. Furthermore, we found that the expression level of Hsp27 was regulated by high-mobility group box 1 (HMGB1), as the functional status of HMGB1 was associated with the expression, translocation and release of Hsp27.
Conclusions: Taken together, these results of our study suggest Hsp27 as a novel regulator of autophagy, and the Hsp27-mediated autophagy maybe exploited as a new target for enhancing the efficacy of chemotherapeutic drugs against leukemia and other types of malignancies.

PUB-0138

A NOVEL OPPORTUNITY TO MEET THE PSYCHOSOCIAL NEEDS OF CHILDREN AND FAMILIES WITH CANCER: CHILD LIFE SERVICES IN THE SCHOOL SETTING

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Purpose/Objective: The role of child life specialists in the psychosocial care of children and families undergoing treatment for cancer is well-established. However, many children and adolescents live significant distances from their pediatric oncology unit and care is increasingly provided on an outpatient basis. When children return to school while receiving cancer therapy, they are particularly vulnerable and in need of psychosocial support.
Materials and Methods: We describe the initiation of child life services at a rural American elementary school and the expansion to seven other schools, focusing on key components of services for children with cancer and challenges to implementation.
Results: The program at Sauquoit Elementary School (Sauquoit, New York; established 2005) was the first school-based child life program in the world. Services are now available to children (5 to 12 years) attending eight public elementary schools in rural New York, who are coping with cancer, other serious illnesses, and grief/loss, including those who have parents or siblings with cancer. The program is supported by the CORE Safe Schools/Healthy Students grant from the U.S. government and has been well-received by parents and children. Services provided by the school-based child life specialist include one-on-one support through activities and play, procedural preparation, education of teachers and students regarding the child's diagnosis and treatment, and coordination with the child's healthcare providers. Challenges have included obtaining funding for expansion of services and continuation after the term of the grant and working with classroom teachers to minimize disruption of the school day.
Conclusions: The school setting presents a novel opportunity to enhance support of children with cancer and their siblings. School-based child life programs have the potential to improve school attendance and performance during cancer therapy. Further research is warranted to evaluate the impact of such programs on long-term academic and psychosocial outcomes for childhood cancer survivors.

PUB-0139

THE SIGNIFICANCE OF DETECTING S100A8 AND S100A9 EXPRESSION IN CHILDHOOD ACUTE LEUKEMIAS.

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Purpose/Objective: S100A8 and S100A9 are two members of the S100 calcium-binding protien family, preferentially form functional heterodimers of S100A8/A9, have been increasingly recognized as new candidates with important roles in various tumors. The purpose of this study was to investigate *S100A8* and *S100A9* expression and their clinical implications in childhood acute leukemia.
Materials and Methods: The study included 102 pediatric patients of acute myeloid leukemia (AML) (AML-M3 were excluded) (de novo = 30, complete remission [CR] = 20) and acute lymphoid leukemia (ALL) (de novo = 32, CR = 20) at different stages and 20 controls without leukemia. *S100A8* and *S100A9* expression levels of bone marrow mononuclear cells were analyzed with real-time reverse transcription PCR (RT-PCR).
Results: Newly diagnosed pediatric patients of AML and ALL had significantly lower transcript levels of *S100A8* and *S100A9*, comparing with patients in CR ($P_{a8} = 0.005$ and $P_{a9} = 0.004$ for AML, $P_{a8\ and\ a9} < 0.001$ for ALL) and control group ($P_{a8\ and\ a9} < 0.001$ for AML, $P_{a8} = 0.004$ and $P_{a9} = 0.005$ for ALL), moreover *S100A8* and *S100A9* expression in de novo AML were higher than in ALL ($P_{a8} = 0.0012$ and $P_{a9} = 0.05$). In the small cohort of AML, high *S100A9* expression level predicted relatively unfavorable early treatment outcome ($P_{a9} = 0.025$), although it was less marked between S100A8 expression and prognosis ($P_{a8} = 0.06$). However, considering the responses of corticosteroid pretreatment and induction chemotherapy, *S100A8* and *S100A9* expression levels had no efficiency to predict early treatment outcome in ALL patients.
Conclusions: This study confirmed S100A8 and S100A9 performed synergic expression and functions in pediatric acute leukemia. *S100A8* and *S100A9* expression levels showed positive correlation with the clinical status in childhood acute leukemia, moreover in de novo AML, they can potentially be markers for predicting early therapeutic efficacy.

PUB-0140

TREATMENT OF LUNG METASTASIS IN HEPATOBLASTOMA INCLUDING HIGH DOSE CHEMOTHERAPY FOLLOWED BY HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Purpose/Objective: Although the treatment of lung metastases in hepatoblastoma (HB) has been usually consisted of aggressive surgery and conventional chemotherapy, they do not always result in cure. In our institute, HB patients with lung metastases have been treated by high dose chemotherapy rescued with stem cell transplantation (HD). In order to evaluate the effectiveness of HD, we retrospectively reviewed our institutional HB patients with lung metastases.

Materials and Methods: Twenty seven HB patients were diagnosed in our institute between 1989 and 2012. Of these, seven patients with lung metastases underwent multimodal treatment including HD. Five had lung metastases at diagnosis and two had lung metastases after the initial treatment. Medical records of these seven patients were reviewed retrospectively.
Results: For five patients with lung metastases at diagnosis, all underwent HD with autologous stem cell transplantation. Although two patients resulted in complete remission, one died of the secondary malignancy. Another patient who did not require lung surgery is alive without disease one year after the treatment. Of the other three of five patients, two are still under the initial treatment including HD, but they have not reached to be complete remission yet. One died of disease without being complete remission. Two patients with lung metastases after the initial treatment were rescued by multimodal treatment consisted of HD followed by lung resection. They have been in complete remission for 8 years, 10 months after the second line treatment respectively. One of two patients was rescued by multimodal treatment consisted of unrelated allogenic stem cell transplantation followed by liver and lung surgeries.
Conclusions: Four of seven HB patients with lung metastases had been rescued by multimodal treatment including HD, although one died of the second malignancy. HD could be a treatment of choice for lung metastases in HB.

PUB-0141

CHILDHOOD CANCER IN MOROCCO

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Purpose/Objective: The aim of this study is to describe the epidemiological characteristics of childhood cancer in Morocco.
Materials and Methods: This is a retrospective analysis of childhood cancer cases, diagnosed and treated at Al Azhar Oncology Center in Rabat between 1994 and 2004.
Results: There were 130 children under the age of 15 diagnosed with cancer at Al Azhar Oncology Center, which was 2.9% of all new cases of cancer reported during the study period. More than half were males with a male-female ratio of 1.45. The average age at diagnosis was 8.2 $\pm$ 3.8 years. Nearly a quarter of these cases were diagnosed during the first five years of life, while the highest rates for males were noted between 5 and 9 years and for females between 10 and 14 years of age, though this pattern varies greatly by tumor type. Leukemia was the most common childhood cancer (34.6%), followed by brain tumors (27.6%). Among all detected cases, 6.9% were diagnosed with metastatic disease and 9.2% died during the study period.
Conclusions: Although rare, cancer in children has a substantial impact on public health in Morocco. A national cancer registry will assist in better planning, resource allocation and management including psychosocial support to improve the quality of life of childhood cancer survivors and their families.

PUB-0142

IQ SCORE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA RECEIVED CNS PROPHYLAXIS: WITH OR WITHOUT CRANIAL RADIATION

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Purpose/Objective: Introduction : Acute lymphoblastic leukemia (ALL) is the most common malignancy diagnosed in children. Children with ALL received cranial prophylaxis with or without cranial irradiation according to risk category. In review literature, cranial radiation therapy CRT) is associated with neurocognitive impairment in childhood ALL survivors

Objective: to evaluate the pattern of Intelligent Quotient (IQ), subsets and index score in Children with acute lymphoblastic leukemia received CNS prophylaxis with or without cranial irradiation.
Materials and Methods: Patients and Methods: ALL children with cure were divided into two groups: group 1 without cranial irradiation (N = 33) and group 2 with cranial irradiation (N = 13). Wechsler Intelligence Scale for Children (WISC) was used to assess IQ which was performed at the end of chemotherapy.
Results: Results: Group 1 had average full IQ score of 95 (verbal score 97, performance score 93 with SD 12) with impairment in certain aspect of symbol search subtest and free from distraction index score. Group 2 had average full IQ score of 86(verbal score 88, performance score 85 with SD 10) with impairment in certain aspect of digit span subtest and processing speed index score. There was significant difference of IQ score between the two groups (independent-sample T-test, p = 0.026)
Conclusions: Conclusion: Children with ALL receiving CNS prophylaxis with cranial irradiation had significantly lower IQ score. In subtest and index score analysis, Children with ALL receiving CNS prophylaxis without cranial irradiation had difficulties in symbol search and free from distraction score whereas Children with ALL receiving cranial irradiation had problems with digit span and processing speed. The retrospective type of study and small number of patients with cranial irradiation is limitation of this study.

PUB-0143

TUMOR IN NEONATE

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Purpose/Objective: Introduction: Solid tumor is uncommon presentation in the neonate. Common solid tumors in neonate are congenital fibrosarcoma and teratoma, however, there was no report of primitive neuroectodermal tumor and malignant nerve sheath tumor in neonates.
Materials and Methods: Method: Case report study
Results: Result; We report two normal full term neonates presenting with huge mass at birth; Case 1 had right axilla 43«34 cms mass, and case 2 had right foot 10«10cms mass. Both cases had normal tumor markers including alpha fetoprotein, b-HCG and LDH. Magnetic Resonance Imaging of mass demonstrated huge malignant highly vascularized mesenchymal soft tissue sarcoma involving at right axillary region, right foot on case 1 and 2 respectively. Both cases underwent an incisional biopsy which reported as primitive neuroectodermal tumor and malignant nerve sheath tumor, respectively. Case 1 received vincristine, doxorubicin and cyclophosphamide alternated to ifosfamide and etoposide in total of 1 $\frac{1}{2}$ courses with partial response then a total tumor removal was performed with serious complication of massive hemorrhage. Tumor was progressively enlarged approximately 3 cms after surgery then the chemotherapy was continued in total of 3 courses with good response. Case 2 received one course of VAC regimen with no response and tumor was progressively enlarged, so a below knee amputation was done with uneventful complication. Both cases still have no recurrent tumor.
Conclusions: Conclusion; Solid tumors in the neonate are uncommon. The mainstay of treatment is complete tumor removal. Chemotherapy, another optional therapy, is to be considered in light of neoadjuvant therapy for tumor reduction or adjuvant therapy for postoperative residual tumor.

PUB-0144

NEONATAL TUMORS: EXPERIENCE ACCUMULATED IN A SPANISH HOSPITAL

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Purpose/Objective: To review all malignant or potentially malignant tumors diagnosed in newborns ($\leq$ 28 days of life) in a general and universitary hospital from 1980 to 2012. To evaluate their association with congenital anomalies, prenatal diagnosis and the prognosis.
Materials and Methods: The medical records of patients with tumors diagnosed (excluded hemangiomas) during the neonatal period in the previous thirt-two years in our hospital were retrospectively reviewed.
Results: The incidence of neonatal tumors during the study period was estimated to be 265 per million live births in our hospital, with a prevalence of 5.8% of the total of diagnosed tumors under 15 years of age (19 cases). The average age at the diagnosis was 6 days $\pm$ 8.7 with prenatal diagnosis 26.3% (50% in the latest 10 years). Most frecuent in female (male/female = 1/1.1). The most frequent histologic diagnoses were neuroblastoma (31.6%) and teratoma/germ cell tumor (TCG) (21%). All neuroblastomas were low risk. TCG were located in sacrococcigeal region (2) and cervical area (2). 21% were associated a congenital abnormality (two Down syndromes, one giant congenital melanocytic nevi and one vesiculoureteral reflux grade V). The treatment was: 57.9% surgery alone (two cervical teratomas needed a second surgery); 26.4% surgery plus quimiotherapy and 15.7% no treatment was received (two transient myeloproliferative disorder and an epedymoma was diagnosed post-mortem). The sequelae for the treatments were observed in 21.1%. The disease-free survival was 84.2%, with a mediam follow-up ranged of 16.5 years.
Conclusions: 1) The most frequently diagnosed tumors in the neonatal period were solid tumors, mainly neuroblastomas and teratomas/germ cell tumors.
2) Most of the neonatal tumors responded well to the oncologic therapy, mainly surgery.
3) The disease-free survival was high, except for brain tumors.
4) A quarter had a prenatal diagnosis and/or were associated with syndromes or birth defects.

PUB-0145

MODIFIED HEAD START PROTOCOL IN YOUNG CHILDREN WITH CNS TUMORS

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Purpose/Objective: There is no standard approach to the treatment of young children with malignant brain tumors. The Head Start (HS) protocol successfully used myeloablative

chemotherapy; however, toxicity of induction chemotherapy was high with up to 10% toxic mortality. To reduce toxicity we modified HSII regimen A2.
Materials and Methods: High-dose methotrexate (HDMTX) was given at reduced dose (270 mg/kg) and prior to cyclophosphamide/cisplatin to decrease mucositis. The dose of cyclophosphamide was reduced as well. Induction chemotherapy consisted of 5 cycles with HDMTX on day 1; vincristine 0.05 mg/kg, days 1, 8, 15; cyclophosphamide 55 mg/kg, days 4 (if MTX level < 0.1 mcmol/L) and 5; etoposide 2.5 mg/kg, days 4, 5, 6; and cisplatin 3.5 mg/kg on day 6. Consolidation myeloablative chemotherapy was the same as in HS II.
Results: Since 2011 we treated a total of 5 patients under 5 years old, including 3 with choroid plexus carcinoma (CPC), one with brainstem PNET, and one with medulloblastoma (MB). Three patients had leptomeningeal spread. The induction chemotherapy resulted in grade 4 hematological toxicity, but no severe infections. We did not observe any significant toxicity related to HDMTX including severe mucositis. Three evaluable patients had partial responses after 2 cycles. All 5 patients are alive. The patient with brainstem PNET had small residual tumors at the primary site and spinal cord and received CSI after ABMT. She is alive with NED at 24 months post-transplant; both patients with CPC who completed treatment are alive with NED at 6 and 14 months. The patient with metastatic MB was in CR after ABMT but developed leptomeningeal recurrence and received ifosfamide-topotecan-carboplatin followed by salvage CSI.
Conclusions: Modified HS protocol proved to be feasible and effective approach in young children with high risk CNS tumors.

PUB-0146

A 13-YEAR REVIEW OF HEPATOBLASTOMA IN A SINGLE INSTITUTE

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Purpose/Objective: To review the management and outcome of all patients with hepatoblastoma treated in a tertiary center in Hong Kong.
Materials and Methods: A retrospective study on hepatoblastoma was carried out for the period between November 1999 and November 2012. Eighteen patients were studied.
Results: The mean age of the 18 children (11 males, 7 females) at diagnosis was 14.0 months, ranging from 0 to 56 months. Majority presented as abdominal distension/ mass (72.2%, n = 13), including 3 (16.7%) with evidence of bleeding. Pre-treatment investigations confirmed 5 PRETEXT II (all except one have either metastasis/ portal vein/ hepatic veins involvement), 9 PRETEXT III and 4 PRETEXT IV diseases.

One patient with PRETEXT II had left lateral segmentectomy done as a primary resection. All of the remaining 17 patients received neoadjuvant chemotherapy (94.4%, n = 17). The three children who initially presented with bleeding further deteriorated during the chemotherapy period and all died without surgery. One patient with main portal vein thrombosis developed liver cirrhosis and signs of portal hypertension required liver transplantation after chemotherapy. Eight patients underwent surgical resection of 2 segments and 4 patients had trisegmentectomy performed.

The mean follow up was 54.57 months (ranged from 2 to 135 months). No recurrence was noted. One child with multiple pulmonary and cerebral metastases showed no response to chemotherapy died at 11th month after right hepatectomy. The overall mortality was 22.2% (n = 4).
Conclusions: With neoadjuvant chemotherapy, current advances in surgical skills and excellent perioperative support, the disease-free survival of neuroblastoma was high even in relatively advanced disease. Despite this, extremely high mortality was expected in patients with tumour rupture or bleeding at presentation.

PUB-0147

ARTHERECTOMY AND PLASTY, SURGICAL TREATMENT OF DIFFUSED MESENTERY LYMPHANGIOMATOSIS IN CHILDREN

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Purpose/Objective: Diffused mesentery lymphangiomatosis is widespread lymphangial malformation of the mesentery. There are nodular mass of different size along the mesentery. The intestinal function is usually affected and leads to protein malabsorption. However, it is difficult for surgery to deal with the widespread disease of the mesentery. Occasionally, we did artherectomy and plasty of mesentery lymphangiomatosis and the outcome revealed good. Hereby, the primary experience is introduced.
Materials and Methods: 5 patients were admmited to this study,2 of them were treated with watch and wait,The other 3 patients accepted surgical treatment.
Results: 2 patients treated with watch and wait for 3 and 5years respectively had obvious protein and calorie malnutrition,In the 3 cases of surgical operation, the postoperative recovery were uneventful. There was no effusion and chyle in abdomen after surgery. In one patient, the symptome of abdominal pain was released 6months after surgery. In the other patient, abdominal chyle was found in inguinal hernia surgery 1 year later and in appendectomy 2 years later. The follow-up of 3 years with ultrasound revealed no relapse of mesentery lymphangioma mass and no malnutrition.
Conclusions: artherectomy and plasty procedure was safe and feasible for diffused mesentery lymphangiomatosis. The effectiveness should be evaluated with long term follow-up and more cases experience.

PUB-0148

PROTON BEAM THERAPY FOR PEDIATRIC PATIENTS WITH PEDIATRIC EPENDYMOMA.

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Purpose/Objective: To evaluate efficacy of proton beam therapy (PBT) for pediatric patients with pediatric ependymoma.
Materials and Methods: From 2009 to 2012, proton beam therapy was conducted to in 6 patients with ependymoma. The patients group consisted of 3 males and 3 females, and the age ranged from 2 to 6 (median: 5) years old. Three patients had recurrent tumor during observation after surgery and chemotherapy. According to WHO classification, the tumor was classified grade 2 and grade 3 for 2 and 4 patients, respectively. The tumor located supratentorial and infratentorial in 3 and 3 patients, respectively. All patients conducted surgery and chemotherapy for the tumor, and subtotal resection and gross total resection was conducted for 3 and 3 patients, respectively. The given doses were ranged 50.4 to 61.2 GyE (median 56.7 GyE). Only one patient received whole ventricle irradiation.
Results: All patients complete planned irradiation. The median follow up period was 2 to 34 months (median: 16.2 months) from start of PBT, and all patients were alive. Local recurrence in the treatment field was observed in one patient 4 months after the PBT with 50.4 GyE. This patient received secondary PBT, but spinal dissemination was appeared. As for toxicities, Alopecia and mild dermatitis were observed in all patients, but none of them experienced severe toxicities. One patient experienced one-time seizure after PBT, and alopecia was prolonged in one patient for 31 months, however, all patients have no trouble with daily life.
Conclusions: PBT may be safe and better alternative to photon radiotherapy for children with ependimoma.

PUB-0149

MANAGEMENT AND TREATMENT OF CHILDHOOD WILMS TUMOR DURING THREE YEARS OF FOLLOW-UP AT A HOSPITAL BASED STUDY

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Purpose/Objective: Wilms tumor is a curable childhood malignancy that can develop in healthy child too. Since 1980, the five-year survival rate of this tumor has been above 90%. The purpose of this topic is to evaluate the Pediatric Cancer Treatment epidemiology, treatment and follow-up of children with Wilms tumor who referred to MAHAK's and Research Center.
Materials and Methods: This cohort study complied children less than 15 years old with favorable Wilms tumor pathology report, who referred to MAHAK's Pediatric Cancer Treatment and Research Center since Jan 2007 to Jan 2010. The standard checklist contained additional information filled for each individual.
Results: The enrolled patients were 33 cases (18 female, 54.5%) with the mean age of 5 $\pm$ 4.4 years old. at the time of diagnosis, the stages of patients were as III (11, 31.3%), IV (8, 25%), I (7, 21.9%), II (6, 18.8%), V (1, 4%) respectively. Tumor involvement were 18 (54.5%) in right and 15 (45.5%) in left kidney. The most common symptoms were as 22 (66.7%) patients with mass of abdomen and 3 (9.1%) with hematuria. All of the patients had nephrectomy surgery at the early diagnosis. Twelve cases (36.4%) had relapsed during or after their treatment that the mean of relapse time was 21 $\pm$ 36.5 months. Out of enrolled patients, there were 24 (72.7%) off treatment, six (18.2%) dead and 3 (9.1%) lost to follow-up. The five years survival was the same as three years survival rate in this study (94% $\pm$ 0.04).
Conclusions: Literature and reviews determine that most children with Wilms tumor are cured and very few of them will have long-term renal problems. Multimodality therapy with surgery and radiotherapy can result in excellent tumor control rate. For achieving the highest survival rate all children with Wilms tumor should be monitor in long-term surveillance programs for the early detection and management of therapy related toxicities.

PUB-0150

ACUTE MYELOID LEUKEMIA: A HOSPITAL BASED RETROSPECTIVE STUDY AT KANTI CHILDRENS' HOSPITAL, KATHMANDU, NEPAL

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Purpose/Objective: To study the clinical features and survival of children with AML
Materials and Methods: This is a retrospective study conducted from March 1998 to March 2012. The data was collected from the hospital records. Bone marrow aspiration showing ≥20% blast cells with morphological and cytochemical features consistent with myeloid series was the criteria for diagnosis of AML.
Results: A total of 624 childhood cancers were reported in this hospital during the study period. Amongst this, the incidence of AML was 12.01% (75) with the most prevalent subtype being M2 (40%) followed by M1 (26.7%). Age group ranged from 4 months to 14 years, with mean age 9.3 years. There was a slight male predominance with M:F ratio of 1.08:1.The most common presenting features were pallor (89.2%) followed by fever (85.0%) splenomegaly (80.1%), hepatomegaly (69.2%), ecchymosis (30.0%), lymphadenopathy (20.0%) gum swelling (10.0%) and facial palsy (2.66%). Cytarabine, Daunorubicin and Etoposide based chemotherapy was given.Out of 75 cases, 30(40.0%) refused treatment, 16 (21.3%) had relapse, 15 (20.0%) died during treatment, 8(10.7%) went into 2 years remission and 6 (8.0%) went into more than ten years remission.
Conclusions: Despite limited resources and bone marrow transplant facilities, we have 10 years survival rate of 8.0%. Efforts should be made to improve survival rate by addressing cytogenetics and molecular studies, bone marrow transplantation, reasons for treatment refusal, relapse and mortality

PUB-0151

A NOVEL SYNTHETIC COMPOUND BISMUTH ZINC CITRATE COULD POTENTIALLY REDUCE CISPLATIN INDUCED TOXICITY WITHOUT COMPROMISING THE ANTICANCER EFFECT

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Purpose/Objective: Background: Cisplatin is a common chemotherapy drug with known neural and nephro-toxicity. We developed an orally administrated compound bismuth zinc citrate (BiZn) which may potentially protect the normal cells from cisplatin induced cytotoxicity.
Materials and Methods: Methods: Cytotoxic effect of BiZn +/− cisplatin on a panel of normal [human mesenchymal stromal cells, human liver cells (MIHA), rat neural stem cells (C17.2), human non-malignant kidney cells (HK-2)] and neuroblastoma cell lines were tested by XTT assay. Orthotopic neuroblastoma (luciferase transduced SKN-LP) xenograft mouse model was adopted. The treatment groups were PBS-untreated (n = 6), BiZn-treated (n = 6), cisplatin-treated (n = 6) and BiZn + cisplatin-treated (n = 6). BiZn (0.14 mmol/Kg) was administered orally 24 hours before and just prior to cisplatin administration and then every two days thereafter. Bioluminescence imaging was performed on all of the mice weekly after tumor implantation. For evaluation of BiZn protective effect on cisplatin induced toxicity, normal mice were used.
Results: Results: BiZn did not have anti-cancer effect on its own and also did not affect the therapeutic effect of cisplatin, both *in-vitro* and *in-vivo*. The protective effects of BiZn on cisplatin treated neuroblastoma cells were not significant in the *in-vitro* setting as compared to the *in-vivo* setting, suggesting BiZn acted indirectly *in-vivo*. Significant tumor shrinkage but no overt toxicity were noted in cisplatin +/− BiZn treated mice and BiZn could significantly reduced the levels of blood urea nitrogen in cisplatin treated mice. Under the lethal dosage of cisplatin, pre-treatment with BiZn significantly increased the survival rate of the mice. We postulated that the mechanism of protection may be related to BiZn induced soluble factors released by the liver and kidney.
Conclusions: Conclusions: Pre-treatment of BiZn can decrease the cisplatin induced cytotoxicity without affecting the antitumor activity of cisplatin *in-vivo*. Since BiZn can be administered orally with good absorption, it can readily applicable as a drug to minimize the adverse effects of cisplatin.

PUB-0152

THE INFLUENCE OF ZEBULARINE ON THE METHYLATION OF WWOX GENE AND THE MRNA EXPRESSION IN LEUKEMIA CELL LINES OF HL-60 AND K562

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Purpose/Objective: To investigate the change of methylation and WWOX mRNA expression after using different concentrations of Zebularine (Zeb) to treat the leukemia cell lines of HL-60 and K562; To analyze the meaning of Zeb.
Materials and Methods: Treated HL-60 and K562 with Zeb, and 5-Aza-CdR as control group. Methylation of the WWOX promoter and exon 1 were determined by MSP and the promoter was determined by bisulfite sequencing; the WWOX mRNA expression and the protein was respectively determined by FQRT-PCR and Westen-Blot. Then analyze the level of methylation both two groups
Results: 1.There were methylated bands, and the unmethylated bands were negative in the region of WWOX promoter, and there were unmethylated bands, while the methylated bands were negative of the exon 1 of K562, and all were detected by MSP before treated; There were unmethylated bands, however the methylated bands were negative of the WWOX promoter and exon 1 of K562 by MSP after treated; There was only one(2.9%) methylated CpG site in the WWOX promoter of K562 after treated, and when compared with the control group, the difference is significant($P < 0.01$).

2. The *WWOX* mRNA and protein expression in K562 was increased after treated, and the difference is significant ($P < 0.05$). There is a significant differences among the different experimental groups treated with different concentration of Zeb($P < 0.05$); However, there is no significant differences among the different experimental groups treated with different concentration of 5-Aza-CdR ($P > 0.05$).

3. There is no significant differences between drug(Zeb and 5-Aza-CdR) treated and untreated group in WWOX mRNA and protein expression in HL-60.

Conclusions: 1. Zeb can play a part in the effect of indemethylation in upregulating the WWOX mRNA and protein expression in K562, nor does HL-60.

2. 5-Aza-CdR can upregulate the WWOX mRNA and protein expression in K562.

PUB-0153

THE FEASIBILITY OF HIGH-DOSE TOPOTECAN, MELPHALAN AND CYCLOPHOSPHAMIDE IN CHILDREN WITH ADVANCED SOLID TUMORS: A SINGLE-INSTITUTION EXPERIENCE

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Purpose/Objective: High-dose chemotherapy (HDCT) with autologous peripheral blood stem cell transplant (PBSCT) has improved the survival ratio in children with advanced solid tumors, however, the preparative regimen is still in development. The aim of this study was to evaluate the feasibility and toxicity of HDCT regimen including topotecan in children with advanced solid tumors.
Materials and Methods: Between January 2011 and January 2013, a total of 17 patients aged 0 to 17 years (median; 7 years) were enrolled. The diagnoses included medulloblastoma/PNET (n = 9), Ewing sarcoma (n = 2), rhabdomyosarcoma (n = 2), sarcoma NOS (n = 2), retinoblastoma (n = 1), and pineoblastoma (n = 1). Seven patients were in complete remission, 8 in partial response, 1 in stable disease, and 1 in progressive disease at HDCT. Patients were treated with topotecan 3.5 mg/m^2/d on days -7 to -3, melphalan 70 mg/m^2/d on days -4 and -3, and cyclophosphamide 1000 mg/m^2/d on days -7 to -5, followed by PBSCT on day 0. The adverse events of the regimen were evaluated in accordance with Common Terminology Criteria For Adverse Events v4.0 (CTCAE), and compared with the former regimen consisted of thiotepa and melpharan in a single institution.
Results: All patients achieved primary engraftment. The median times to neutrophil and platelet recovery were 10 days (8-13) and 18 days (14-74). There was no treatment-related mortality. Most common non-hematological adverse events were grade 3 mucositis (n = 7), grade 3 diarrhea (n = 6), and grade 3 febrile neutropenia (n = 10). No other grade 3 or greater non-hematological toxicity was observed. Twelve of 17 have remained alive at a median of 360 days.
Conclusions: These findings suggest that the HDCT regimen consisted of topotecan, melphalan and cyclophosphamide might be tolerable and be less toxic than those with the former regimens in children. The efficacy of this regimen should be confirmed on a larger cohort of patients.

PUB-0154

THE STUDY OF A REAL-TIME PCR ASSAY IN DIAGNOSIS OF INVASIVE FUNGAL INFECTION AMONG PEDIATRIC PATIENTS WITH HEMATOLOGICAL AND NEOPLASTIC DISORDER

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Purpose/Objective: Purpose: We established a real-time PCR(RT-PCR) assay for the detection and strain identification of Candida species and Cryptococcus neoformans rapidly,accurately,specificity,and quantify the content of the fungus. these fungus are clinical common species including Candida albicans, Candida glabrata, Candida tropicalis, Candida parapsilosis and Cryptococcus neoformans. the Result will give the doctors a conduction in the therapy.
Materials and Methods: Methods: GenBank(NCBI) was searched for sequences of the genes of those four Candidas and Cryptococcus neoformans and find the specifical regions of

each species. specific Primers and probes for those fungus were designed using the Primer premier 5.0. Isolate the DNA from fungal strains to select the specifical primers and probes and the best condition of the PCR reaction. And test 62 clinical strains of all the five fungal specises.
Results: Results: Each of the primer and probe in the assay was specific,the sensitivity can achieve 10CFU with good stability, repeatability. The result of the tests of clinical strains was the same with the detection of Microbiology laboratory.
Conclusions: Conclusions: The established real-time PCR assay is a useful tool for the rapid, accurate identification of Candida species and Cryptococcus neoformans and can give each a quantification. This technology will be variously used in the diagnosis of invasive fungal infection.

PUB-0155

RELATIONSHIP BETWEEN SERUM ALPHA-FETOPROTEIN LEVEL AND CLINICAL FEATURES OF CHILDREN WITH HEPATOBLASTOMA

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Purpose/Objective: A retrospective study of 74 cases of hepatoblastoma to analyze the relationship between its clinical features and serum alpha-fetoprotein level.
Materials and Methods: We summarized the clinical stages, treatment, prognosis,AFP value information, and made statistical analysis.
Results: In this patients group, Stage I and II patients, average AFP 36333ng/ml.stage III and IV patients, average AFP78346ng/ml. Patients who received preoperative chemotherapy were measured of alpha-fetoprotein values ??before and after chemotherapy respectively. The results show that in 49 cases AFP value decreased, among which, 44 cases show an AFP decline greater than 50% after chemotherapy, and 20 cases show an AFP decline greater than 90%.. 15 patient cases were measured serum AFP levels on the first postoperative day, among which 10 cases were reported AFP declines by over 50% comparing with preoperative values; 3 cases were reported AFP declines by less than 50%; 2 cases were reported AFP value increase. The postoperative follow-up. Of 74 patients in this group a total of 52 cases received postoperative follow-up, among which:45 cases tumor-free survival, with overall 3 year-survival rate of 86.5%;7 cases of recurrence. Among recurrence cases, 4 cases were reported of alpha-fetoprotein level decrease back to normal 1 month after the first surgery, significantly lower than patients of tumor-free survival group; 1 case returned to normal 3 months after the first surgery. accounting for 14%, similar to tumor-free survival group; 2 cases never returned to normal level; 1 case maintained normal level ??after recurrence.
Conclusions: 1.For Stage III and IV cases, Alpha-fetoprotein value was significantly higher than the Stage I and II cases;
2. Preoperative chemotherapy can significantly decrease the AFP values, and it can be used to estumate the effect of chemotherapy
3. The speed of decline of Hepatoblastoma patients' postoperative alpha-fetoprotein can be used as an important indicator of prognosis, calling for attention in follow-up process.

PUB-0156

DISTINCT FEATURES OF PLEUROPULMONARY BLASTOMA: AN AGGRESSIVE INTRA THORACIC NEOPLASM OF CHILDHOOD.

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Purpose/Objective: Pleuropulmonary blastoma (PPB) is a rare and aggressive malignant tumor that affects children and adults. This neoplasm histologically characterized by primitive blastema and a malignant mesenchymal stroma that often demonstrates multidirectional differentiation. Literature showed poor prognosis despite the introduction of multimodal therapy, our aim is to review our King Hussein Cancer Center (KHCC) experience.
Materials and Methods: We reviewed medical records of PPB patients seen at KHCC during the period from January 2003 to December 2011. Age, Clinical data, surgical notes, pathologic findings, and summaries of chemotherapy and current patient status were obtained.
Results: The series included 5 patients (2 males and 3 females) with a median age of 36 months (range 22 to 65 m), Respiratory distress was the most common clinical symptom. The tumor involving the right side in 3 patients, and 2 in the left. Tumor is solid in one patient and solid-cystic in 4 patients. In 2 patients (40%) it's associated with cystic nephroma of the same side kidney. All patients treated with neoadjuvant multiagents chemotherapy followed by surgery, radiotherapy was not used in any patient. Four patients (80%) are alive and healthy after median follow up of 37 months (range 6 to 56 m), one patient (20%) died after disease progression.
Conclusions: PPB is an aggressive neoplasm of early childhood, but with appropriate neoadjuvant chemotherapy and surgery good outcome can be achieved. cystic nephroma is a well known assotiation and here its found in 40% of cases.

PUB-0157

10 YEARS FOLLOW-UP ON ACUTE LEUKEMIA IN INFANTS AND YOUNGER CHILDREN IN CHINA: REPORT FROM SINGLE CENTER

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Purpose/Objective: To evaluate the long-term prognosis of acute leukemia (AL) in infants (< 1-year-old) and younger children (1-2 years old) that underwent different chemotherapy regimens in a Chinese population.
Materials and Methods: Totally 28 young children (< 2 years) diagnosed as AL that were admitted from Jan, 2000 to Dec, 2009. Patients that were admitted before 2003 were treated with China-98 ALL or AML regimens. ALL patients admitted from Jul, 2003 to Mar, 2008 underwent BFM 2002 protocol and CCLG-ALL 2008 protocol started after Mar, 2008. AML patients treated with MRC 10 chemotherapy regimen from Jul, 2003 to Jul, 2005 and after Jul, 2005, AML patients underwent CHFU-AML 2005 protocol (based on BFM 98 and MRC 10).
Results: 5-year events free survival (EFS) rate of ALL cases was 64.0% while that of AML CASES was 40.0%. The relapse rate of ALL and AML cases were 22.2% and 33.3% respectively. Compared with our previous report, the younger ALL cases in this study had worse EFS and higher relapse rates ($P < 0.01$). The EFS rate of infant AL cases was worse than that of AL cases of 1-2-year-old but no significant difference showed.
Conclusions: More improved chemotherapy regimen should be well designed to improve the prognosis of ALL in such age group. Support treatment and BMT remains to be reinforced in developing countries.

PUB-0158

CLINICAL SUMMARY OF THE HIGH INTENSITY FOCUSED ULTRASOUND LEADING COMPREHENSIVE TREATMENT OF 11 CASES WITH HEPATOBLASTOMA

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Purpose/Objective: To study a comprehensive treatment protocol based on high intensity focused ultrasound (HIFU) ablation of children hepatoblastoma with stage III and IV.
Materials and Methods: There were 4 patients with stage III and 7 patients with stage IV disease. Comprehensive therapy protocol include preoperative 3-6 sessions chemotherapy, transarterial chemoembolization (TACE), HIFU and postoperative 6-8 sessions chemotherapy. After whole treatment the longest follow-up for 24 months.
Results: After preoperative Chemotherapy the metastasis tumor completely disappeared and the primary tumour had diminished obviously from 16cm × 6.5cm to 6.2cm × 3.3cm. Except 2 patients with portal vein tumor embolus 9 patients were treated by TACE result in tumor boundary clear and few blood flow. After HIFU all of them entire ablation were 7 cases and part ablation were 4 cases (include 2 patients with portal vein tumour embolus, 1 central type patient and 1 patient with mutiple hepatoblastoma). Total energy of HIFU was from 247250J to 944340J. After HIFU the AFP of 2 patients decreased to normal in 1 month, 5 patients in 2 months, 3 patients of part of the ablation beyond 2 months. After HIFU liver functions of all patients recovered normal in 1or 2 week. There have been 3 patients suffering costal malformation.
Conclusions: Our preliminary experience suggests that HIFU based comprehensive therapy is a non-invasive solution of Local treatment for children with advanced hepatoblastoma. However, further study is needed for investigating the long-term survival rate and side-effect.

PUB-0159

IRF4: COMMON REGULATORY ROLE IN CHILDHOOD LEUKEMIA?

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Purpose/Objective: Childhood leukemia is characterized by chromosomal translocations. Of significant interest are the transcriptional alterations that might affect the characteristics of leukemic stem cells, such as the ectopic re-activation of the genes responsible for self-renewal. Our hypothesis is that the aberrant expression of such genes could be involved in the development of certain leukemic subtypes, so correlations could exist between gene expression and certain diagnostic characteristics. We also examine whether differential gene expression could be related to specific leukemic cell maturation stages.

Materials and Methods: We investigated the expression levels of *HOXA9, MEIS1, AML1* and *IRF4*, in 58 children with acute leukemia and in 4 leukemic cell lines. By using cytogenetic, immunophenotypic and gene expression data we attempt to find possible correlations between the expression of these genes and the different leukemic subtypes.
Results: Differential expression of the aforementioned genes did not directly correlate to immunophenotype and/or cytogenetics or any particular leukemic subtype. *HOXA9* over-expression was significantly more up-regulated in females, possibly highlighting developmental differences between the two genders. *MEIS1*, *AML1*, and *IRF4* were significantly over-expressed and co-expressed in 20% of the patients and one cell line, independent of leukemic subtype, hinting at a possible synergistic relationship. In addition, *IRF4* over-expression appeared in various leukemic subgroups, suggesting that it may have a common regulatory role among leukemic subtypes.
Conclusions: The results suggest that the above genes may act as important regulators of both hematopoietic development and leukemic formation. Only through the identification of these regulators, and of their downstream targets, will we gain a better understanding of how deregulated transcription on key developmental pathways leads to leukemogenesis.

PUB-0160

CANCER CHILDREN CHARACTERISTICS IN THE SOUTH OF VIETNAM

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Purpose/Objective: To describe the epidemiologic, clinical and laboratory characteristics of cancer in children managed at a regional children's hospital.
Materials and Methods: In a retrospective- case series analysis, all children under 15 years admitted to the Onco-Haematology Department at Children Hospital 2 Ho Chi Minh City with a cancer diagnosis, from March 2011 to March 2012 were evaluated.
Results: There were 116 cases with male: female rate was 2:1. The mean age was 42.8 $\pm$ 5.3 months with patients aged from 12 to under 60 months accounted for the highest percentage (59.5%). The most common cancers identified were Leukemia (46, 39.7%), Neuroblastoma, NBL (22, 19.0%), Wilms Tumor, WT (12, 10.3%), and Langerhans cell histiocytosis, LCH (9, 7.8%).

For Leukemia, the most type was B- lineage Acute lymphoblastic leukemia with 86.7%.

For NBL, a high percentage were diagnosed in late stages, with stage III and IV diagnosed 18.1% and 81.8%, respectively. There were no cases of stage I or II. Nearly all cases showed heterogeneous masses with calcification at adrenal or paraspinal region (95.5%) on CT scan.

For WT, the most common symptom was a painless abdominal mass (91.6%). The abdominal CT scan images consisted of large renal masses of that removed or surrounded the renal vessel (58.3%) but did not cause hypertension.

For LCH, the two most common subtypes of the disease identified were multisystem with involvement of risk organ and single system with CNS-risk lesions. Both classifications accounted for 44.4% of cases.
Conclusions: The most common cancer of children was Leukemia, and the most common malignant solid tumor was Neuroblastoma as expected. The overwhelming predominance of high-risk stages at which NBL was diagnosed in this cohort suggests that improved education and surveillance techniques to identify these tumors earlier could have a great impact on overall survival.

PUB-0161

INSULAR-TYPE COMPONENT FOLLICULAR THYROID CARCINOMA IN A 15-YEAR-OLD GIRL—CASE REPORT

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Purpose/Objective: The clinical history of a pediatric patient with metastatic insular-type component follicular thyroid carcinoma will be reviewed. Previously reported cases will be examined to allow for comparison of prognosis.
Materials and Methods: Ultrasonography and technetium 99m 2-methoxyisobutylisonitrile scan) revealed characteristics of malignant tumor of the thyroid gland (about 5-6 cm in diameter). Surgical intervention included total thyroidectomy with bilateral paratracheal neck dissections (level VI)
Results: Final histological examination follicular carcinoma with insular-type component(30% presence), vascular invasion into a blood vessel of capsulae tumor. Three month later, were revealed left-sided neck lymph node metastasis of insular-type component follicular thyroid carcinoma. Surgery consisted of left-sided unilateral cervical lymph nodes dissection. Final histological examination was revealed metastasis insular component thyroid carcinoma in lymph node of jugular vein group and adjacent muscles and metastasis in platisma. Ten month later, revealed metastasis in left-sided supraclavicular lymph nodes were revealed. Final histological examination was insular carcinoma with infiltration of capsulae of the lymph nodes. Postoperatively, the patient underwent radioactive iodine I 131 therapy.
Conclusions: Pediatric metastatic insular thyroid carcinoma is an uncommon form of thyroid malignancy requiring aggressive surgical treatment and adjuvant radioactive iodine.

PUB-0162

TUMOUR MARKERS IN CYSTIC CRANIOPHARYNGIOMAS: PART OF THE GERM CELL TUMOUR FAMILY? A JOURNEY THROUGH THE LABORATORY AND THE LITERATURE.

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Purpose/Objective: Intracranial cystic teratomas and craniopharyngiomas may share similar clinical and radiological features. It is no longer considered best practice to treat intracranial germ cell tumors (GCT) empirically based on radiological features alone as up to 20% may prove to be tumors other than GCT. Cystic fluid and cerebrospinal fluid (CSF) can be tested for tumor markers such as alpha fetoprotein (α-FP) and beta human chorionic gonadotrophin (β -hCG). However these are tested on platforms designed for urine and serum testing. We aimed to determine if the South African chemistry laboratories could validate an assay to test these markers accurately in CSF. A secondary aim was to review the literature on craniopharyngiomas and intracranial germ cell tumors to determine the significance of tumor markers in the diagnosis of cystic craniopharyngiomas.
Materials and Methods: Communication with staff of the National Health Laboratory Services as well as with the major private laboratories to enquire about validation of assays and the possibility of setting up validated assays for tumor markers in CSF. Literature review to elucidate normal values using validated assays.
Results: Currently, there is no laboratory in South Africa which runs a validated assay for these markers in fluid other than serum and urine. Worldwide, laboratories may issue results based on unvalidated assays, which are then used to diagnose and prognosticate in GCTs. The scanty available literature supports the finding that craniopharyngiomas express β-hCG and suggests normal and pathological levels.
Conclusions: Detection of high levels of β-hCG in cyst fluid of intracranial lesions may aid in the diagnosis of craniopharyngioma, especially in settings where neurosurgical outcomes are suboptimal. Measuring levels of CSF tumor markers in intracranial germ cell tumors is essential in diagnosis, prognostication and treatment stratification. The absence of this modality in South African laboratories is problematic and we recommend that assays be validated to improve patient outcomes.

PUB-0163

CHILDREN'S CANCER IN NIAMEY, NIGER

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Purpose/Objective: This study was conducted to determine the epidemiological aspects of cancer in children under the age of 15 years in Niamey region.
Materials and Methods: A descriptive retrospective analysis of childhood cancer cases, reported between 1992 and 2009 to the Niger Cancer Registry, was performed.
Results: During the study period, 331 children were diagnosed with cancer; representing 6.7% of all cases of cancer collected during this period.The average age of diagnosis was 7.75 $\pm$ 3.97 years. Childhood cancer was more common among males (58.3%) than females (41.7%). The most prevalent ethnic group was the Djerma-Sonrai (55%). According to recorded data, the most common groups of cancers in children were lymphomas (29%), bone tumors (11.48%), leukemias (7.25%), renal tumors (5.13%) and nervous system tumors (3.32%). Among the 325 cases for whom the evolution is known, 47 (14.5%) of them died during the study period.
Conclusions: Children's cancer remains a serious public health problem in Niger. The discovery of the tumor in late stage characterizes the population because of lack of awareness about cancer in children.

PUB-0164

UNUSUAL PRESENTATION OF NON HODGKIN LYMPHOMA

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Purpose/Objective: Lymphoma generally presents with lymphadenopathy and hepatosplenomegaly. However unusual presentations may occur sometimes. This may delay

the diagnosis, which may affect outcome. Some of the unusual presentations of lymphoma like pleural effusion, septic arthritis, pott's spine etc have been mentioned in literature. Hence we report five cases of Non Hodgkin Lymphoma with unusual presentations.
Materials and Methods: Retrospective analysis of NHL cases with unusual presentation since January 2010- December 2012.
Results: Case1: A 2.5 years old female child presented with tibial swelling of around 2×2cm along with pelvic mass involving retroperitoneum, pancreas, left ovary & bilateral kidneys. Biopsy of tibial swelling confirmed B cell lymphoblastic lymphoma. Additionally she also had right atrial mass on CT chest, suspected to be metastasis of lymphoma which resolved on chemotherapy. Case2: 6.5 yrs old female child presented with progressive left eye proptosis over last 6 months with multiple convulsions. CT brain was suggestive of retroorbital mass. Biopsy of retroorbital mass proved to be tdt positive B cell lymphoma. CSF cytospin showed lymphomatous involvement. Case3: 11 years male child with HIV infection presented with multiple fractures at neck and epiphyseal region of bilateral femur. MRI bone was suggestive of nonhomogenous mass involving both femurs which on biopsy proved to be Non Hodgkin lymphoma. Case4: 7 years old male child came with a non healing wound over left leg since one month, which required amputation. Histopathology of amputed leg was suggestive of Non Hodgkin Lymphoma. Case5: 12 years old male child presented with left sided massive pleural effusion. Pleural fluid cytology was confirmative of T cell lymphoblastic lymphoma.
Conclusions: Hence high index of suspicion and early workup is required to avoid upstaging of lymphoma in children.

PUB-0165

IMPROVEMENT IN PEDIATRIC CANCER SURVIVAL IN A DEVELOPING COUNTRY THROUGH COLLABORATION WITH NONGOVERNMENTAL ORGANIZATION.

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Purpose/Objective: Lokmanya Tilak Municipal General Hospital is a municipal corporation run tertiary care hospital catering to the population from the lowest socioeconomic strata. PurposeÑTo evaluate the improvement in cancer survival in paediatric patients at our centre through funding for personell by a nongovernmental organization(NGO).
Materials and Methods: Method–
Study design- A retrospective analysis of case records enrolled.
Study sample- Children with cancers enrolled between 2005 to 2011.
A comparision was made pre(2005-2008) and post(2009-2011) collaboration with JivDaya foundation (a NGO based in USA). Through JivDaya foundation we got extra personell exclusively for pediatric oncology patients(4 staff nurses,1 medical social worker,1data manager and 1outreach worker)and we evaluated the impact of these personell on patient care and outcome.
Results: ResultsÑChildren abandoning treatment reduced from 60.6%($n = 66$)in 2005to 2008 to around 24.07%($n = 55$)in each year from 2009 to 2011($p < 0.001$).Additionally the number of children completing treatment increased from 8($n = 66$) in 2005 to 2008 to 26($n = 55$) in 2011($p < 0.001$). The overall survival rate has improved from 20% in 2005-2008 to 51.85% in 2011($p < 0.001$).These results show a significant impact on patient management and outcome.
Conclusions: ConclusionÑImprovement in overall outcome of cancer depends on the infrastructure which includes manpower and financial aid and collaboration with such NGO's such as JivDaya Foundation had a very positive impact on patient care and survival benefit to children with cancers.

PUB-0166

PROPHYLACTIC FIRSTLINE ANTIBIOTICS REDUCE INFECTIOUS FEVER AND SHORTEN HOSPITAL STAY DURING CHEMOTHERAPY-INDUCED AGRANULOCYTOSIS IN CHILDHOOD ACUTE MYELOID LEUKEMIA IN CHINA

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Purpose/Objective: To study the safety and efficacy of prophylactic antibiotics during chemotherapy-induced agranulocytosis to reduce bacterial infections and infection-related mortality in childhood acute myeloid leukemia (AML) in China.
Materials and Methods: From January 2011 to October 2012, we retrospectively analyzed infectious fever in 31 males and females (3-16 years) with AML receiving intensive chemotherapy (96 cycles). The prophylactic group patients ($n = 16$) were given the combination of vancomycin and cefepim or single-use opiperacillin/tazobactam to prevent bacterial infection during agranulocytosis and observed for 35 treatment cycles. The control group patients ($n = 15$) receiving no preventive antibiotics treatment were observed for 61 treatment cycles. The difference in infection incidence and average length of hospital stay was analyzed with χ^2-test and *t*-test using SPSS statistic software.
Results: Relative to the control group, the preventive group had less frequent fever (1.6 times vs 3.1 times, $p = 0.014$), longer interval to fever (3.9 days vs 2.4 days, $p = 0.011$), and shorter duration of hospitalization (22.6 days vs 28.3 days, $p = 0.005$). Prophylactic group had fewer children with lung infection than the control group (45.7% vs 90.2%, $p = 0.005$). A rash occurred in one patient in prophylactic group during the application of vancomycin, subsiding after withdrawal. No other antibiotic-related effects were observed in prophylactic group.
Conclusions: Prophylactic firstline antibiotics used during strong chemotherapy-induced agranulocytosis in childhood AML can effectively reduce the incidence of infectious fever and shorten the average length of hospital stay, increasing treatment success and quality of life in pediatric patients. Larger controlled clinical studies are needed to verify our findings.

PUB-0167

TREATMENT OF ACUTE MYELOID LEUKEMIA WITH THE MRC AML 10 REGIMEN IN CHINESE CHILDREN: A SINGLE CENTER STUDY

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Purpose/Objective: The objective of the present study was to investigate the therapeutic efficacy and feasibility of MRC AML 10 regimen in the treatment of acute myeloid leukemia (AML; excluding acute promyelocytic leukemia) in Chinese children.
Materials and Methods: Nineteen children with AML treated with the MRC AML 10 regimen were recruited from December 2001 to December 2009, and the clinical data were retrospectively analyzed. Several children received concomitant hematopoietic stem cell transplantation. Kaplan Meier method with Log-Rank testing was employed for survival analysis.
Results: The complete remission rate was 94.7%. Follow-up was for a median 69 months (range: 24*106 months). The predicted 5-year overall survival (OS) rate and leukemia free survival (LFS) rate were 73.7% and 68.4%, respectively. The LFS rate was similar in low risk children and non-low risk children (87.5% vs 54.5%, respectively; $P = 0.181$). The OS rate was similar in children receiving chemotherapy alone and in children receiving chemotherapy plus hematopoietic stem cell transplantation (81.8% vs 50.0%, respectively; $P = 0.147$). The LFS rate was dramatically different between children with AML M1 or M2 and children with AML M4, M5, or M7 (84.6% vs 33.3%, respectively; $P = 0.026$).
Conclusions: UK MRC AML 10 trial can also improve the outcome of childhood acute acute myeloid leukemia (non acute promyelocytic leukemia) in experienced center in China. For non low-risk patients, routine hematopoietic stem cell transplantation can not improve the prognosis in our experiences.

PUB-0168

NEPHROTIC SYNDROME- A RARE PARANEOPLASTIC PRESENTATION OF HODGKIN DISEASE

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Purpose/Objective: Nephrotic syndrome is a rare paraneoplastic presentation. It has been described in association with hodgkin disease in adults but rarely from pediatric age group. We hereby report a nine year old boy with this rare association.
Materials and Methods: A nine year old boy presented to our hospital with isolated left cervical lymphadenopathy. There was no history of significant weight loss, fever or contact with tuberculosis. A biopsy of the lymph node revealed it to be a classical mixed cellularity hodgkin lymphoma with CD 30 and CD 15 positivity. During this process of evaluation, he also developed facial puffiness and pedal edema. Investigations were suggestive of nephrotic syndrome (nephrotic range proteinuria, hypercholesterolemia, hypoalbuminemia) and hence a diagnosis of hodgkin lymphoma with nephrotic syndrome was considered.
He was risk stratified as stage 3A after staging investigations and was started on chemotherapy as per protocol along with steroids (prednisolone) 60 mg/m^2/day for nephrotic syndrome. Response evaluation after two cycles showed a good response. He was also in remission from nephrotic syndrome. Presently, he has completed therapy and is doing well at follow up.
Results: Association of nephrotic syndrome in a child with hodgkin disease is a rare coincidence. The incidence reported in literature for this association is 0.17-0.4%. Review of literature revealed only twelve cases being reported in children worldwide. The mechanism behind it is still elusive. Some studies have attributed it to T cell dysfunction and recent studies have reported role of protein c-mip. Remission from lymphoma is associated with remission and relapse of nephrotic syndrome is associated with recurrence of lymphoma.
Conclusions: We are hereby reporting this case for its rare association and few cases being reported in pediatric literature. Pediatric oncologists need to be aware of this association since it will require a multidisciplinary approach in management.

PUB-0169

PRIMARY MUCINOUS ADENOCARCINOMA OF THE THYMUS

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Purpose/Objective: Primary thymic adenocarcinomas are rare neoplasms. The mucinous subtype has been recently described. It is an extremely rare variant of thymic adenocarcinoma which behaves aggressively. There are only a few case reports in the literature. To our knowledge, it is the second case described in a child.
Materials and Methods: Retrospective case report.
Results: A 15-year-old boy presented with chest pain. A chest X-ray followed by a chest computed tomography (CT) revealed an 8 cm × 5 cm anterior mediastinal mass. The serum beta-HCG and alpha-fetoprotein levels were within the normal range. Endoscopic examination demonstrated an extrinsic bronchial compression. A CT-guided percutaneous needle biopsy of the mediastinal mass yielded necrotic material. The patient underwent anterior mediastinotomy. Intraoperative ?ndings included a mediastinal mass with vascular invasion and multiple disseminated nodules in the pleura. Biopsies were performed. The pathological diagnosis was primary mucinous adenocarcinoma of the thymus. After four courses of chemotherapy with ADOC regimen (cisplatin + doxorubicin+ vincristine+ cyclophosphamide), evaluation showed an increase of tumor size. Multiple metastases appeared in both lungs, mediastinal lymph nodes, ribs, iliac bone, tibia and vertebreas with spinal cord compression. The patient underwent decompressive radiotherapy. He died four months after the initial diagnosis.
Conclusions: Clinicians and surgical pathologists should include thymic mucinous adenocarcinoma in the differential diagnosis of a mediastinal mass. Prognosis is very poor.

PUB-0170

THE MANAGEMENT OF SYMPTOMATIC METASTATIC LESIONS OF MEDULLOBLASTOMA

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Purpose/Objective: Medulloblastoma is a malignant tumor of the developing CNS with highly metastatic potential. Though, many clinical trial and discussions have been made to fight this neoplasm, the cure of this disease is still challenging. And in terms of the metastatic lesion of medulloblastoma, there is no conclusive management for them. Then in this study, we reviewed our medical strategy for the metastatic lesions and the results of treatments.
Materials and Methods: We have 4 patients suffering from medulloblastoma with residual metastasis in our institution after standard therapies including surgical removal, radiation therapy, and chemotherapy. They all have difficulty to walk and/or severe sensory disorders.
Results: Before starting maintenance chemotherapy, we performed tumor removal and laminoplasty for 3 patients and focal radiation surgery for 1 patient. The Karnofsky performance status and Brunnstrom stages of all patients were improved within 1 month.
Conclusions: The management of metastasis from medulloblastoma is controversial. Our cases suggested that the adequate interventions for metastatic lesions may lead to improve the patients' performance status even patients were in the terminal phase of the disease.

PUB-0171

QUALITY OF LIFE IN CHILDREN WITH CANCER: THE STATE OF THE SCIENCE

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Purpose/Objective: Survival rates have markedly improved over the last three decades in children with cancer. In children with brain tumors (BT) and acute lymphoblastic leukemia (ALL), the five*year survival rates are approximately 70% and 80% respectively. Quality of life (QOL) is considered an important outcome measure due to the increasing survival rates. The purpose of this systematic literature review is to describe the state of the science related to quality of life in childhood cancer.
Materials and Methods: CINAHL and PubMed were searched for publications of research findings using the terms: *childhood cancer, quality of life*, and *health-related**, for papers published between January 1, 2002 and April 28, 2012 in English language. Exclusion criteria were non-research articles, literature reviews, and participants > 18 years old, children at end of life, and childhood cancer survivors.
Results: Fourteen articles met all the inclusion criteria. All included studies focused on aspects of QOL including physical, psychosocial, social, and spiritual functioning in children with cancer. The most commonly affected QOL domain was physical with symptoms of fatigue, pain, and nausea most commonly associated with decreased QOL. Impaired psychosocial functioning was also associated with decreased QOL. Children who received cancer treatment within the previous12 months experienced more emotional outbursts and behavioral problems than those who received treatment more than 12 months ago. Children with hematologic malignancies such as ALL had better QOL compared to those with other types of childhood cancers.
Conclusions: This review indicates that children with cancer experience changes in QOL related to treatment and specific diagnoses. Impairments in two QOL dimensions, physical and psychosocial functioning, were most often associated with decreased QOL. Future research is needed to examine the changes in the physical and psychosocial QOL domains with a focus on those diagnoses at higher risk for lower QOL.

PUB-0172

EPIGENETIC REMODELLING ON INK4A-ARF (CDKN2A) TUMOR SUPPRESSOR LOCUS BY EZH2 IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA.

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Purpose/Objective: T cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematologic malignancy and the deletion of the *INK4A-ARF* (*CDKN2A*) tumor suppressor locus is a frequent genetic alteration. The INK4A/ARF locus coding for two negative regulators of the cell cycle, p16 and p14, respectively. The histone methyltransferase EZH2 is a key component of the polycomb repressive complex 2 (PRC2), overexpressed in many cancers. It has been observed that the presence of EZH2 at the level of the promoter of INK4A can directly contribute to its epigenetic silencing through DNA methylation. Aim of our study was to analyze expression levels of EZH2 and epigenetic control on cell cycle regulators as p16 and p14 in children with T-ALL.
Materials and Methods: We analyzed EZH2 expression levels by Real time PCR and Western Blot analysis in 20 T-ALL patients treated to Paediatric Oncology Service of Second University of Naples. Total RNA from cells was extracted with Triazol reagent and random primers were used for reverse transcription. Chromatin Immunoprecipitation (ChIP) analysis was carried out on Jurkat cell line and on lymphoblasts of two pediatric patients to analyze INK4a/ARF locus using an antibody for EZH2. Normal bone marrow was used as control.
Results: ChIP analysis showed that immunoprecipitated DNA using an antibody for EZH2 exhibited no amplified in INK4a/ARF promoter region analyzed. Our data show that EZH2 RNA expression level is higher in our samples compared to the control. EZH2 protein (80 kDa) was expressed in 16/20 samples T-ALL as in Jurkat cell line respect to controls, where this protein is absent.
Conclusions: Our preliminary results showed that EZH2 does not contribute to epigenetic silencing of INK4a-ARF locus

PUB-0173

WILMS TUMOR TREATMENT RESULTS AFTER RADIATION THERAPY AT THE CHILEAN NATIONAL CANCER INSTITUTE

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Purpose/Objective: Wilms Tumor (WT) is the most common kidney malignancy in children. Treatment in Chile is based, depending on stage and presentation, on early surgery, radiotherapy and chemotherapy according to the PINDA protocol. The objective of this publication is to review the historical patient series of the Chilean National Cancer Institute (CNCI).
Materials and Methods: A retrospective review of every patient treated with WT at the CNCI was performed. We describe the patient population, radiotherapy treatments delivered and overall survival. Prognostic factors were explored.
Results: Between September 1993 and December 2010 110 children were treated. Median age at diagnosis was 3.6 years. Median follow-up was 128 months from the end of radiation therapy and only 3 patients were lost to follow-up. At the time of analysis in June 2012 of the 107 patients with complete follow-up 19 had died of disease progression. All patients who died did so within the first three years of treatment. Overall survival at 2, 4 and 12 years was 82%, 78% and 78% respectively. In multivariate analysis time to RT was a negative predictor of outcome (P = 0,04).
Conclusions: Treatment of WT has an excellent prognosis. Overall survival is stable after the first 3 years after treatment, independent of the patient«s initial grouping. Amongst prognostic factors, in patients with indication of RT treatment should star as early as possible after surgery.

PUB-0174

INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH CANCER

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Purpose/Objective: Invasive fungal infection (IFI) in oncologic children are life threatening events. The purpose of this study was the assessment of clinical course of IFI in neoplastic children according to the diagnostic and therapeutic difficulties based on our institution experience.
Materials and Methods: 28 patients with cancers and IFI were enrolled to this study: 17 pts (60,7%) with solid tumors and 11 pts (39,3%) with leukemia. We analyzed clinical course of IFI based of initials symptoms, diagnostic difficulties, patogens and treatment results.
Results: All of patients (n = 28) presented symptoms of IFI during neutropenic period (WBC 0,4-0,1 K/ul) with characteristic clinical picture such persistent fever, cough, chest pain, poor signs in physical examination. All of 28 pts presented lung location, 1 pt had additionary liver foci of the fungal infection, 1 pt was diagnosed as having CSN mycosis. Each patient was diagnosed with IFI base on clinical manifestation, radiologic picture (CT,MRI), blood culture results, galactomannan, PCR and histopatology. Diagnosed patogens: Candida albicans (11pts),Candida tropicalis (1pt), Aspergillus sp. (8 pts), in 9 pts unidetified patogens. In the studied group 27 pts achieved complete remission of IFI, 1 pt died as the result of lungs aspergillosis progression. Antifungal therapy was applied in the period of 2 weeks to 6 months. A delay in oncologic treatment ranged from 14 days to 6 months..
Conclusions: Invasive fungal infections are serious infectious complication in children with cancer becouse of dignostic and therapeutic difficulties, clinical course and in the cosequence delay of the oncologic treatment. Deep neutropenia play fundamental role in the IFI development.

PUB-0175

FOCAL NODULAR HYPERPLASIA IN CHILDHOOD CANCERS: DIAGNOSIS AND CLINICAL COURSE

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Purpose/Objective: Even though focal nodular hyperplasia (FNH) is rare in childhood, it is reported at increased rates in treated pediatric cancer patients. They are considered as hyperplastic (regenerative) response to hyperfusion and there are characteristic abnormal arteries at the centres of the nodules but pathogenesis still remains controversial. Aetiology is also unclear, the use of high dosage of alkylating agents, the occurence of venoocclusive disease, graft versus host disease, hematopoetic stem cell transplantation are risk factors for developing of FNH. The aim of this study to describe the patients diagnosed as FNH after primary malignancy and describe radiologic findings and analyze the clinical course of FNH.
Materials and Methods: We retrospectively evaluated the diagnostic work-up, radiologic findings, clinical course and outcome of 6 patients, diagnosed as FNH after pediatric cancer treatment at the Department of Pediatric Hematology-Oncology of the Kanuni Sultan SŸleyman Training and Research Hospital and Istanbul University, Oncology Institute, between 1993 and 2009.
Results: FNH lesions were diagnosed in 6 patients after an average interval of 5.6 years, since the conclusion of the antineoplastic therapy. Five patients had a history of neuroblastoma and single patient had a history of primitive neuroectodermal tumor.FNH was incidentally found at USG or MRI performed for routine controlling. Two children underwent surgical biopsies to rule out liver metastases. No dysfunction was identified in liver function tests. Alpha-fetoprotein levels were within normal ranges. The dimensions of the lesions were between 1 and 4 cm and in the form of a solitary lesion in 3 patients and had a multifocal appearance in the other 3 patients. The lesions were stable within 1-10 years follow-up, no malign transformation was detected.
Conclusions: FNH can be misdiagnosed as liver metastasis in pediatric cancer patients. It should be considered the differential diagnosis of hepatic mass previously treated for pediatric solid tumor.

PUB-0176

LEPTIN CONCENTRATION AND NUTRITIONAL STATUS IN THE COURSE OF TREATMENT IN CHILDREN WITH BRAIN TUMOURS - PRELIMINARY REPORT

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Purpose/Objective: The assessment of the nutritional status of children with malignant brain tumours in the course of treatment in correlation with the concetration of leptin.
Materials and Methods: The study involved 44 children treated for CNS tumours. The controled group was composed of 20 healty children. Each child's weight and height were measured 7 times in determined time period to calculate the body mass index SDS BMI. to calculate the body mass index SDS BMI.. Leptin markers were analysed three times: before the beginning of the treatment (G1), during the maintenance treatment (G2) and after its completion (G3)
Results: The initial parameters of the nutritional status * the SDS BMI means in children with diagnosed malignant tumours of the CNS - were not different from the control group respective parameters. In the course of treatment the average values of SDS BMI decreased, reaching their lowest level during the maintenance treatment and were significantly statistically lower compared to the control group. Immediately after the completion of treatment anthropometric indicators were higher than during the maintenance treatment. During the therapy an increase in the concentration of leptin and its decrease after the completion of the therapy was observed. There was no statistically significant correlation between the concentration of LEP and the average concentration of SDS BMI.
Conclusions: .In coclusion, in children with brain tumours there are quantitative disorders of the nutritional status which correlate with the period of the treatment. The most significant disorders in the nutritional status are observed during maintenance chemotherapy. The overall survival of children with CNS tumors does not seems to depend on the initial nutritional status. the correlation between the concentration of leptin and the nutritional status of children with brain tumours was not explicitly confirmed, it may suggest a need for analysing this issue with more patients enrolled.

PUB-0177

HEALTH STATUS AND HEALTH-RELATED QUALITY OF LIFE OF LONG-TERM SURVIVORS OF BRAIN TUMOURS IN CHILDHOOD

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Purpose/Objective: Self-reported health-related quality of life (HRQL) provides insight into morbidities experienced by individuals within the context of daily living. Our group previously identified an unanticipated burden of pain in survivors of brain tumours in childhood. Subsequent HRQL studies have reported pain inconsistently, with limited investigation into the burden of this morbidity. The purpose of the current study was to explore the HRQL, with a focus on pain, in survivors greater than 10 years from diagnosis of a primary brain tumour in childhood or adolescence.
Materials and Methods: A cross-sectional study was undertaken using Health Utilities Index (HUI2/3) questionnaires. Pain was characterized using a coloured analogue scale for self-perceived severity and a homunculus to identify the location of pain, as well as comparison of the single-attribute HRQL scores for participants with and without pain. The stability of pain was established using HUI2/3 data of the same cohort collected at 5 and 10 years prior.
Results: Twelve males and 13 females (mean time from diagnosis of 19.7 years) were found to have multi-attribute HRQL scores of 0.79 for HUI2 and 0.69 for HUI3. Thirteen (52.0%) participants experienced pain in the past week, with individual differences in severity, location and number of areas of discomfort within the body. Comparison of single-attribute HRQL scores for participants with and without pain revealed significantly higher burdens of morbidity in sensation and emotion among the former. Pain also increased from the initial interview (10 years prior) to the present interview.
Conclusions: Long-term survivors of brain tumours in childhood have overall decreased HRQL. Pain appears to be a persistent and significant burden with implications for other attributes of HRQL. The findings of this study provide further insight into a poorly characterized phenomenon of this survivor cohort and warrant further study. Support by HUInc Student Grant is gratefully acknowledged.

PUB-0178

FREQUENCY AND RISK FACTORS FOR THE COLONIZATION AND INFECTIONS OF VANCOMYCIN RESISTANT ENTEROCOCCI (VRE) AND CLINICAL OUTCOME IN PEDIATRIC HEMATOLOGY/ONCOLOGY PATIENTS

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Purpose/Objective: VRE has become a serious problem especially in immuno-suppressed patients in hematology-oncology clinics. In this paper we tried to define the VRE infected and colonized groups determi-ne its risk factors, incidence and evaluate treatment appro-aches to these infection and their clinical outcomes.
Materials and Methods: 32 patients who were admitted to pediatric hematology oncology department and bone morrow transplantation unit between January 2007 - June 2010 and had VRE colonizati-on at culture samples were included in this study. We assessed the clinical, laboratory and treatment outcomes retrospectively.
Results: 56% of VRE colonized patients were male and they had a mean age of 106.7 $\pm$ 64.6 months (5-216 months). Some (26/32 patients) of them were admitted to hematology oncology depart-ment, and 6 of the cases were in-patients in the BMT unit and 14 of them were ALL. We determined the most important risk factors as central catheter (93.8%), chemotherapy and immunosuppressi-on (90.6%). During the last 3 months of treatment, amikacin, tei-coplanin, meropenem, cefepim, ciprofloxacin were the mostly used antibiotics. The most common colonization sites were rectal samp-les (25 patients). 9/32 patients had

VRE infection. 14% of coloni-zed ALL patients, 50% of coloni-zed AML and BMT patients had VRE infection. Linezolid was used for the treatment of 22 VRE patients, and 25% of VRE infected patients expired. The most commonly concomitant infection in most patients was pulmonary fungal infection (6/8).
Conclusions: VRE is one of the most important nosocomial patho-gens in immunocompromised patients, so good practice in antibi-otic usage, isolation precautions and VRE surveillance studies are very important. VRE by itself is not a cause of serious infection, but together with the risk factors, morbidity and mortality might be higher. Surveillance studies including rectal sample cultures for risky patients to decrease VRE spread should be recommended.

PUB-0179

STUDY OF THE ROLE OF PALLIATIVE RADIOTHERAPY IN THE MANAGEMENT OF INCURABLE PEDIATRIC MALIGNANCIES.

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Purpose/Objective: : To evaluate the role of palliative radiotherapy in the management of incurable pediatric malignancies
Materials and Methods: : Patients coming to the department of radiotherapy S.M.S Hospital were included in the study.36 pediatric patients were selected between Nov 2010 to Nov 2012. All of these 36 children received palliative radiotherapy for symptom control. Palliative radiotherapy was given either as single modality or in addition to surgery, chemotherapy. Information recorded for each patient included age, sex, and extent of disease, histological types, symptomatology, treatment methods and symptom relief. The various dose schedules were used (1) 625cGy/week for 3 week.(2)20 Gy in 5 fractions (3) 30 Gy in 10 fractions.
Results: : There were 26 males and 10 females in the age group of 1 to 19 years, with a median age of 14 years (range of 1-19 years). Predominant symptoms were swelling with or without pain, bleeding, and weakness of limbs. The median duration of symptoms was 80 days (range of 4-40 days). The histological diagnosis of these children, most in the group of malignant round cell tumors (17), retinoblastoma (6), neuroblastoma (5), Ewing's sarcoma (8). All patients presented with advanced stages of disease. Out of 36 patients 18 (50%) had disseminated disease at presentation. Six patients underwent surgery while 30 patients received chemotherapy and all patients received palliative radiotherapy. Three patients showed complete resolution, 18 patients showed good, while 14 patients had little, 1 did not have any relief in their symptoms. At the completion of multimodality treatment, 16 patients had partial response, 6 patients had progressive disease, 8 had stable disease and 2 patients had complete response. The disease status of 4 patients could not be known.
Conclusions: Radiotherapy provides better symptom relief, so the role of radiotherapy is very important as palliative modality in children with locally advanced lesions

PUB-0180

AN ADOLESCENT WITH HYPEREOSINOPHILIC SYNDROME DIAGNOSED AS CHRONIC EOSINOPHILIC LEUKEMIA WITH THE FINDING OF FIP1L1-PDGFRA MUTATION

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Purpose/Objective: Hypereosinophilic syndrome is a rare disease particularly in childhood with peripheral eosinophil count of $>1{,}500/mm^3$ that is not due to secondary causes. An adolescent diagnosed with chronic eosinophilic leukemia with the presence of FIP1L1-PDGFRA mutation and no blastic infiltration in the bone marrow is presented.
Materials and Methods: A 16-year-old boy with symptoms of bone pain, fever and chills for the last 6 months was referred to our center. In physical examination, he was pale, had 1cm lymphadenopathies in the cervical and inguinal region and 3cm splenomegaly. Complete blood count showed WBC:28,000/mm^3, Hb:7.4g/dL, Hct:22.8%, MCV:103.7 fL, PLT:81,000/mm^3 with absolute eosinophil count 16.400/mm^3. In peripheral smear, there was hypereosinophilia with no blast. He had low folate and very high vitamin B12 levels. Erythrocyte sedimentation rate was 78/1.hr. In blood chemistry, no pathologic finding was present.
Results: Bone marrow aspiration revealed increased young and old eosinophils with no blasts. Flow cytometry supported the findings of the bone marrow. Genetic investigation showed the presence of FIP1L1-PDGFRA mutation. He had no end organ damage with normal echocardiography and respiration function tests. Corticosteroid treatment did not resolve the findings of eosinophilia. He responded to imatinib therapy (100mg/d) at the first week. He was in morphological remission but low levels of FIP1L1-PDGFRA insisted at first month of imatinib. He is under imatinib treatment for 3 months now and in search for genetic remission.
Conclusions: This case is presented since hypereosinophilic syndrome is rare in childhood and secondly he was diagnosed as chronic eosinophilic leukemia with the sole presence of FIP1L1-PDGFRA mutation.

PUB-0181

CASE REPORT: 15 CASES OF OPTIC NERVE SHEATH MENINGIOMAS UNDER 15 YEARS-OLD

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Purpose/Objective: To analyze the features of optic nerve sheath meningiomas in chindren
Materials and Methods: According to the 2007 WHO classification of tumors of central nerve system, 15 patients were diagnosed as obital meningiomas which occur in childhood at the department of pathology, Zhongshan Opthalmic center of Sun-yat sen university. The 15 patients (7 male, 8 female) had a mean onset age of 9.3 years (3 to 14 years). All 15 patient were undergo meningioma resection in our hospital. There were seven meningothelial type cases in all fifteens, there were three fibrous type cases, one microcystic type case and two anaplastic type cases.
Results: There was a marginal predominance of female patient in our study, which was different from what people found before. The main reason that these patients came to hospital to receive surgical treatment is losing their eye sight, and they has more chance to get recurrence (4 of 15) as well as malignant (3 of 15). All the tumours have more or less some malignant behaviors such as bone and mesenchym invasion or involve the nerve system.
Conclusions: The optic nerve sheath meningiomas in children are rare tumors, they are more malignant and more easily have recurrence than other meningiomas. They also are more dangerous because of their special location. We should take them seriously, and reconsider the definition of benign tumours.

PUB-0182

ACUTE MIXED LINEAGE LEUKEMIA TREATMENT OUTCOME: A 5 YEARS SINGLE INSTITUTE EXPERIENCE

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Purpose/Objective: To investigate treatment outcome of pediatric, Mixed-lineage acute leukemia's (MLL) patients diagnosed and treated at the National Cancer Institute, Cairo University during a 5 years period.
Materials and Methods: Retrospective review of patient charts with newly diagnosed histologically proven MLL, diagnosed and treated at the Pediatric Oncology Department, National cancer institute, Cairo University in the period between January 1st 2005 till end of December 2010 was performed. All patients were followed up till the end of June 2012. Clinical and laboratories data of these patients were retrospectively followed and evaluated.
Results: Twenty seven patients were included in our study. Age of patients ranged between 8 months - 17 years, median 9 years. They were 17 males and 9 females. Follow Up period ranged from 4-93 months, median of 12.3 months.

Total leucocytic count (TLC) at diagnosis ranged between 1.5 to $546 \times 10^3/m^2$ with a median $21.4 \times 10^3/m^2$. Bone marrow was suggestive of ALL in 9/27 patients (33.3%), AML in 5/27 patients (18.5%), and MLL in 13/27 patients (40.7%). Immunophenotyping showed Myeloid+ T (M + T)cell in 37%, whereas M + B in 63%. Seven patients received ALL induction like therapy, while 20/27 patients received AML like treatment. Post induction CR rate was 63%. *Disease outcome*: 17/27 (63%) of patients died due to chemotherapy related toxicities and fungal chest infection. By the end of the study OS at 5 years was 20% with no statistical difference between the two subtypes.
Conclusions: Mixed-lineage acute leukemias carry an extremely poor prognosis in our institute. There is a strong need for implementing a standardized protocol of therapy offering early HSCT as well as a better supportive care and further improving the infection control setup.

PUB-0183

BLOODSTREAM INFECTIONS RELATED TO CENTRAL VENOUS CATHETERS IN CHILDREN WITH CANCER - EXPERIENCE IN A SINGLE SOUTH AFRICAN CENTRE

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Purpose/Objective: Central venous catheters (CVC's) are an essential tool in the management of childhood cancer. Catheter-associated bloodstream infections (CABSI's) are associated with increased morbidity, mortality and amplified health care costs. In a resource limited country with limited nursing numbers and patients that are often immune compromised this additional burden is undesirable. To our knowledge, this is the first study of its kind in a developing country. Information gained will help structure better use of indwelling central lines.
Materials and Methods: This is a retrospective review of CABSI's between November 2011 and December 2012. 76 catheters inserted [25 Totally implantable venous access systems

(TIVAS), 44 Tunneled central vascular catheters (TCVC's), 2 Central vascular catheters (CVC's), 5 were excluded (n = 71), total of 8,135 catheter days (c.d.)] were studied.
Results: 24 episodes of CABSI's with subsequent line removal were documented. The overall CABSI rate were 2.95/1000 c.d. (TCVC's = 5.38/1000 c.d., TIVAS = 1.41/1000 c.d.). Of catheters prematurely removed, 86% were removed secondary to CABSI's. A total of 14 different organisms were cultured (blood cultures/catheter tips). Most frequent were Fungal organisms (n = 6). Children with solid tumours and haematological illness had a 26% and a 42% incidence of CABSI's respectively (AML = 55.5%; ALL = 47%). Type and position of catheters, HIV status, patients' BMI, neutropenia, time to next dose of chemotherapy did not play a role. Patient- nurse ratio (mean, per week) was consistently high.
Conclusions: The rate of CABSI's and premature removal of CVC's in our unit is of concern. Fungal organisms were most frequently cultured. Type of malignancy is a risk for developing a CABSI. The patient-nurse ratio in our unit is unacceptably high. More careful selection of the patient, type of line used and adherence to infection guidelines will be implemented to prevent further infections.

PUB-0184

CLINICAL PROFILE AND OUTCOME OF INTRACRANIAL GERM CELL TUMOUR IN A SINGLE INSTITIUTION

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Purpose/Objective: Children with Intracranial Germ Cell Tumours (ICGCT) are about 13% of Paediatric Brain Tumour in our Institute. It is curable disease. However, there were some relapsed cases and some of them were refractory to treatment.
Materials and Methods: We retrospectively reviewed the paediatric patients with ICGCT in KK Hospital from 1997 to 2012 to analyse the clinical profile, protocol of chemotherapy with radiotherapy and outcome of disease. The datas were obtained from Singapore Children Cancer Registry. We diagnosed ICGCT based on histopathology and tumour markers in which BhCG > 50 IU/L or AFP > 25ng/ml.
Results: Forty five patients were diagnosed as ICGCT within 15 years (May 1997 to May 2012). We excluded 5 patients as 4 patients were transferred to other institutes and one was congenital ICGCT who died before any treatment. Among 40 patients, 22 were Non-secreting Germ Cell Tumours (NSGCT) and the rest were Secreting Germ Cell Tumours (SGCT). There were Chinese 28, Malay 7 and Indonesian 5, male 27(68%) and female 13(32%). Median age was 11 (1-16) year. Majority of patients (70%) were above 10 years of age.

Most of the patients, 37(93%), received chemotherapy. Thirtyfour patients had Chemotherapy and Radiotherapy and 3 patients received Chemotherapy after debulking surgery. Radiotherapy after surgery was given in 2 patients. Autologous Stem Cell Transplant was done in 3 patients and one died of transplant related sepsis. One infant underwent surgery but died of intracranial haemorrhage during operation. Mortality was found in 6 patients(15%). OS and EFS were 84% and 68% overall and SGCT(79% and 60%), NSGCT (87% and 75%), respectively.
Conclusions: Overall survival of NSGCT had better outcome than SGCT as in other centers. However, the outcome of ICGCT in our Institute was slightly lower than other International review(> 90%). We may need to do more analysis and review to improve our outcome.

PUB-0185

OUTCOME OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) TREATED ON A RISK-STRATIFIED PROTOCOL (PALL08) BASED ON LOCAL EXPERIENCE

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Purpose/Objective: To evaluate outcome of a protocol with risk-stratification based on results of our previous protocols and treatment strategy based on internationally published reports.
Materials and Methods: Prospectively collected data on 180 children with ALL treated at our institution on our PALL08 protocol from 2008 and 2012 were analyzed.
Results: Median age was 4.6 years (1.1-13.3, 5.5 ± 0.24) and 58.3% were male. 160 patients with B-ALL were categorized as low risk (LR) if within good-risk ranges for age and WBC count and if good-risk cytogenetics (hyperdiploidy or *RUNX1-ETV6*) were positive. Children with CNS3 status or with > 5% blasts on Day 14 BM evaluation were considered very high risk (VHR). All others, including children with CNS2, were considered high risk (HR). Twenty patients with T-ALL were stratified according to WBC count and CNS positivity into LR (4) and HR (16). Forty-six (25.6%), 103 (57.2%) and 10 (5.6%) children with B-ALL were treated on LR, HR and VHR protocols. Two patients (1.1%) died during induction. 172 patients (95.6%) achieved complete remission at end of induction. Ten (5.8%) patients relapsed at a median of 12.1months (3.5-37, 15.6 ± 3.8) from remission. With a median follow up period of 2.3 ± 0.124 years the overall survival (OS) was 86.2% and event free survival (EFS) was 83.8% compared to 82.5% and 69.9% on our previous protocol (OS p = 0.1 and EFS p = 0.02). There was no difference in survival between T- and B-ALL (OS = 85.5% v. 93.8% and EFS = 84.5% v. 78.9%; p = NS). CNS3 status was associated with poor outcome (EFS = 40%) while trisomy 4/10 (EFS = 97.4%) and *RUNX1-ETV6* (EFS = 96.3%) conferred good prognosis.Infectious toxicity continues to be high.
Conclusions: Although relapse rate on this protocol has decreased from our previous results (21.7%) longer term follow-up to look at relapse and toxicity outcomes is needed. Risk-stratified approach to ALL therapy based on local results is essential to improve outcomes.

PUB-0186

EFFECTS OF A STRUCTURED WEB-BASED SUPPORT GROUP FOR ADOLESCENTS WITH CANCER: A PILOT STUDY

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Purpose/Objective: In response to the advancements in technology, there has been a growing interest in developing web-based support groups which are more flexible and convenient in fostering mutual support among patients with similar illness experiences than conventional face-to-face support group. Given that adolescents nowadays are used to communicate through digital means, this study aimed to investigate the effects of a 12-week structured web-based support group on health-related quality of life, psychological distress, and social support among adolescents with cancer.
Materials and Methods: This was a controlled quasi-experimental study which allowed observation of changes in sequential fashion. Thirty cancer patients who were aged between 13 and 18 years and currently receiving active treatment at the time of recruitment were recruited to the study. Prior to the intervention, their psychosocial status were monitored for 12 weeks as baseline data. Then, they were invited to a 12-week nurse-facilitated structured web-based support group which enabled the participants to interact with other patients with similar illness experience. The 12 weeks following the intervention were the posttest period, in which follow-up measurements were taken to account for history effects. Outcome measures, including health-related quality of life, psychological distress, perceived social support and satisfaction towards web-based support group, were taken continuously at 6-week interval throughout the 36 weeks.
Results: We are still in the data collection progress and preliminary data analysis will be available by August.
Conclusions: This study is funded by The Children's Cancer Foundation Peter Nash Paediatric Oncology Research Grant. Findings of this study will be of significant value for local clinical practice since this is a pioneer study providing evidence on the effects of a professional-facilitated web-based support group in the Chinese community.

PUB-0187

ANTHRACYCLINES INDUCED CARDIOTOXICITY AMONG SURVIVORS OF CHILDHOOD CANCER

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Purpose/Objective: Anthracyclines can result in acute or chronic cardiotoxicity. The reported frequency of cardiotoxic effects in children is 0 * 16%.We planned this study to evaluate cardiotoxicity in children who have received anthracyclines
Materials and Methods: Children who received anthracyclines and were at least 2 years from receiving the drug were studied. Echocardiography was done to assess: Left atrial size; left ventricular internal diameter (LVID); Left ventricular ejection fraction; Mitral valve flow velocity; Peak early diastolic velocity & Peak late diastolic velocity. MUGA scan measured left & right ventricular ejection fraction. Data pertaining to age at the time of diagnosis and study, sex, drug received, cumulative dose, drug infusion rate & adverse reactions during therapy was retrieved from patient files. Any abnormal values of LVEF, RVEF, LVID, left atrial size or mitral valve flow velocity was defined as cardiotoxicity, with cut-off for LVEF & RVEF abnormality being < 50% & < 45%.
Results: Forty children were studied. Mean age was 12.1 years [6- 23]; median: 11.75 years. Cumulative dose of anthracyclines: mean - 239mg/m$^{2.}$ [90 - 480 mg/m^2]. No child had clinical cardiovascular abnormality. Prevalence of subclinical cardiotoxicity in this cohort was 65%. Abnormal left atrial size was seen in 35% and abnormal left ventricular dimension in 30%. Ten percent had an abnormal left ventricular ejection fraction with 20% having abnormal right ventricular ejection fraction. Male sex was found to be more predisposed to cardiotoxicity [p = 0.044]. Slow infusion of drug versus bolus significantly affected the occurrence of cardiotoxicity [p = 0-06]. Age at diagnosis, anthracycline used, cumulative dosage and nutritional status did not influence cardiotoxicity.

Conclusions: The prevalence of subclinical cardiotoxicity may be much higher than what is predicted. Patients who receive anthracyclines need regular cardiological evaluation and a long-term follow up. The long-term morbidity of these patients needs further exploration.

PUB-0188

DIET QUALITY IN AUSTRALIAN CHILDHOOD CANCER PATIENTS RECENTLY AFTER TREATMENT.

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Purpose/Objective: Optimal nutrition support is crucial throughout the childhood cancer trajectory. Growing evidence suggests that poor nutrition after childhood cancer treatment is associated with obesity, type 2 diabetes, heart disease, and osteoporosis in survivorship. This study aimed to determine the prevalence of poor diet quality in childhood cancer patients recently off treatment in an Australian population.
Materials and Methods: Diet quality of childhood cancer patients (2-18 years, <5 years after treatment), were assessed using The Australian Child and Adolescent Eating Survey (ACAES). To determine a child's diet quality, the Australian Child and Adolescent Recommended Food Score (ACARFS) was generated. This score reflects the relationship between their dietary diversity and nutrient adequacy (maximum score is 72, a good diet quality score is >50).
Results: Fifty-five parents provided dietary information on their child with cancer (child's mean age: 9.35 years). Twenty-nine percent of patients were overweight/ obese, greater than the Australian population rate of 24.9%. The mean overall ACARFS was 31.33 (SD 9.0, range 10-47). The mean ACARFS vegetable intake was 9.96 out of a possible 21, 6.26 out of 12 for fruit, 4.55 out of 11 for dairy and 2.25 out of a possible 7 for meat protein. The mean average daily energy intake of 9496kJ was higher than the national Australian average for children of 8922.4kJ. Patient's total average fat (81.44g) and sugar (140.88g) intake were also higher than the national average for children of 75.8g (fat), 135.4g (sugar).
Conclusions: Low ACARFS scores in this population indicate suboptimal diet quality, suggesting that these patients consume a limited variety of healthy foods. This suggests that poor diet intake may be manifesting early off treatment. Early dietary intervention may prevent this suboptimal nutritional state translating into increased metabolic risk as dietary habits established early in life are likely to continue into long-term survivorship.

PUB-0189

INFECTION RELATED MORTALITY DURING INDUCTION THERAPY OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN A SINGLE TERTIARY CARE ONCOLOGY CENTRE IN SOUTH INDIA

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Purpose/Objective: Morbidity and mortality due to infection during the induction phase of childhood acute lymphoblastic leukemia (ALL) continue to be a major concern in developing countries.Objective of this study was to analyze the epidemiology of infections in patients undergoing ALL induction therapy
Materials and Methods: We did a retrospective analysis of 154 patients treated as per UK MRC induction protocol over a span of 5 years from 2007 to 2012
Results: Out of 154 patients, 59 (38.3%) had febrile neutropenia. The commonest site of infection was the respiratory tract (18 patients, 30.5%). Microbiologically proven infections were recorded in 23(39%) of patients. Most of the bacterial isolates were gram negative bacteria 13 (57%), predominantly Escherichia coli, Pseudomonas and Acinetobacter, 2 (9%) were gram positive isolates namely Alpha hemolytic streptococcus and Staphylococcus epidermidis. Six patients (25%) had documented fungal infection, predominantly aspergillus and candida. Two patients (9%) had viral infection positive for influenza virus (H1N1). Out of these patients, only one (0.6%) died who had panresistant Acinetobacter sepsis. All the other patients with documented infections survived.
Conclusions: Gram negative bacteria were the predominant organisms causing infection in our ALL patients undergoing induction chemotherapy. Fungal infections should also be seriously considered in these patients. Even in developing countries the infection related mortality in childhood ALL can be minimized with good supportive care

PUB-0190

CLINICAL CHARACTERISTICS AND TREATMENT RESULTS IN CHILDHOOD HODGKIN'S LYMPHOMA: SINGLE CENTER EXPERIENCE

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Purpose/Objective: Childhood Hodgkin lymphoma varies from in developing countries to developed countries with epidemiological, clinical and histological features. In this study we aimed to investigate the clinical features and treatment results in childhood Hodgkin's lymphoma.
Materials and Methods: Eighty six patients, previously untreated, diagnosed as Hodgkin Lymphoma with biopsy were included in this study. The patients were treated with chemotherapy and involved field radiotherapy according to the stages. Patients were treated 2 cycles of ABVD in stage I and IIA, four cycles in IIB and IIIA, and six cycles MOPP/ABV in IIIB and IVA,B. Demographic features and treatment outcome were evaluated. Event-free survival and overall survival were estimated according to Kaplan-Meier.
Results: Male/female ratio was 66/21 (76%/24%) and the age was 84 ± 44 months (30-193 months). The most common histologic type was mixed cellular type (59%). The most common localization was head and neck (68%). Patients were classified as 7% in stage I, 55% in stage II, 23% in stage III, and 15% in stage IV. B symptoms were detected in 41% of patients.

Five and 10 year overall survival were 85% and 81%, event free survival were 80% and 76% respectively. According to stage, overall survival was 100% in patients with stage I, 95% for stage II, 78% for stage III and 78% for stage IV. There was significant relationship between stage and survival($p = 0.02$).
Conclusions: There is a predominance of mixed cellularity subtype, male sex and younger age in our study population. Results obtained with a combined modality therapy consisting of chemotherapy, modified according to stage are satisfactory. Survival rates improved over time by increasing support therapies.

PUB-0191

CHROMOGRANIN A IN NEUROBLASTOMA: CORRELATION TO STAGE AND PROGNOSTIC FACTORS

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Purpose/Objective: The aim of the study was to correlate blood concentrations of chromogranin A (CgA), chromogranin B (CgB), and neuron-specific enolase (NSE) to clinical course and prognostic factors in children with ganglioneuroma (GN) and neuroblastoma (NBL).
Materials and Methods: Blood samples from 69 controls and 31 patients with non-NBL or GN tumors and leukemias, and 89 patients with GN ($n = 8$) and NBL ($n = 81$), were analysed and clinical data extracted from the hospital records.
Results: CgA and NSE blood concentrations were significantly higher in neonates and infants with NBL ($P < 0.001$ and $P < 0.0001$) compared to controls. CgA and NSE concentrations were significantly higher in patients having advanced stage (stage 3-4) disease ($P < 0.05$ and $P < 0.005$, respectively, students T-test), MYCN amplified tumors ($P < 0.05$ and $P < 0.0001$, Mann-Whitney test), and tumors with loss of heterozygosity at the short arm of chromosome 1 ($P < 0.05$ and $P < 0.0005$, Mann Whitney test). Only NSE was correlated to tumor related death ($P < 0.05$, Mann Whitney test).
Conclusions: This study has shown elevated plasma and serum concentrations of CgA and NSE in patients with NBL and that the levels correlated to clinical stage and the presence of unfavorable genetic aberrations. This indicates that CgA and NSE may be used as prognostic markers when advanced molecular biology analyses are not available.

PUB-0192

TAKING THE EARLY WARNING SIGNS OF CHILDHOOD CANCER TO THE RURAL AREAS OF GAUTENG IN SOUTH AFRICA: TRAINING HEALTH PROFESSIONALS

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Purpose/Objective: Two thirds of children with cancer in South Africa never reach a specialist centre for treatment. The majority of those who present have advanced disease. In most cases the Health Professionals are not aware of the Early Warning Signs of Childhood Cancer, how to refer the children or where to refer the cases to.
Materials and Methods: CHOC Childhood Cancer Foundation has embarked on an awareness campaign in partnership with the Gauteng Department of Health and Social Development in South Africa to train every professional working in the local rural clinics to train them about the Saint Siluan Warning Signs of Cancer in Children and the work that CHOC does.
Results: The finding was that a longer and more formal education time was needed to improve the referral of earlier stage of disease. It was also apparant from the fall-off of the number of new patients over a period of time, that the educational awareness campaign needs

to be on-going and that the failure of improving the earlier stages of referral of paediatric cancer cases might be due to the time limit of the educational campaign.
Conclusions: Our aim is to reach cancer children at an earlier stage, to increase the survival rate, to have less disabilities and to ensure that every Health Professional are trained on the Early Warning signs of Childhood Cancer.

PUB-0193

RISK FACTORS FOR UNDERLYING VIT D DEFICIENCY IN CHILDREN WITH CANCER AT THEIR DIAGNOSIS FOR CANCER

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Purpose/Objective: There is increasing interest in the possible association between cancer incidence and vitamin D (Vit-D). Our recent study results showed a prominent Vit-D deficiency in our pediatric cancer patients during their fist admition to our clinic. This study has been designed as a questionare based research to find out possible risk factors for Vit-D deficiency.
Materials and Methods: Sixty patients that have been newly diagnosed as cancer and defined as Vit-D deficiency enrolled the study between 2010-2012. A questionare which included 32 questiones has been performed to each patient's family. Questiones are designed to determine risk factors for Vit-D deficiency like; daily sun light exposure, consumption of food that known as source of the Vit-D, suplementation during pregnancy, lactation periods or during infancy etc. Results were stuied with SPSS 11.5 program for istatistical analyses.
Results: Seventy patients with leukemias, lymphomas and solid tumors were included in the study. Fourtysix (66%) males and 24 females (34%) were between 6 months to 17 years old. Almost 60% of the patients have been borned during autumn or winter. During pregnancy 64% and during lactation 83% of the mothers have not been supplemented with Vit-D. Seventy four percent of the mothers did not have any knowledge about importance of the Vit-D. Supplementation of the Vit-D during infancy was not avaliable for 58% of the patients. Daily exposure to the sun light was between 0 to 6 hours (median:2.2 hours). Monthly consumption of fish and egg was between 0 to 5 times (median:1.3 time) and between 0 to 45 eggs (median:13.9) respectively. Daily consumption of the milk was between 0-2 glasses (median:1 glass).
Conclusions: Acording to our study, famillies are not aware of the importance of Vit-D. A special attention has to be given for education of parents for Vit-D supplementation during pregnancy, lactation and infancy.

PUB-0194

CYTOGENETIC FINDINGS IN ACUTE MYELOID LEUKEMIA: A DEVELOPING COUNTRY EXPERIENCE

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Purpose/Objective: Cytogenetics has now been well established as one of the most valuable prognostic factors in acute myeloid leukemia (AML). We describe cytogenetic findings and response to therapy in children with AML.
Materials and Methods: This is a retrospective study describing the cytogenetic findings and response to therapy in children diagnosed with AML from January 2006 to January 2013
Results: The cytogenetics could be done only for 34 out of 75 children diagnosed with AML. Clonal chromosomal abnormalities were detected in 29/34 (85.29%) of the patients. The chromosomal changes seen in this study in order of frequency were: t (8;21) in 6 (17.6%), t (15;17) in 6 (17.6%), trisomy 21 in 5 (14.7%), normal in 5 (14.7%), complex karyotyping in 4 (11.7%), 45 XO in 4 (11.7%), monosomy 7/del (7q) in 1 (2.9%), trisomy 8 in 1 (2.9%), t(11;17) in 1 (2.9%), inversion 16 in 1 (2.9%). We also categorized the patients in to favorable 13 (38.2%), intermediate 16 (47%), and unfavorable 5 (14.7%) prognostic groups. Notably, complete remission rates after first cycle of chemotherapy (CR1) was 11/13 (91.6%), 8/16 (50%) and 0/5 (0.0%) in favourable, intermediate and unfavorable group respectively. In favourable group one died in induction and 1 abandoned treatment. In intermediate 3 died in induction and 5 abandoned. In unfavorable 2 went in CR after two cycle of chemotherapy and 3 were refractory. The overall sustained CR1 rates were 5/11 (45.5%) [3 relapsed and died, 3 abandoned treatment] in favourable group, 3/8 (37.5%) [3 relapsed and died, 1 abandoned treatment, 1 relapsed patient is on treatment] in intermediate group and 0.0%[2 refractory patients died, 1 refractory patient is on treatment, 2 relapsed and died] in unfavorable group.
Conclusions: Cytogenetics affects outcome for children with AML even in the developing world settings despite high abandonment and sepsis as confounding factors.

PUB-0195

LEIOMYOSARCOMA OF INFERIOR VENA CAVA IN PEDIATRIC AGE- AN UNKNOWN ENTITY

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Purpose/Objective: Around 300 cases of leiomyosarcoma have been reported worldwide. Except for a 2-year-old child with leiomyosarcoma of a saphenous vein, no other case reports of leiomyosarcoma of vascular origin has been described in the pediatric age group
Materials and Methods: We collected data of children diagnosed with leiomyosarcoma at our centre from 2005-2012.
Results: We found only one case of leiomyosarcoma out of 800 children with cancer. He was a 13-year-old male, who presented with polycythemia, jaundice, dyspnea and right-sided abdominal pain. Chest x-ray was done in view of dyspnea which showed retrocaval shadow. On 2D ECHO mass abutting on the right atrium pushing the heart superiorly. CT-chest revealed a large 14.2×10.7cm supra-diaphragmatic mass lesion invading the IVC, superiorly abutting the right atrium and inferiorly depressing the diaphragm with no pulmonary metastasis. CT angiography confirmed the same and also revealed hepatic venous obstruction. The tumor was resected completely by a team of cardiac and hepatobiliary surgeons. The IVC and the right atrium were reconstructed using bovine pericardial grafts and the diaphragm with proline mesh. The tumor in hepatic veins came out as embolus during surgery, there was no resection of liver done. Post operative period was uneventful. The histopathology report along with immunohistochemical-staining positive for smooth-muscle-actin suggested a malignant mesenchymal tumor consistent with leiomyosarcoma of IVC/ right atrium. The final diagnosis was leiomyosarcoma of IVC of segment III with sub acute Budd-Chiari syndrome. The patient refused chemotherapy and got transferred to another centre.
Conclusions: Leiomyosarcoma involving right atrium and IVC is difficult to remove but a skilled team of surgeons can make it possible

PUB-0196

TUBERCULOSIS IN PEDIATRIC ONCOLOGY– A DEVELOPING WORLD EXPERIENCE

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Purpose/Objective: Tuberculosis (TB) is an important differential diagnosis of children with malignancies who have uncontrolled persistent fever, especially in the setting of high prevalence as in developing countries
Materials and Methods: Retrospective analysis of data of TB in pediatric-oncology patients admitted at our hospital between 2005-2012.The diagnosis was made on clinical and standard laboratory tools {Biopsy,Quantiferon- gold test, Adenosine-deaminase levels(ADA)}
Results: Eight cases of TB were diagnosed among 800 newly diagnosed cases of childhood cancer. The median age was 5.5 (2.9-13.5) years. The underlying diseases were five acute lymphoblastic leukemia, two acute myeloid leukemia and one Hodgkins lymphoma. The disease categories were two pleuro-pulmonary -TB, one cutaneous-TB, one hepatic-TB and one disseminated-TB. None had a positive family history of TB. The clue of TB was persistent fever in all except for one who was incidentally diagnosed during the pre-stem cell transplant investigations, one had skin eruptions and three had chronic cough with chest pain. We diagnosed one case by AFB positive on liver biopsy, another by positive quantiferon gold with elevated pleura- fluid-ADA, skin biopsy of another showed erythema nodosum and the rest clinically. We treated all cases with 4 drug anti-tubercular treatment (ATT) .There were 3 therapy-related mortalities, not attributable to TB. One child has completed treatment and is off ATT for 6 months, other two are on ATT, one had a very early CNS relapse and the other is doing well.
Conclusions: Tuberculosis is an uncommon but significant cause of PUO in the oncology setting, especially hemato-lymphoid malignancies

PUB-0197

MEDULLOBLASTOMA IN CHILDREN: REPORTS OF A SINGLE INSTITUTION

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Purpose/Objective: report clinical and epidemiological characteristics in patients over 3 years old with localized medulloblastoma (MBT), and compare overall survival (OS) and event free survival (EFS) with previous results and the published data.
Materials and Methods: retrospective analysis of records from patients admitted with diagnosis of medulloblastoma between November 2000- August 2008. At the same period 807 patients with solid tumor entered, 37 (4,58%) were medulloblastoma, 12 were older than 3 years old and had localized disease. They recived chemotherapy with vincristina, cisplatin and lomustine and craneospinal radiotherapy.

Results: The mean age at diagnosis was 7,4 years old (range 4,6 to 11,9 years). Male to female ratio was 5:1.

75% (9/12) classic MBT, and desmoplastic 25% (3/12). Most common symptoms were headache and vomiting (66,66%), ataxia (58,3%) weigth lost (33,33%), and visual disturbans (25%). Total resection was done in 75%,partial in 25% and RDT in all of them. (EFS 77,7% vs 33, 33%). Four patients discontinue treatment (1: by infection, 3: by hearing loos). Progresions occurred in 2 patients (1: local, 1: meningeal), relapses in 2 patients (1: local 2: meningeal), all died. Event Free survival was 66,6% and OS was 66,6%. Median follow up was 7,9 years (range 0,8 to 9,7 years). Most common sequel were endocrinol—gic (75%), gait disturbances, learning and hearing loss (50%).

Conclusions: Comparing our results with previous protocols, the patients achieve better survival. The total reseccion was an independent prognostic factor. The OS and EFS in our cohort were lower than literature. Probably our patient had bigger tumors and worst perfomance status at diagnosis. Our objective is improve early diagnosis and support therapy.

PUB-0198

PEDIATRIC MESENTERIC NEUROENDOCRINE TUMOR: A CASE REPORT FROM DHARMAIS CANCER HOSPITAL, JAKARTA, INDONESIA.

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Purpose/Objective: Neuroendocrine tumors are a diverse group of neoplastic entities identified by specific symptoms related to hormonal secretion, and are recognized by their immunohistochemical staining patterns. We report a pediatric case from the Dharmais Cancer Hospital, Jakarta, the largest oncology hospital in Indonesia.

Materials and Methods: A 10 year old boy presented at a private hospital in Jakarta with severe vomiting, pallor, anorexia, prolonged diarrhea and weight loss. A palpable abdominal mass was confirmed on CT scan; a mesenteric tumor measuring approximately 10 cm was detected. Surgical resection was done. Histopathological examination, combined with imunostaining positivity for synaptophysin, established the diagnosis of neuroendocrine tumor. He was discharged home, but two to three weeks later presented at Dharmais Hospital with a left neck mass. PET scan revealed increased uptake in the left neck as well as the primary site in the mesentery.

Results: The patient received two cycles of chemotherapy with cisplatin and etoposide, after which the left neck mass resolved. PET scan following the third cycle of cisplatin/etoposide returned to normal. Urinary 5HIIAA excretion, measured after completion of six treatment cycles, was not elevated. He remains clinically free of tumor three weeks post completion of chemotherapy.

Conclusions: Pediatric neuroendocrine tumors, though rare, are amenable to surgical resection and respond to chemotherapy. Long term follow up and monitoring is required to ensure durable remissions.

PUB-0199

CYTOMEGALOVIRUS INFECTION AND DISEASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose/Objective: CMV infection has significant morbidity and mortality in immunocompromised children undergoing HSCT. Data on CMV infection in patients on standard chemotherapy is limited. Our study objective was to evaluate CMV infection and disease in children with Acute Lymphoblastic Leukemia (ALL) on standard chemotherapy.

Materials and Methods: Prospective evaluation for CMV infection was done in newly diagnosed ALL children (< 12 years). Baseline CMV IgG and IgM, CMV pp65 antigen assay and CMV RT-PCR were done at diagnosis. CMV pp65 antigen and PCR were repeated after induction, intensification, and early maintenance. Children with prolonged febrile neutropenia (FN) [$>$ 7 days] were also screened for CMV.

Results: Fifty four children (median 6.0 years[1-12]) with ALL were serially monitored. Fifty two had baseline CMV IgG positive and 13/54 were IgM positive. No child demonstrated pp65 antigenemia. Seven children were positive by PCR at various time points. Three after intensification, two post-induction, one child twice: at diagnosis & intensification, one after starting maintenance. Patients were largely asymptomatic. However, three had prolonged neutropenia. All episodes resolved without specific therapy.

Nineteen episodes of prolonged FN were evaluated. Three (16%) were positive for CMV PCR. CMV pp65 antigen assay was positive in 2/3. Two had pneumonia (1 with added GI symptoms), one CMV retinitis. Two children were treated successfully with Ganciclovir, one child succumbed to pneumonia.

Conclusions: Fifty two (96%) children had been exposed to CMV prior to diagnosis of ALL. Seven children, essentially asymptomatic, had CMV infection during therapy. Sixteen percent of children with prolonged FN had CMV disease. CMV pp65 antigen assay is not reliable in this patient subset. We recommend investigating for CMV infection in prolonged FN. Large multicentric studies will identify the magnitude of this infection in patients with malignancies.

PUB-0200

ACUTE PROMYELOCYTIC LEUKAEMIA(APL): A SINGLE CENTRE EXPERIENCE IN AFRICA.

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Purpose/Objective: To review all the cases of APL diagnosed and treated over a ten year period at Red Cross War Memorial Children's Hospital (RCWMCH).

Materials and Methods: A retrospective analysis of the charts of children treated for APL at RCWMCH between January 1999 and December 2009.

Results: In this 10 year period, 98 children were diagnosed and treated for Acute Myeloid Leukaemia (AML). 15 of these 98 children had APL. These diagnoses were made on bone marrow morphology, flow cytometry and cytogenetic analysis of the patient's blasts. Each child in this group had clones carrying the classic translocation (15; 17) mutation. The age of presentation of these children was between 35 to 149 months. There were 10 females and 5 males. All of these children were treated with ATRA 45mg/m^2 for 30 days, with a further 60 days of ATRA if there was a response to therapy. 12 were treated with a modified Berlin-Frankfurt-MŸnster (BFM) 87 protocol. 3 received treatment with a protocol based on United Kingdom Medical Research Council (UK MRC) AML 15. All, except 2 of these patients were alive at 20months after completion of therapy. 1 had died due ATRA syndrome 4 days after diagnosis; the other was in remission when killed in a motor vehicle accident within 1 year of treatment completion.

Conclusions: APL comprised 15.3% of all patients diagnosed and treated for AML between 1999 and 2009. All patients demonstrated the classic t (15; 17). There was an excellent 20 month survival rate (Overall survival 90%).

PUB-0201

COMPARING PATIENTS WITH WILMS' TUMOR IN KHCC REGISTRY AND THE SEER DATABASE

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Purpose/Objective: Wilms' tumor is the most common malignant renal tumor in children. It is characterized by high sensitivity to chemotherapy and radiotherapy and by its good prognosis.

Materials and Methods: We conducted a search for patients with Wilms' tumor in both the POND database (adopted by KHCC since 2006) and the SEER database (26% of patients with cancer in US are recorder). Pediatric patients (< 18 years at diagnosis) were selected.

Results: We compared 60 patients treated at KHCC (2006 till 2012) to 778 patient registered in the SEER database (2004 till 2009). The median age of patients was similar (KHCC, 2.7 years; SEER, 3 years). Gender distribution was similar (KHCC, 50% females; SEER, 53% females; $P = 0.45$). There was no significant different in the rate of metastatic disease (KHCC, 20%; SEER, 25%; $P = 0.53$) and bilateral renal involvement (KHCC, 17%; SEER, 8%; $P = 0.051$). There was no difference in the use of radiotherapy among the 2 groups ($P = 0.37$). The 2-year survival was similar in the 2 groups (log-rank test, $P = 0.16$).

Conclusions: Our analysis showed similar features and outcomes of patients with Wilms' tumor treated at KHCC to those registered in the SEER database.

PUB-0202

EVALUATION OF DO NOT RESUSCITATE ORDERS AT A SINGLE CENTER IN JORDAN

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Purpose/Objective: DNR orders are crucial in planning end-of-life care. Successful discussion of these orders depend on family background, care giver's perceptions and patients conditions

Materials and Methods: We retrospectively analyzed charts of patients who had DNR orders placed between January 2006 and December 2011. We analyzed demographics, DNR order documentation, and timing of DNR orders in relation to diagnosis and death.

Results: We evaluated the charts of 76 patients (44 males). The median age at diagnosis was 5 years (range, 0 to 16.7). DNR orders were obtained from first attempt in 55 patients (76%). The majority of orders were obtained by primary oncologist (92%), while the rest were placed by palliative care team and intensive care consultants. Orders were placed in the outpatient clinic (48%), in-patient unit (41%) or intensive care unit (11%). The median duration from DNR order placement to death was 2.1 month (range, 0 to 25) and was

significantly longer for patients with solid tumors (3.4 months) in comparison to CNS tumors (1.6 months) and Leukemia/Lymphoma patients (0.4 months); $p = 0.022$.
Conclusions: Our study showed no clear obstacles in placing DNR orders among our patients. We believe that better analysis requires better documentation of the process including all unsuccessful attempts to place the order. Patients with leukemia/lymphoma in our center should have end-of-life planning done at an earlier stage.

PUB-0203

RECURRENT MONOPHASIC WILMS' TUMOR IN PELVIC KIDNEY - A THERAPEUTIC CHALLENGE

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Purpose/Objective: To report an unusual case of repeated loco-regional recurrences in a patient with stage I low-risk monophasic (epithelial variant) Wilms' tumor (WT) of pelvic kidney requiring aggressive therapy over a decade.
Materials and Methods: Hospital database was reviewed.
Results: One year boy presented with lower abdominal lump (6×5cm). Investigations showed WT in left ectopic kidney. Left nephroureterectomy was done; HPE confirmed WT with predominant tubule formation, minimal atypia and mitosis (stage I). Repeat CECT a month later showed thrombus in infra-hepatic inferior vena cava (IVC) and right common iliac vein with paraaortic and iliac lymphadenopathy. This was followed by early abandonment of therapy; the patient received only 2 cycles of VAC. Local relapse in retroperitoneal lymph nodes occured after 7 years. After 6 cycles of ICE chemotherapy, RPLND was done but HPE showed no tumor. Second recurrence ocurred 14m later in mesocolic lymph nodes that was completely excised; followed by 6 cycles of IE chemotherapy and 20 Gy whole abdominal irradiation. Histopathology was similar. 3rd recurrence - a large pelvic mass ($15 \times 8 \times 7$cm); trucut biopsy showed epithelial predominant WT. 6 cycles of Paclitaxel based salvage chemotherapy followed by excision of the retro-vesical tumor and boost radiotherapy of 10.8 Gy to the pelvis given. A year later, though free of local or distant relapse, has acute renal failure owing to radiation nephritis of contralateral kidney, is on regular dialysis and waiting for renal transplantation. We plan to excise the persistent calcified thrombus in subhepatic IVC that could be harboring a nidus of tumor cells before renal transplantation is contemplated.
Conclusions: Inert tumor cells in the calcified IVC thrombus has possibly caused the repeated loco-regional recurrences of a low-risk localized monophasic WT. The importance of initial completion of therapy and need for long term follow-up cannot be overemphasized.

PUB-0204

OVEREXPRESSION PRMT5 IN BONE MARROW CELLS OF CHILDHOOD WITH ACUTE LYMPHOBLASTIC LEUKEMIA INDICATES POOR PROGNOSIS

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Purpose/Objective: To verify the change of expression Protein arginine methyltransferases 5(PRMT5)in children with acute lymphoblastic Leukemia (ALL) in different therapy time point and it's clinical value in individual chemotherapy.
Materials and Methods: Bone marrow of children with ALL at diagnosis and follow-up different therapy time point were detected PRMT5 expression by quantitative PCR;At the same time PRMT5 values will be compared to those values such as BCL-ABL,TEM-AML1 and E2A-PBX1 in the patients, PRMT5 values will be compared to minimal residual disease level monitoring by flow cytometry detecting the abnoraml immnunephenotype of blast cell in the different therapy time point.
Results: The PRMT5 level of the blast cell is more higher than that of normal bone marrow cell. With the proceeding of chemotharepy, the PRMT5 level of the blast cell is decreasing. The PRMT5 level of the relapse patients's blast cell re-increaseing when relapse. The PRMT5 level of the older patients (age more than 10 years) is strongly higher than the patients whose age are less than 10 years and more than 1year($p = 0.000$). The PRMT5 level of the patients with BCR-ABL fusion gene is strongly higher than the patients without fusion gene($p = 0.021$). The PRMT5 level of the patients T cell ALL is strongly higher than the patients with prognitor B cell ALL($p = 0.025$).
Conclusions: Form our study PRMT5 level have the positive relativeship with the blast cell load. Overexpression PRMT5 in bone marrow cells of childhood with acute lymphoblastic Leukemia indicates poor prognosis. It would be a useful factor for re-classifying the risk and readjust the chemotherapy, it will important affect in the individal therapy for the patients with ALL.

PUB-0205

ANAPLASTIC LARGE CELL LYMPHOMA'S IN CHILDREN. A SINGLE EXPERIENCE OF MOROCCAN INSTITUTION.

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Purpose/Objective: Anaplastic large cell lymphoma (ALCL) represents 10% of children lymphomas in literature. Our objective is to study clinical features and outcome of children ALCL treated in Casablanca university medical center in Morocco, and address the difficulties to manage such tumors.
Materials and Methods: Data of patients aged less than 20 years diagnosed with ALCL from January 2003 to December 2012 were retrospectively collected. The diagnosis was histologically made. The treatment was according to the HM 91 protocol before 2009. Since 2009, the treatment was based on ALCL 99 protocol.
Results: Sixteen patients were enrolled. ALCL represents 6% of newly diagnosed pediatric lymphomas and 1.4% of all children hematological malignancies. The median age was 13 years with a range from 5 to 2o years. The H/F ratio was 3. The annual incidence was 1.5 cases per year. The average diagnosis delay was 4 months. The most common primary site was: lymph nodes in 56% of cases, mediastinum in 19% and skin in 12%. The ALCL was histologically T type in 82% of cases and null type in 28%. The immunohistochemistry to identify the Alk protein was performed in 10 patients (62%), it was positive in 7 patients (70%).Three patients had lung metastases. Five patients (37.5%) kept maintained complete remission after a median follow-up of 59 months. Four patients (25%) relapsed and underwent 2nd line chemotherapy. Two patients died by progressive disease and five patients (31%) were lost to follow-up. The 5-year EFS and OS were 42% and 78% respectively.
Conclusions: ALCL is a very good prognosis tumor in children. The high rate of patients lost to follow-up is still high in our conditions which made difficult the management of such disease.

PUB-0206

PARASPINAL NEUROBLASTOMA WITH OPSOMYOCLONUS ATAXIA SYNDROME

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Purpose/Objective: To report a toddler with paraspinal thoraco-abdominal Neuroblastoma (NB) with opsomyoclonus ataxia (OMA) syndrome who was successfully treated with combination of surgery, chemotherapy and immuno-modulators.
Materials and Methods: Hospital database and the case report were reviewed.
Results: A $1\frac{1}{2}$-year-old girl presented with classical features of OMA syndrome (progressive ataxia, gait disturbance, difficulty of speech, and opsoclonus). To start with, she had pyrexia of unknown origin at the age of 1 year. Detailed neurological workup was negative for any organic CNS pathology. Further evaluation revealed 5.2×2.3 cm solid mass in the right paraspinal region abutting D_{10}-L_1 vertebral bodies without intra-spinal extension. The family did not seek any treatment for next 4 months. Repeat imaging in our hospital revealed no increase in size of the tumor. Trucut biopsy of the lesion showed a malignant blue round cell tumor. 24- hour urinary VMA and metastatic workup were negative. Trans-diaphragmatic resection was done through the abdominal route; R_1 resection was done. HPE and IHC confirmed Stage 2A low risk (COG) Neuroblastoma. Flowcytometry showed an aneuploid population with a DNA index of 1.47 and total S- phase fraction of 10.39%. FISH analysis was negative for N-Myc amplification. Postoperatively, she was given 4 cycles of chemotherapy (Cyclophosphamide, Doxorubicin and Vincristine). She also received IVIG and prednisolone for the OMA syndrome, but her cerebellar symptoms progressed. Rituximab therapy was then started and continued for total 4 weeks without any side effects. She has been followed up for 21 months with no recurrence (MIBG proven) and near resolution of OMA Syndrome.
Conclusions: OMA syndrome is a rare neurobehavioral paraneoplastic disorder in children with neuroblastic tumors. The neurologic symptoms are generally treated with a number of immunosupressive and immunomodulating agents. We add evidence that Rituximab is a promising, and safe therapy for OMA syndrome in children with neuroblastoma.

PUB-0207

A RAPIDLY EXPANDING INFANTILE FIBROSARCOMA OF HAND: CASE REPORT

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Purpose/Objective: Infantile fibrosarcoma (IF) is the most frequent soft tissue tumor in the first year of life. Surgery is the mainstay of treatment but it can be mutilating dependig on the tumor«s size or location. Chemotherapy (CHT) may shrink the tumor to facilitate surgical resection.
Purpose: To report a case of IF of hand

Materials and Methods: Description of clinical features, diagnosis, treatment modalities, and patient outcome.
Results: A 4-month-old male was admitted at our hospital with a rapidly expanding mass noted during the first week of life, involving his right hand on the second intermetacarpal space and initially considered as a vascular tumor. At the age of 3 months a biopsy was performed in another institution, with inconclusive diagnosis. At our hospital, a large, firm, red-wine colored mass, with ulcerated and bleeding area that involved almost all the hand was observed. Staging workup was performed and no metastatic disease was detected. The preliminary biopsy«s report described a small-blue-round cell tumor. Due to life-threatening tumoral bleeding and judged by surgeons to require a hand amputation, empiric chemotherapy with Vincristine/ Actinomycin D (VA) was started while waiting for final biopsy diagnosis. A clinical response was observed within a few days. The definitive diagnosis of IF was confirm with the positive rearrangement of ETV6 gene. The regimen of chemotherapy was completed according to E*pSSG*nonRMS2005 Protocol with *Very Good Partial Response* and a conservative surgical tumor«s resection could be performed. The patient developed moderate drug-related toxicity (Anaemia, catheter related infection and febrile neutropenia grade 3).
Conclusions: As other literature reports, our case showed that IF is a chemosensitive tumor and chemotherapy allowed a conservative surgery. Initial surgery is only recommended if tumor is potentially resectable without mutilation. A chemotherapy regimen based in VA without anthracyclines and alkylating agents have high rates of response, with acceptable toxicity.

PUB-0208

RISK AND BENEFIT OF PREOPERATIVE CHEMOTHERAPY FOR PEDIATRIC RENAL TUMOR: A REPORT FROM THE SINGLE INSTITUTION IN JAPAN

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Purpose/Objective: The current treatment strategy of Wilms tumors in Japan has been based on the regimen of JWiTS (Japanese Wilms Tumor Study) established in 1996. The regimen is based on the NWTS/COG (National Wilms Tumor Study/Children's Oncology Group) protocol characterized by initial radical operation followed by postoperative adjuvant therapy. In our department, the strategy is fundamentally based on the regimen of JWiTS, however, the regimen of SIOP (International Society of Pediatric Oncology) characterized by preoperative chemotherapy has been administered for some unresectable cases. Our current strategy of pediatric renal tumor has been assessed, especially, the risk and benefit of preoperative chemotherapy.
Materials and Methods: Sixty-two cases of renal tumor was treated in Kyushu University hospital from 1963 to 2011. Eleven cases were initially treated by preoperative chemotherapy. Clinical features and outcome was analyzed.
Results: Intraoperative complication including tumor rupture or spillage was not recognized. Reduction in size was observed in 7 of 11 cases (63.6%) and down-staging was accomplished in 6 of 7 cases (85.7%) (stage3 & 4). Inappropriate regimen was performed for two cases (CCSK and MRTK). In addition, 3 cases of stage 5 did not show effective volume reduction by preoperative chemotherapy. In that case, the mesenchymal histology might affect the result.
Conclusions: In the cases of good responder for preoperative chemotherapy, down-staging and the risk of intraoperative complication can be decreased. Although the effect of decreasing in size was recognized, long-term preoperative chemotherapy includes a risk of undertreatment for unfavorable histology cases. For the cases which showed an insufficient volume reduction by preoperative chemotherapy, early conversion for operation should be considered.

PUB-0209

THE ROLE OF PREOPERATIVE CHEMOTHERAPY IN TREATMENT OF HEPATOBLASTOMA; A SINGLE INSTITUTIONAL EXPERIENCE.

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Purpose/Objective: To analyze treatment results of children with hepatoblastoma in a Japanese single institute.
Materials and Methods: Medical records of consecutive 21 patients who were diagnosed and treated at Kanagawa Children's Medical Center between 1991 and 2011 were reviewed.
Results: Median age at diagnosis was 21-month-old (range 0 * 132 months). Median serum AFP value at diagnosis was 313650 ng/ml (441 * 2×10^6 ng/ml). PRETEXT was I to II in 4, and III to IV in 17 patients. Three had distant metastases at diagnosis. Curative surgery, including liver transplantation (n = 2), was performed in 18 patients (85.7%). Fifteen patients received chemotherapy before curative surgery. Preoperative chemotherapy was started with cisplatin and THP-Adriamycin (CITA) in all cases. Six patients received CITA repeatedly, and 9 patients received CITA plus other regimens before curative surgery. Postoperative chemotherapy was performed in 8 patients. Overall survival in 21 patients was 64.6%. Survival of patients with localized disease (PRETEXT I or II) was 100%, whereas survival of patients with advanced disease (PRETEXT III or IV) was 56.1%. Initial response to chemotherapy, that was evaluated by AFP decline, was tended to be associated with prognosis. Among patients who had advanced disease and received preoperative chemotherapy (n = 14), survival of 6 patients in whom AFP decreased more than 1 log after the first CITA was 83.3%, compared with 33.3% of survival in 8 patients whose AFP decline was less than 1 log (P = 0.123). Among patients who had advanced disease and received preoperative chemotherapy and curative surgery (n = 11), median AFP level at surgery relative to the value after the first CITA was 0.05 or 1.03 in patients who received repeated courses of CITA or other regimens after CITA (P = 0.046).
Conclusions: Effective salvage chemotherapy regimen for poor CITA responders is needed to be developed.

PUB-0210

SYNOVIAL SARCOMA IN CHILDREN AND ADOLESCENTS: REPORTS OF A SINGLE INSTITUTION

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Purpose/Objective: Report epidemiology and overall survival in patients with diagnosis of synovial sarcoma (SS) and compare them with the publicated data.
Materials and Methods: Retrospective analysis on records from 14 patients admitted between January 1997- December 2012. Risk stratification was based on IRS staging. All received surgery plus chemotheraphy and radiotherapy according to differents SIOP protocols
Results: 154 patients with sarcomas tumors were admitted, 54 patients with diagnosis of soft tissue sarcomas, 14 of SS. The mean age at diagnosis was 11.75 years (range 5.3 to 16.5 years). The male to female ratio was 1.8:1. Three patients refuse or abandon treatment (one at the beginig and two averaging treatment) so that, they were excluded.
The most common primary tumor sites were lower extremities n = 12 (85%),
Disease groups, according to IRS were: GI n = 5; GII 2,; GIII 4, and GIV 1. Not known: 2
Tumor size was greater than 5 cm in 11 of 13 (85%) patients
10/11 patients recieved surgery and chemotherapy.
1/11 was irresecable (mediastinum)
6/11 recived radiotherapy
Median follow up was 4.8 years from diagnosis (range 1 to 6.25 years) Progresions occurred in 2 patients (both dead) Relapses occurred in 2 patients (1 local and 1 combined) All survive after multiple recurrences (local and distance)
Event Free survival was 63% and Overall survival was 81%.
Conclusions: Like reported in literature multimodality treatment, based in adecuate resection surgery plus chemotherapy and radiotherapy seems to be the best approach to increase cure rates in children and adolescents with SS.We also have high survival rate for initial and relapsed desease
Multicenter randomized clinical trials with a larger number of patients are needed to determine a risk-based treatment for these patients.

PUB-0211

DATA ANALYSIS OF DAY CARE AND OUTPATIENT FACILITIES AT CHILDREN'S HOSPITAL LAHORE, PAKISTAN: ARE WE DOING ENOUGH?

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Purpose/Objective: In developing countries there is a lot of emphasis on ward facilities but good daycare and outpatient facilities are very important for good outcomes for patients whose treatment may last for 2-3 years. An efficient daycare facility and minor procedure room play an important role in reducing the burden on the ward. The Children's hospital is a tertiary government center with 6-bedded chemotherapy bay along with a transfusion room and procedure room. The Oncology department receives over 500 new cancer patients per year. The purpose of this study was to analyse the data of patients enrolled in day care center from 1.1.12 -31.12.12 to look for efficiency of its working, to evaluate the workload and assess how it can be improved further.
Materials and Methods: The day care services are supported by the social welfare department, clinical psychologist and up-to-date oncopharmacy and charity-run hostel. Retrospective review of patients with ALL and biopsy proven solid tumors was done. Data regarding age, sex, diagnosis, histopathology, chemotherapy and intrathecal sessions and outcome were recorded and analyzed.
Results: Total 340 patients were included with age range 1-16(44% = < 5 yrs). 125(37%) were females. The diagnosis was Acute Lymphoblastic leukaemia in 187(55%), Hodgkin

Lymphoma 49(15%), Wilm tumor 38((12%), Germ cell tumour 14(4%), Retinoblastoma 12(3.6%), Langerhans Cell Histiocytosis 10((3.4%), Neuroblastoma 24(7%) and Nonhodgkin lymphoma in 6(2%).patients Total 8,050 chemotherapy and 1,940 IT sessions were given during this time period, with average of 620 chemo sessions and 150 ITsessions.
Conclusions: Our day care clinics have reduced the ward workload and the number of patients being admitted for chemotherapy.All this has enhanced the quality of care being provided. In future we want to improve our pain management facility and to involve more social support groups to reduce lack of attendance, and in turn improve final outcome.

PUB-0212

PROTON MAGNETIC RESONANCE SPECTROSCOPY AS A PREDICTOR OF SURVIVAL IN CHILDREN WITH DIFFUSE PONTINE GLIOMA

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Purpose/Objective: To investigate metabolite changes in diffuse pontine gliomas using proton magnetic resonance spectroscopic imaging (^{1}HMRSI), thereby predicting tumor response and prognosis
Materials and Methods: Five children (6-9 years old) diagnosed with diffuse pontine gliomas were evaluated using 1H MRSI technique on a 1.5Tesla scanner. MR spectral data was obtained using ^{1}HMRSI point-resolved spectroscopy sequence (PRESS TR/TE = 1000/144ms) corresponding to voxels overlaid on FLAIR images. Metabolite abnormalities were determined by calculating choline (Cho), N-acetyl aspartate, (NAA), myo-Inositol (mI) and lactate (Lac) values relative to creatine (Cr). Cho/NAA, Cho/Cr and mI/Cr ratios in the tumor affected region were compared with normal brain tissue.
Results: In two patients, Cho/Cr (2.0-2.6 vs 1.13) and mI/Cr (0.47 vs 0.34) ratios were elevated but NAA/Cr (1.50-1.60 vs 1.62) ratio was close to normal. In the other three patients NAA/Cr ratios were reduced (1.20-1.27 vs. 1.62), while Cho/Cr (2.06-2.50 vs. 1.15) and mI/Cr (0.49-0.53 vs. 0.34) ratios were elevated. Lactate was elevated in all the spectra but no lipid peaks were obtained. Two patients responded well to radiotherapy with survival rate greater than 1 year while the other three children survived only six months despite radiotherapy.
Conclusions: Normal NAA/Cr ratio and elevation of Cho indicates intermingling of tumor cells with neurons and no neuronal destruction suggesting better prognosis and response to treatment. Reduced NAA/Cr accounts for neuronal destruction which portends graver prognosis. Hypoxia and hypoxia-inducible factor-1 (HIF-1) pathways are associated with angiogenesis and tumor progression. Elevation of Cho/Cr and mI/Cr ratios (suggesting rapid cell turnover) and lactate build-up due to hypoxia suggest tumor progression. ^{1}HMRSI metabolite mapping of tumors serves as biomarkers for tumor progression and predictor of response to treatment.

PUB-0213

CONGENITAL NEOPLASMS IN NEWBORNS

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Purpose/Objective: The incidence of malignant neoplasms in newborns is 1.8 - 3.6 per 10,000 livebirths. Several multicenter studies demonstrated an association of congenital neoplasms with different malformations. Epidemiology and stratification of neoplasms in the neonatal period is of particular interest as the data are very limited. The goal was to study the stratification of congenital neoplasms and malformations and to evaluate the methods of early diagnosis.
Materials and Methods: Retrospective study was conducted that included 3,654 patients ranged in age from 6 to 28 days admitted to the Pediatric Service between 2008 and 2011
Results: Of 3,654, 108 patients (2.95%) were diagnosed with benign or malignant neoplasms. Hemangioma was the most predominant neoplasm and was present in 84 cases (77.7%). Other solid tumors were present in 24 (22.3%) cases: kidney neoplasm (Wilms tumors) in 3(2.7%), adrenal neuroblastoma in 2 (1.8%), brain tumor in 1 (0.9%), tumor of the eye - retinoblastoma in 1 (0.9%), soft tissue tumor in 1 (0.9%). Teratoma was diagnosed in 4(3.7%) cases: sacrococcygeal (3) and ovarian (1). One patient had abdominal yolk sac tumor and sacrococcygeal teratoma. Neoplasms of oropharynx in 2 (1.8%), liver in 5 (4.6%) and lien in 3(2.7%) cases were cystic. Prenatal diagnosis of anomalies and fetal tumors is based on US characteristics, and organ specific and tumor specific symptoms. Signs suggestive of fetal neoplasms were distortion of the contour, shape, size, fetal anatomy, changes of the moving pattern, polyhydramnios and fetal hydrops. Congenital neoplasms were diagnosed prenatally by US in 22 (20%) cases.
Conclusions: Congenital malignant tumors in newborns are rare. Diagnostics of tumors in neonatal and particulaly prenatal period is difficult. Inerdisciplinary approaches is required for early diagnosis and correct management of newborns with neoplasms

PUB-0214

HEPATOPATHY-THROMBOCYTOPENIA SYNDROME (HTS) IN A CHILD WHILE RECEIVING ACTINOMYCIN-D THERAPY FOR WILMS TUMOR (WT)

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Purpose/Objective: HTS is a severe complication very similar to vein occlusive disease in children receiving chemotherapy for WT. It's characterized by fever, hepatomegaly, ascites, weight gain, jaundice, elevated levels of transaminases and severe thrombocytopenia. Actinomycin-D (Act-D) is the probable cause of this syndrome. We report a case of severe HTS in a child while receiving Act-D containing chemotherapy for WT.
Materials and Methods: A six-year-old girl was admitted in our unit for the complaint of abdominal pain. Radiological findings identified a well-defined solid mass ($12 \times 11 \times 9$ cm) in the left kidney.
Results: The patient was enrolled in Turkish Pediatric Oncology Group (TPOG) WT Study protocol and received preoperative chemotherapy regimen consisting of vincristine, 1.4 mg/m^2, once weekly, for 4 weeks and Act-D, 15μg/kg/day, x5 days, the first week. The patient was subsequently managed with complete resection of the mass with left radical nephroureterectomy and histology revealed a WT with diffuse anaplasia. She received postoperative chemotherapy and external radiotherapy according to TPOG WT Study-Stage III Unfavorable histology protocol. After the first administration of Vincristine and Act-D, the patient was hospitalized because of fever and oral mucositis. Blood tests revealed pancytopenia. On the third day of antibiotherapy her clinical condition worsened with abdominal distension. Abdominal ultrasound confirmed a moderate enlargement of liver and spleen with ascites. Hepatic and portal venous flows were normal. Blood tests showed severe thrombocytopenia (1000 /μL) and very high levels of hepatic enzymes (AST/ALT: 2354/1088 IU/L). The coagulation parameters were abnormal. The patient was treated with life support treatment (blood, plasma and platelet transfusions, fluid and albumin infusion, diuretics, dopamine) but clinical conditions did not improve and the patient died of pulmonary hemorrhages on the fifth day.
Conclusions: Although Act-D related hepatotoxicity is a historically well-known problem, HTS is rare, life-threatening and often not well-recognized condition in children with WT receiving Act-D containing chemotherapy.

PUB-0215

RELAPSE OF ALL AT CHILDREN IN KYRGYZSTAN

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Purpose/Objective: To study the features of relapse in children with ALL who were treated on a protocoll ALL-BFM-96 in Kyrgyzstan.
Materials and Methods: From 2001 to 2012, was under the supervision of 850 patients with ALL, of whom 178 patients had relapsed disease in 22%. Early relapse was 9%, and late relapse of the disease in 13%. Bone marrow relapse was 18%, CNS and testicular relapse in 4%.
Results: Early relapses at 1 year of treatment 16.5% were in children with high-risk disease, the initial leukocytosis in these patients ranged from 100 to 300 white blood cells, of which 6% of patients had T-cell ALL,2.5% of testicular and 5% had CNS relapses. The most frequent relapses were after 20-24 months from the remission. In 65% relapse was caused by failure to comply with maintenance treatment in the second year of treatment. Parents are leaving home did not comply with maintenance therapy, they were not given time to drugs mercaptopurine and methotrexate, they did not study of blood. Survival of patients with late relapse who underwent PSCT was 60%, without it 10%. In Kyrgyzstan about 80% of households are families with many children, almost all patients had transplants from siblings donors. Patients with early relapse of high leukocytosis and T-cell immunophenotype, testicular relapse, CNS died in the first months of therapy.
Conclusions: In Kyrgyzstan, in children with ALL was observed in 22% of late relapses of the disease, of whom 16.5% of late relapses of the disease. Almost all later relapse were the fault of the parents, because they did not comply with treatment in the second year of treatment, while at home the children were not given supportive therapy mercaptopurine and methotrexate. PSCT was from sibling donor and survival 60% and survival 5% without it.

PUB-0216

PROFILE OF FEBRILE NEUTROPENIA IN CHILDREN - A STUDY FROM A TERTIARY CANCER CENTER IN INDIA

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Purpose/Objective: Febrile neutropenia (FN) is common in patients undergoing chemotherapy. The objective of this study was to study the profile of FN in pediatric cancer patients.
Materials and Methods: All children less than 18 years with FN admitted at our center between January 2011 and November 2012 were analyzed for their demographic characteristics, clinical profile, microbiologic isolates and mortality.

Results: There were 144 episodes of FN during the study period. The mean age was 8.371. Leukemias comprised 129 (89.6%) and solid tumors accounted for 15 (10.4%) episodes of FN. Induction related episodes were higher compared to other phases of treatment (38.2% vs 31.3% in consolidation vs 11.1% in maintenance). First line antibiotics (cefipime, Cefaperazone- Sulbactum + aminoglycoside), second line antibiotics (carbapenam) and antifungals were used in 58.3%, 10.4% and 25.6% cases respectively. Amphotericin B was the commonest antifungal used followed by Voriconazole (18.1% vs 2.1%). Antifungals were started empirically in 21(56.75%) episodes and preemptively in 16(43.25%) episodes. Gram positive agents were needed in 20 (13.8%)episodes. Indications for use were pneumonia (8 patients), MRSA (2), mucositis (6) and line infections (4). Blood culture isolates was seen in 20 patient episodes (13.9%). Gram negative organisms were the commonest organisms isolated in 11 patients. Pseudomonas, Klebsiella and E.coli were recovered in 5,4 and 3 cases respectively. All the isolates of E. coli and pseudomonas were sensitive to Carbapenams while two isolates of Klebsiella were carbapenamse producing strains sensitive only to Colistin and tigecycline Mean days of neutropenia, growth factors and antibiotic use was 7.89, 3.81 days and 8.81 days respectively. There were 2 deaths in the study.
Conclusions: Leukemias are the leading cause of FN in pediatric cancer patients undergoing chemotherapy. Appropriate antibiotics against gram negative organisms which are the most commonly isolated ones reduces the morbidity and mortality from this condition.

PUB-0217

SEVERE AND SYMPTOMATIC HYPERAMMONEMIA AFTER ASPARAGINASE THERAPY IN TWO LEUKEMIC CHILDREN

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Purpose/Objective: Asparaginase is one of the most important chemotherapy agent in childhood leukemia. This agent is a catalyser enzyme that transforms asparagine and glutamine to aspartic acid and glutamic acid. Ammonium is a natural result of this reaction. In chemotherapy regimen transient hyperammonemia will be seen and usually well tolerated without any symptomatic treatment. We represent two cases in which symptomatic hyperammonemia occured and treated properly.
Materials and Methods: Cases: First case is a 45 days old baby boy treated for infant leukemia since November 2012 in terms of COG9407 protocol. According to treatment regimen vincristine, corticosteroids, doxorubicin were given and L-Asp 6000 u/m2 every other day. After third day of L-Asp treatment patient's activity and feeding reduced, hypersomnia noticed, blood ammonium level was measured 250 µmol/L (Maximum value according to age: 136 µmol/L).

Second case is a four years old girl who has been treated for relapse/ refractory AML since February 2012. During treatment regimen she had PEG-Asp (2500 U/ m2) intramuscular injection, after two weeks patient had weakness and hypersomnia. Her blood ammonium level was measured 146 µmol/L (Maximum value according to age: 60 µmol/L).
Results: Both cases were treated with protein diminished diet, sodium benzoate and iv glucose infusions and blood ammonium level reduced properly. Both cases were investigated for urea cycle defect (eg. Ornithine transcarbamylase deficiency), non were detected.
Conclusions: There are case reports that L-Asp can provoke hyperammonemia, but no proper treatment regimens for this situation were suggested. L- Asp is a common used agent in protocols and treatment protocols must inform about management of this side effect.

PUB-0218

CENTRAL VENOUS CATHETERS AND COMPLICATIONS IN OUR CENTER - TEN YEARS EXPERIENCE AND COMPARISON OF DECADES

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Purpose/Objective: Central venous catheters provide a long term entry for pediatric patient group and can be used safely in most cases. But major complications like infections or thrombosis may end up with the loss of central access and cause severe morbidity and mortality. Catheter related infections are affected by the type of catheter, duration time and sterile precautions.This study was designed to find out the major complications in use of central venous catheters for a ten year period (2002-2012) at Ankara University Medical School, Turkey.
Materials and Methods: Ten years period were retrospectively analysed for central venous catheter's, type, duration, and complications. The results were compared the previous data of our clinic, the similarities and differences were reviewed.
Results: A total of 94 catheters were placed in 84 children for long-term chemotherapy with a total experience of 31.087 catheter days. Fifty patients were boy and 34 patients were girl and median age was 8. Twenty-six patients had acute leukemia, 25 patients had lymphoid malignancies, and 33 had solid cancers. Thirteen patients had port catheters while the other 71 patients had double-lumen catheters. There were 39 catheter related infections and rate of catheter-related sepsis was 1.15 episodes per 1000 catheter days. Most common reasons for the removal of catheters were infection and thrombosis. Fifteen of infected catheters had to be removed because of Candida, Acinetobacter, Pseudomonas and Staphylococcus species and the others were treated by both systemic and antibiotic/anticoagulant lock therapy. None of the patients were lost by catheter related sepsis.
Conclusions: In a comparison our results are much better than previous years of our clinic (rate of catheter-related sepsis was 4.9 episodes per 1000 catheter days before 1999) but we still have issues about proper usage and sterility like other developing countries.

PUB-0219

SEPTIC SHOCK AND ITS EMERGENT MANAGEMENT IS ESSENTIAL IN THE PEDIATRIC ONCOLOGY CLINICS

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Purpose/Objective: It is not as common as febrile neutropenia, but some children suffer from sepsis and septic shock during or after chemotherapy. In this study, we aimed to document our septic shock experience in children treated for cancer.
Materials and Methods: We have retrospectively analyzed the patient records who were treated for sepsis and septic shock during cancer treatment between 2009 and 2013. The study included 22 septic shock episodes of 21 children.
Results: Median age was 15 years (3-18) and there were 12 female and 9 male. Diagnosis was leukemia or lymphoma in 14 patients whereas solid tumors in 6 and histiocytosis in 1. At the time of diagnosis, absolute neutrophil count was less than 500/mm^3 in 12 episodes (54.5%), 500-1000/mm^3 in 2 (9%) and more than 1000/mm^3 in 8 (36.4%). Twenty out of 22 (90.9%) episodes had fever at onset.

Trimetoprim prophylaxis was given in 15 (68%) out of 22 episodes. Twelve (54%) patients were on steroid treatment before septic shock episode. Upon the findings of septic shock patients were given aggressive intravenous fluid replacement and triple antibiotics (glycopeptides, carbapenems and aminoglycosides). In 20 (90.9%) episodes, inotropic agents such as adrenaline, nor-adrenaline, dopamine and dobutamine) were used. Four patients were ventilated for ARDS. Three patients had also multiorgan failure.

Median hospitalization day in PICU was 3 days (1-16). Seventeen (77%) episodes had less than 5 days of hospitalization. Eighteen of 22 episodes were treated succesfully, but 4 patients deceased of whom 2 were not in remission of their primary disease.
Conclusions: We can conclude that septic shock is a serious problem, especially in children with fever, either severe neutropenic or not. The morbidity and mortality is high, and its proper management is essential. Many episodes can be reversible by giving aggressive fluid replacement and proper antibiotics started.

PUB-0220

OSTEOSARCOMA AS A SECONDARY MALIGNANCY IN AN ADOLESCENT MALE PREVIOUSLY TREATED FOR HODGKIN'S LYMPHOMA

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Purpose/Objective: Osteosarcoma, are among the secondary malignancies that occur most frequently after childhood cancer. Previous chemotherapy (with alkylating agents but also with anthracyclines) has been implicated as a contributing factors in the development of secondary bone sarcomas.
Materials and Methods: We report a rare and interesting case of osteosarcoma as a second cancer occurring in an adolescent male who had a history of Hodgkin's disease, treated with ABVD. Eight years later, he was subsequently diagnosed as suffering from a localised osteosarcoma of left distal femur, considered to be a second malignancy (therapy associated). Due to a low left ventricular ejection fraction (anthracycline - associated cardiotoxicity), he was not deemed fit to be enrolled into the EURAMOS protocol, thus following an anthracycline - free variation.
Results: Therefore, he was treated preoperatively with 5 cycles of high dose Methotrexate (HDMTX) of 12g/m^2 and 2 cycles of Ifosfamide/Etoposide (14 g/m^2 / 500 mg/m^2) which was well tolerated. He subsequently had his distal femoral replacement. He had made an excellent recovery from surgery and gained gradually full function. The histology of the resected tumour showed complete excision with soft tissue margin and wide bone margins. There has been a good response to neoadjuvant chemotherapy with greater than 90% tumour necrosis. He continued with post-operative chemotherapy, in which he completed 7 more courses of

high dose Methotrexate and 3 courses of Ifosfamide and Etoposide. He was put under regular surveillance post chemotherapy. He carried out 2 monthly chest x-rays and 6 monthly chest CT-scan and 4 monthly imaging and follow-up of his limb for the first year. The boy is now in his second year of follow-up and he is disease and relapse free. Long-term surveillance is mandatory.
Conclusions: In conclusion, the same principles that are applied to the treatment of primary osteosarcoma, should also be used for osteosarcoma presenting as a second malignancy.

PUB-0221

FEBRILE NEUTROPENIA AND AVAILABLE BIOMARKERS AMONG CHILDREN WITH HEMATOLOGICAL MALIGNANCIES

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Purpose/Objective: Febrile neutropenia in children with hematological malignancies is related to substantial morbidity and mortality. We prospectively monitored episodes of febrile neutropenia, complications and evaluated available biomarkers.
Materials and Methods: Prospective data collection on all episodes of febrile neutropenia (absolute neutrophil count < 1000 cells/mm$^{3)}$ in children with hematological malignancies were monitored for one year period. Endpoints were documentation of bacterial, viral or fungal infection and estimation of mortality. C-reactive protein (CRP) and procalcitonin were evaluated as predicting biomarkers
Results: There were 423 admissions and 3189 bed-days during the studyperiod. A total of 78 episodes of febrile neutropenia (88% during induction chemotherapy) were identified in 37 children with median age 5 yeras old (range 1-14) and 67% females. The majority of patients w (72%) were diagnosed with acute lymphoblastic leukemia. Documented bacterial infections were found in 22/78 episodes (19 bloodstream infections, 1 urinary tract infection and 2 other). The leading pathogen was Coagulase-Negative-Staphylococci (49%), followed by Escherichia coli (18%), Klebsiella spp (8%) and Pseudomona aeruginosa (8%). It is noteworthy that 4%% among Klebsiella spp and 39% among E.coli isolates were extended beta-lactamase producers (ESBL). There aws one documented CMV infection and 1 hepatosplenic candidiasis. A total of 3 deaths occured but only one was infection related. The median CRP in children with documented bacterial infection was 80.7, while in children without documented bacterial/viral or fungal infection was 29.3, respectively ($p = 0.019$). Positive procalcitonin (> 0.0 mcg/l) was significantly associated to proven bacterial infections ($p = 0.039$)
Conclusions: Bloodstream infections remain the main complication of febrile neutropenia. Gram-positive bacteria have become more commonly isolated etiologic pathogens. Nevertheless, gram-negative episodes need special attention due to the growing incidence of antimicrobial resistance as a consequence of the widespread use of antibiotics. CRP and procalcitonin may provide useful and important assistance for guiding prompt treatment of episodes of febrile neutropenia in children with hematological malignancies.

PUB-0222

OUTCOMES OF PROGRESSIVE QUALITY IMPROVEMENT IN THE CARE OF CHILDREN WITH CANCER

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Purpose/Objective: *Purpose:* This is a prospective observational study at HHS where we introduced quality improvement (QI) interventions and analyzed disease outcomes.
Materials and Methods: *Methods:* The HHS has 17 beds; 45 (average) new cancer patients are admitted yearly .To improve quality of care, (1) we organized our infection prevention and control (IPC) team; (2) we began data collection of admissions including infections and their risk factors; and (3) we introduced QI interventions. Interventions fall into hygiene, vaccination, and antibiotic prophylaxis categories. We used education to raise QI awareness and skills of staff and families. During Period 1(Nov2010-Nov.2011), we began surveillance, and hygiene of environment, hands, and patient; and enforced influenza vaccination. These initiatives continued and improved in Period 2(Dec.2011-Dec.2012), and introduced guidelines of hygiene, infection care and antimicrobial prophylaxis. We compared outcomes (number of admissions, length of stay (LOS), LOS in the Intensive Care(IC), bacteremias, and deaths) in Period 1 and 2.
Results: *Results:* During the two years, the HHS had 409 admissions; the mode length of stay (LOS) was 4 days (range = 0*98), there were 58% males, 307 admissions for Acute Lymphoblastic Leukemia, 53 for Lymphomas, 44 for Acute Myeloid Leukemia and 2 for Chronic Myeloid Leukemia. There were 12 admissions in IC, median LOS of 5 days (range = 0.5*16). We observed reduction of infection from 42/100 discharges in the first 3 months of Period 1 to an average of 36/100 discharges during both periods. LOS and HAI rates were similar in both periods; however, infections of skin and soft tissue, blood stream and gastrointestinal tract decreased from Period 1 to Period 2.
Conclusions: *Conclusions:* QI interventions improved rates of infections at the HHS. Our model of gradual improvement provides objective information to leaders of hospitals. Rational investments in QIs will redound in better outcomes in the care of children with cancer.

PUB-0223

TREATMENT OF RELAPSED CHILDHOOD HODGKIN'S LYMPHOMA WITH BRENTUXIMAB VEDOTIN: A CASE REPORT

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Purpose/Objective: A case report is presented to describe response of a patient with relapsed Hodgkin Lymphoma (HL) after brentuximab vedotin treatment.
Materials and Methods: A 13 year-old teenager presented October 2008 with a five-day history of nocturnal fever (39C), diaphoresis, with no response to antibiotics. Neck ultrasound revealed cervical lymphadenopathy, diagnosed with mixed cellularity HL IIIBE (liver infiltration), histologically confirmed, CD15+, CD30+, CD45-, CD20-.

After 4 ABVD cycles presented progression, given then four ICE cycles, with partial response providing external beam radiation 30Gy to compromised fields, remain partial response, administrating four ICE cycles with complete response, cessation of chemotherapy March 2010.

December 2010 presented relapse with lymphadenopathy in mediastinum, abdomen, and hepatosplenomegaly, initiating BEACOPP with relatively good response, after 8 cycles were detected tumour on left mammary area, right pulmonary node and hepatosplenomegaly, biopsy confirmed HL infiltration, not candidate to transplant for a pneumophaty secondary to bleomicyn and radiotherapy, received ADE 4 cycles with partial response, December 2011 brentuximab vedotin 1.8 mg/Kg was started alone, each 21 days.
Results: After 4th cycle of brentuximab vedotin presented reduction of mammary tumour size, after 9th no mass was observed but presented infectious testicular process, therefore, treatment was temporarily suspended. After 10th inguinal and retroperitoneal lymphadenopathies were detected, splenomegaly and bilateral nephromegaly (5cm tumour), pelvic and abdominal radiotherapy with inverted Y technique was administered (36Gy). Brentuximab vedotin treatment was reinitiated one month later with doxorubicin and cyclophosphamide after three cycles presented good response, remaining on treatment.
Conclusions: Because of the small number of patients that fail to primary therapy, no uniform salvage treatment strategy exists for this patient population. Brentuximab vedotin showed an objective response rate of 50% in adults phase II study; we saw a good response in our patient but it is necessary more pediatric studies to determine whether they respond differently than adult patients.

PUB-0224

A 30 YEAR REVIEW OF CANCERS IN INFANCY IN A TERTIARY CENTER IN SINGAPORE

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Purpose/Objective: Cancers in infants (0 * 1 year old) is relatively rare. Malignancies of infancy represent 10% of all childhood cancers in children younger than 15 years of age. The average annual incidence of infant cancers is 233 per million infants in the US. There is paucity of data in Asia.
Materials and Methods: We retrospectively reviewed case records of patients managed in our center in the past 31 years (1981 * 2012). Patients were from Singapore and regional countries. Data was retrieved from the departmental database and was reviewed using electronic records system. We reviewed age at diagnosis, gender, nationality / race, diagnosis and outcome.
Results: There were 83 patients reviewed; of whom 78 had complete data. There were 40 males and 43 females (ratio 0.9). Majority of the patients were Chinese (48%); the remaining were Malay (17%), and others (35%) (Bangladeshi, Caucasian, Filipino, Indian, Indonesian, Myanmese, Sri Lankan, Vietnamese). Median age at diagnosis was 0.68 (range, 0.01 * 1.00) years. Neuroblastoma was the most common diagnosis (22%), followed by acute leukaemia (16%), retinoblastoma (13%), germ cell tumours (12%), brain tumours (medulloblastoma and astrocytoma) (11%), hepatoblastoma (8%) and Wilms tumour (7%). Of these patients, 71 are alive (85%), 7 died (8.5%), and no records can be found for the remaining 5 (6%). All patients with a diagnosis of acute leukaemia survived.
Conclusions: In our series, the epidemiology of cancers in infancy mirrors worldwide trend. In contrast to cancers in the older age group where acute leukemia is the commonest; neuroblastoma predominates in this age group. Prognosis in this age group appears favorable with many long-term survivors.

PUB-0225

SUCCESSFUL TREATMENT OF RELAPSED ALL IN A FANCONI ANEMIA PATIENT WITH DOUBLE CORD BLOOD TRANSPLANTATION

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Purpose/Objective: Allogenic hematopoietic stem cell transplantation(HSCT) is the only therapeutic choice to restore normal hematopoiesis in Fanconi anemia(FA). Moreover, concomitant acute lymphoblastic lukemia(ALL) hastens HSCT due to extremely sensitivity to the chemotherapy in FA patients.
Materials and Methods: A 12-year-old male patient with Fanconi anemia who developed ALL underwent a double unrelated cord blood stem cell transplantation, using conditioning regimen consisted of fludarabine 30mg/m^2/day on day -8 to -3, cyclophosphamide 5mg/kg/day on day -5 to -2, and rabbit antithymocyte globulin (Thymoglobulin$^{®}$, Sanofi, Germany) 2.5mg/Kg/day on day-3 to -1. And graft versus host disease (GVHD) prophylaxis was consisted of cyclosporine A and mycophenolate mofetil.
Results: Neutrophil engraftment was achieved at 16days without platelet count recovery. Gastrointestinal GVHD, cytomegalovirus infection were developed from 3 months post HSCT, but they are controlled successfully within a few months. At 12 months post HSCT, the patient demonstrated normal blood counts with platelet recovery ($> 20 \times 10^9$cells/L without platelet transfusion), sustained donor chimerism, and no evidence of ALL relapse, GVHD.
Conclusions: Childhood FA with ALL could be successfully treated with double cord blood transplantation in the absence of human leucocyte antigen-matched related or unrelated donors, by fludarabine based, reduced intensity conditioning.

PUB-0226

CARDIAC FUNCTION IN CHILDREN WITH MALIGNANCIES DURING ANTHRACYCLINES CONTAINING CHEMOTHERAPY

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Purpose/Objective: To determine the frequency and type of cardiac dysfunction during anthracyclines containing chemotherapy in a population of children with malignancies.
Materials and Methods: Retrospective analysis by the of routine echocardiography (Echo) data for the six-year period, when we investigated 727 patients treated for malignancies with anthracyclines (AAB) was conducted. At next step of investigation in dynamics of chemotherapy containing middle/high doses of AAB coursework (160-495 mg/m2) were examined by extended Echo 82 children with Hodgkin's lymphoma (42), osteogenic sarcoma (24), acute promyelocytic leukemia (16) aged from 1 year to 17 years.
Results: It is established that from 20% patients with malignancies, receiving different AAB have been with systolic dysfunction of any degree of severity from subclinical manifestations (77%), that diagnosed only by instrumental methods, till clinical signs by NYHA CHF classes 2-4 (23%). In patients receiving chemotherapy in a dose 160-495 mg/m2 AAB identified the following types of cardiac dysfunction, as well as their combinations. Increased contractility of myocardial (FS $>$ 44%, EF $>$ 77%). In the course of therapy AAB was recorded in 23% of patients. Signs of non restrictive LV diastolic dysfunction (E/A for transmitral flow < 1) were presented at various stages of chemotherapy - in 11% of children. The increase in afterload (wall stress - WS(merid) $>$ 75g/cm2) characterizes afterload left ventricular and it remodeling, which is associated with it dilation, change in shape and wall thickness - in 35% of patients. Systolic dysfunction (FS $<$ 31%, EF $<$ 60%) was present in 32% of cases. In 8% of cases we determined the accumulation of fluid in the pericardial cavity in combination with a reduction in myocardial contractility or without.
Conclusions: Subject to limits in the control group of norms (M $\pm$ 2SD) quantitative analysis Echo pointed to a number of pathological conditions that characterize cardiac function mainly in sub clinical level.

PUB-0227

DEVELOPMENT OF AN ALGORITHM FOR THE MANAGEMENT OF FEBRILE PEDIATRIC ONCOLOGY PATIENTS IN DAVAO CITY, PHILIPPINES

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Purpose/Objective: The risk of mortality due to infection in pediatric oncology patients undergoing chemotherapy is well documented. In pediatric cancer centers (PCCs) in high-income countries (HIC), evidence based guidelines to standardize care and improve outcomes for patients with febrile neutropenia are available. By contrast, in the PCC in Davao City, Philippines, where the epidemiology of fever is different, analogous decision support tools are not available. We developed an algorithm for management of pediatric oncology patients presenting with fever to the Southern Philippines Medical Center (SPMC), tertiary care facility in Davao based on available antimicrobials and diagnostics capability.
Materials and Methods: During a three-week period, we surveyed current practice and interviewed pediatric infectious disease and oncology practitioners at SPMC. In addition, we directly observed nursing and resident workflow and reviewed the inpatient charts of patients admitted with fever. Information gathered included pricing and availability of selected antibiotics, radiographic and laboratory diagnostics, and description of current practice.
Results: Our initial investigation revealed that interpretation of fever, its workup, urgency, and approach to management differed amongst pediatric resident and nursing team members. Following this, in consultation with local care providers, we formulated an algorithm for the care of children undergoing chemotherapy and presenting to the hospital with fever. Management considerations discussed include neutropenia, vital sign instability, persistence of fever, and development of high-risk complications, such as mucositis. Guidelines stipulate mandatory laboratory evaluations, studies to consider, and recommended antimicrobial therapy.
Conclusions: Algorithms for management of fever in oncology patients in resource limited settings, tailored to site-specific resources, offer an opportunity for process standardization that may improve patient outcomes. Future directions of study will include user training in algorithm use, evaluation of whether the algorithm is followed, and patient outcomes in order to prompt revisions as part of ongoing quality improvement efforts.

PUB-0228

OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKAEMIA-INSTITUTIONAL EXPERIENCE FROM INDIAN SUBCONTINENT

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Purpose/Objective: Approximately 20% of childhood leukaemias are of myeloid origin, the majority of them being acute myeloid leukaemias(AML). There is a paucity of data addressing the outcome of pediatric AML from Indian subcontinent. We analyzed the outcome of pediatric AML from our institute.
Materials and Methods: Case records of all childhood AML patients (1-19 years) from January 2007 to December 2012 were studied. Event Free Survival (EFS) is defined as relapse, death, lost to follow up and treatment drop out, Overall Survival (OS) is defined as death due to any cause from the date of diagnosis. Graph pad prism is used for statistical analysis.
Results: Sixty three children were registered during the study period. Median age was 14(range 2 - 19), males constituted 39 and females 24. Most common presenting symptom was fever (87%), followed by fatigue (73%) and bleeding manifestations(38%). Acute Promyelocytic Leukaemia(APML) was the most common subtype(30%), followed by AML-M2(25%). None of the children had any inherited disorder. Eighteen out of 63 patients refused treatment. Out of the 45 children who took treatment, 66% (30/45) achieved complete remission following standard induction regimens (All trans retinoic acid + Daunomycin for APML and 3 + 7 regimen for other AMLs), whereas 22% patients failed induction. The remission rates for APML were significantly higher at 88% as compared to 54% for other AMLs. Five out of 45 patients abandoned treatment before the completion of the planned chemotherapy. Median follow up of the study is 11 months (range 1-60). The median EFS is 11months, median OS being 15 months. The 3 year OS for APML is 61% as compared to 14.8% for other AMLs ($P = 0.0126$).
Conclusions: Treatment of childhood AML is still a challenge for the Pediatric Oncologist. Though the survival rates for APML is encouraging, little success has been achieved in the treatment of other AMLs.

PUB-0229

OUTCOME OF RETINOBLASTOMA PATIENTS IN A DEVELOPING COUNTRY; SINGLE INSTITUTION EXPERIENCE

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Purpose/Objective: Retinoblastoma(RB) is rapidly progressive cancer of developing retina. Almost 90% children affected by RB belong to developing countries, where late diagnosis leads to advanced disease at presentation, which not only makes the eyes unsalvageable, but sometimes saving life is also impossible. We studied the outcome of pediatric patients with retinoblastoma, presenting to a tertiary care cancer hospital in Pakistan.
Materials and Methods: Retrospective review of medical records of RB patients presenting at Shaukat Khanum Memorial Cancer Hospital and Research Center, Pakistan, between January 2007 till December 2011.
Results: Total of 134 patients with 191 affected eyes were studied. Out of these, 84 were males and 50 females with M:F of 1.7:1. Median age was 25 months with range of 1 * 120

months. Sixteen (12%) patients had positive family history of retinoblastoma and 57 (42.5%) had bilateral disease.

Only 12 out of 191 eyes were salvaged, while 12 patients had to go through bilateral enucleation. Fourteen (10.4%) patients had upfront enucleation with no adverse histopathological features and did not receive any chemotherapy. Fifty five (41%) patients abandoned treatment, out of which about 50% left before initiation of therapy. Sixty three (47%) patients achieved complete remission. Of these 87% (n = 55) patients are on regular follow-ups.

Fourteen (10.4%) patients died, 11 due to disease progression and 2 deaths were attributable to treatment related toxicity. One patient who presented with very advanced disease died even before initiation of therapy.

Conclusions: RB is still costing eyes and lives of children in developing countries mainly due to advanced disease stage at presentation. Abandonment was a significant problem in this series needs to be addressed.

There is an urgent need of awareness/education among general public and primary health care workers and to develop smooth and swift referral system to trained ophthalmologist and pediatric cancer hospital.

PUB-0230

CYTOGENETIC ABNORMALITIES IN CHILDHOOD ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROME AND PROGNOSTIC SIGNIFICANCE

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Purpose/Objective: Cytogenetics analysis is probably the most important prognostic factor for AML. We studied the cytogenetic abnormalities of children with AML and Myelodysplastic Syndrome (MDS), treated in our Unit in a 20-year period and their prognostic significance.

Materials and Methods: Data was retrospectively collected by the clinical records of all 50 patients treated to our unit from January 1991 until February of 2011.

Results: The most frequent abnormality was MLL rearrangement (11q23), in 5 children (10%), 3 without other cytogenetic abnormalities and 2 with coexistent complex abnormalities. Inversion 16 was found in 3 patients (9,09%) and other 3 had the characteristic for ?3, t(15;17) translocation. Two children had t(8;21) translocation. Regarding specific chromosome findings, 4 children had abnormalities of chromosome 7, three of chromosome 5, two of chromosome 3, five of 11 and two of 12p. Complex cytogenetic abnormalities had 22 children (44%).

The prognosis for children with t(15;17) and inv16 was excellent, since all of them are alive. The survival of children with 11q23 rearrangement was 60%, as 2 of them died from disease progression. One of the two children with t(8;21) died from disease. The survival for children with normal caryotype was 40%. The children with complex cytogenetics had also poor prognosis (OS 31,82%). Survival rate for those with chromosome 7 abnormalities was 75%, while only one child with 12p abnormalities survived. Similarly bad was the prognosis for children with chromosome 5 (33,33%) and chromosome 3 abnormalities (50%).

Conclusions: The prognostic significance of certain cytogenetic abnormalities in AML / MDS has been studied in our population and confirmed favorable for inversion 16 and t(15;17) and unfavorable for chromosome 3, 5 and 12p abnormalities. Complex cytogenetic abnormalities have poor prognosis. The translocation t(8;21) and chromosome 7 abnormalities, have not been adequately studied due to the small number of patients.

PUB-0231

THE CHARACTERISTICS OF MEDIASTINAL NEUROBLASTOMA IN CHILDRENHOOD.

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Purpose/Objective: To study the clinical characteristics of mediastinal neuroblastoma.

Materials and Methods: From 2008 March to 2012 September, 110 cases of neuroblastoma has been admitted, including 26 cases of mediastinal neuroblastoma and 84 cases of other neuroblastomas. To compare the clinical manifestation, tumor markers, biological prognostic factors of mediastinal neuroblastoma with other neuroblastomas.

Results: The average age of mediastinal neuroblastoma group is 25.5M,which is very similar to other neuroblastomas.88.5% of mediastinal neuroblastomas had syndrome at newly diagnosis, and so did 60.7% in other neuroblastomas ($P < 0.05$). The early stage (???) cases of mediastinal neuroblastoma group were 34.6%, higher than that of other neuroblastomas which were 8.3% ($P < 0.05$). 21.4% of serum NSE levels of Mediastinal neurobJastoma group risen more than 100 ng/L, lower than 86.1% ($P < 0.05$) in other neuroblastomas. All the cases in mediastinal neurobJastoma had a N-myc copy number of less than 10 copies, while 23.1% in the other neuroblastomas' were more than 10 copies ($P < 0.05$).The 4-year overall survival rate was 80% in mediastinal group and 44% in the other neuroblastomas. Of the cases whose primary tumors were in localized neuroblastoma, the 4-year survival rate was 100%, significantly higher than 82%in other neuroblastomas.

Conclusions: Majority of the mediastinal neuroblastoma cases perform early clinical stage and favorable biological prognostic factors.These may associated with the prognosis of mediastinal neuroblastoma.

PUB-0232

WHAT CAN BE RATIO BETWEEN REGRESSIVE AND PROGRESSIVELY GROWING FORMS OF NEUROBLASTOMA IN THE PERINATAL PERIOD?

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Purpose/Objective: To numerical definition of the ratios of the regressing and progressing forms of neuroblastoma in the fetus and newborn.

Materials and Methods: The study group included 15 newborns of both sexes. From 9 of them (abdominal neuroblastoma) have been the potential of malignancy, 6 - with a clinical diagnosis retroperitoneal, predominantly of solid tumor, suspected to neuroblastoma (without morphological evidence). Group was selected from infants that admitted to the clinic with abdominal neuroblastoma: 1999 to 2012.

Results: No there were confirmed cases of prenatal detection for patients who had morphological evidence of retroperitoneal neuroblastoma and adrenal neuroblastoma. Although from 2 patients was a significant tumor volume (91 and 149 cm^3), which allowed to assign them to the category of "definitely for prenatal detection". Group of six infants with diagnosed during pregnancy retroperitoneal and adrenal formations was interesting both in terms of predictive value of prenatal ultrasound data, and in terms of the study of the biological properties of the tumor. Tumors were found in II-III trimester of pregnancy and then have been submitted results of observation related to their regression. Their postnatal volume was, on average 2 times less than that from the undiagnosed prenatally, but with installed potencial of malignant growth.

Conclusions: Share of the regressing and of the malignancy forms of neuroblastomas from fetus can be determined in ratio 6:2. In the neonatal period ratio changes by increasing the number of diagnosed tumors with an aggressive course.

PUB-0233

A PREFERENCE FOR PUBLIC CORD BLOOD BANKING IN JORDAN

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Purpose/Objective: Cryopreserved units in private cord blood banks (CBB) outnumber those stored in public CBB, yet a significantly higher number of transplants ($\approx$650 times) utilize public CBB sources. This predicament is exacerbated in developing countries where CBB is dominated by costly private companies that may seemingly misguide public perception of CBB benefits in addition to overlooking the establishment of public CBB.

Materials and Methods: A prospective self-administrated survey of 461 anonymous pregnant women during a routine antenatal visits was conducted at 4 public and private hospitals throughout Jordan. A verbally consensual multiple-choice questionnaire was provided to participants.

Only 40.6% of participants were aware of CBB benefits with 56.8% willing to donate cord blood from their child. Those willing to donate preferred the use of public (77.1%) rather than private (19.5%) CBB. The main reasons were: cost (34.4%), safety (24.5%), lack of knowledge (19.8%) and privacy concerns (11.9%). The preference for public CBB was not related to insurance status, level of education, age, or parity.

Results: Only 40.6% of participants were aware of CBB benefits with 56.8% willing to donate cord blood from their child. Those willing to donate preferred the use of public (77.1%) rather than private (19.5%) CBB. The main reasons were: cost (34.4%), safety (24.5%), lack of knowledge (19.8%) and privacy concerns (11.9%). The preference for public CBB was not related to insurance status, level of education, age, or parity.

Conclusions: The study demonstrates a significant preference for public CBB in Jordan. National initiatives should be taken to increase public awareness of CBB and future planning to establish CBB for public usage.

PUB-0234

HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF HIGH-RISK PEDIATRIC RHABDOMYOSACROMA PATIENTS

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Purpose/Objective: High-risk rhabdomyosarcoma patients (disseminated forms, relapses, alveolar subtype) present a therapeutic challenge due to their aggressive course and resistance to conventional treatment. The aim is evaluating effectiveness and safety of high-dose chemotherapy with autologous hematopoietic stem cell transplantation (HDCT with auto-HSCT) in patients with high-risk rhabdomyosarcoma.
Materials and Methods: Eight pediatric patients (mean age 8 years) with resistant/relapsed embryonal (n = 3) or alveolar (n = 5) rhabomyosarcoma were included in the study. All the patients received surgical treatment, irradiation and chemotherapy according to treatment standards, although only 1 patient achieved CR, while in 7 cases only the partial response was observed. The patients proceeded to single HDCT (n = 6) or tandem HDCT (n = 2) with auto-HSCT according to toxicity burden and the quality of available autograft. All the patients received busulfan16 mg/kg and melphalan140 mg/m^2, for tandem HDCT recipients carboplatine 500 mg/m^2 - etoposide 300 mg/m^2 and 900 mg/m^2- etoposide 45 mg/m^2- cyclophosphamide 120 mg/m^2 regimens were also conducted. The graft source was bone marrow, the mean CD34+ cells count was 6,05 ? 10^6/kg.
Results: The conditioning regimens were characterized by moderate toxiticy (WHO Grade I-II). Median follow-up time is currently 370 days. All patients achieved good partial response with 60-90% decrease of target lesions volume. Nevertheless, the median progression-free survival was as short as 142 days. Only 3 of 8 patients are currently alive: 1 in CR (follow-up 165 d.), 1 patient in stable PR (follow-up 30 d.), 1 local relapse (follow-up 25 d.).
Conclusions: Although HDCT with auto-HSCT provides a short-term response in very high-risk rhambomyosarcoma patients population, in most cases it is not a curative. More aggressive post-HDCT local control or preemptive immunoadoptive cell therapy could probably improve the prognosis.

PUB-0235

AWARENESS OF THE THERAPEUTIC BENEFITS OF UMBILICAL CORD BLOOD INCREASES WILLINGNESS TO DONATE

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Purpose/Objective: Umbilical cord blood (CB) is an effective and safe treatment alternative for a spectrum of diseases. This has lead to a rapid increase in private CB banking in the Middle Eastern. Ethical concerns have surfaced including whether the decision to store CB is guided by knowledge of its benefits or misguidance.
Materials and Methods: A prospective self-administrated survey of 461 anonymous pregnant women during routine antenatal visits was conducted at 4 hospitals throughout Jordan. A verbally consensual multiple-choice questionnaire was provided to participants consisting of demographic data and knowledge of CB benefits.
Results: Median age of participants was 28 years (range, 17-42), with an average of 3 pregnancies (range, 1-13), and $>65\%$ received some form of higher education. When asked if they had ever heard of CB banking or were aware of its benefits, 59.4% and 57.3% respectively responded negatively with education level having a direct correlation with positive responses ($p < 0.0001$). Willingness to donate was higher (70.1%) in the group that was aware of the benefits compared to those lacking awareness (47.1%). Most awareness came from media sources (41.2%) and 91.1% believed their obstetricians should discuss CB collection during the antenatal period.
Conclusions: Understanding the therapeutic benefit of CB increases willingness to donate. Public awareness initiatives are required to improve current CB banking practices.

PUB-0236

TEMOZOLOMIDE IN THE TREATMENT OF NEWLY DIAGNOSED DIFFUSE BRAINSTEM GLIOMA IN CHILDREN: EXPERIENCE AT A SINGLE INSTITUTION

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Purpose/Objective: The purpose of this study was to assess the efficacy and toxicity of radiotherapy (RT) with concurrent temozolomide (TMZ) chemotherapy followed by adjuvant TMZ in children with diffuse intrinsic pontine glioma (DIPG).
Materials and Methods: Patients younger than 18 years with newly diagnosed diffuse brainstem glioma were enrolled. Histologic confirmation was not necessary for any patient in whom typical magnetic resonance imaging scans revealed a DIPG. No previous therapy, excluding corticosteroid treatment, was permitted. Children were treated with focal RT to a dose of 54 Gy along with concurrent daily TMZ (75 mg/m^2/day). Four weeks after completing the initial RT*TMZ schedule, adjuvant TMZ (200 mg/m^2/day, days 1*5) was given every 28 days up to 12 cycles or progression disease.
Results: Fifteen children with a median age of 9 years (range 3-14) were enrolled in this clinical trial. There were 6 males and 9 females. All patients completed RT. A median number of 3 courses was administered per patient (range: 2-9). The toxicity associated with TMZ was primarily hematopoietic (grade III/IV thrombocytopenia and leucopenia). At a median follow-up of 15 months 13 children have died, 1 child was alive with progressive disease and 1 with stable disease. No patient experienced CR. The median time to progression was 7.3 months (range 3,4*17,3 months).
Conclusions: Chemoradiotherapy with TMZ followed by adjuvant TMZ did not improve the PFS and is associated with higher toxicity when compared with radiotherapy alone in treatment of children with DIPG.

PUB-0237

PHOTOVOICE, OUR SURVIVORS' VOICE THROUGH EXPRESSIVE ART

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Purpose/Objective: Research has discovered that cancer changes how adolescent survivors see themselves; whether the change is positive or negative or both depends on the meaning given to the experience. Therefore, it is important to give survivors the opportunity to make sense of their cancer experiences. Photography enables the individual to expand their focus from the introspective to the wider external world, while giving them a sense of control and empowerment in making choices on what to capture in their pictures. At the same time, a snapshot depicts a metaphor of ourselves: our values, perceptions and expectations that determine when and how a photograph is taken (Weiser, 1988).
Materials and Methods: The Therapeutic Photography workshop for childhood cancer survivors, age 13 to 23, was completed in 2012. The workshop began with an instructional component where survivors learn how to take good photographs with professional cameras. Then they were given freedom to take photographs that represent their cancer experiences. Followed by a group sharing which facilitated by social workers. Survivors were assisted to process through some of the common topics and themes brought out by the photographs.
Results: Thus through the medium of photography, survivors were given the opportunity to capture what they would like to express about their cancer experiences in a safe and non-threatening way and find affirmation, closure and/or new insights about their cancer experiences.
Conclusions: This presentation seeks to share some of our survivors' photos and may many others 'hear' their voice. In addition, we will also be presenting findings on the therapeutic experience of 15 survivors who participated in these experiential workshops.

PUB-0238

A DIAGNOSTIC ALGORITHM FOR RULING-OUT AND DIAGNOSING LEUKEMIA IN A RESOURCE-LIMITED SETTING

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Purpose/Objective: Over the past several decades, new technologies have changed the way childhood leukemia is diagnosed in high-income countries. By contrast, in low and middle-income countries where immunohistochemistry and flow cytometry are not routinely available, morphology and cytochemical stains remain the primary means of diagnosis. Recognizing the lack of guidelines tailored toward resource-limited settings, we developed a rule-out leukemia algorithm for a large tertiary care center in Davao City, Philippines.
Materials and Methods: Initial data gathered included pricing of laboratory and radiology modalities and the time currently required for each test to be performed at the Southern Philippines Medical Center (SPMC). We then utilized a structured process-mapping tool to determine the major delays to diagnosis and assess areas for systems improvement. Finally, best practices of pediatric oncologists on-site were discussed. The above data was reconciled in a final deliberative process utilizing local and international expert opinion.
Results: We created an algorithm for pediatric residents and nurses formatted as a decision-tree. It is organized into two phases, each with an expected time frame to completion. The first phase focuses on identifying which patients should undergo a bone marrow aspiration based on history and physical and basic diagnostics. A comprehensive site-specific

differential diagnosis is also included. The second phase details a mechanism for the differentiation of acute lymphoid from myeloid leukemias.
Conclusions: In many low and middle-income countries, the diagnostic tools available for the diagnosis of leukemia are limited due to cost and access. In addition, there are very few trained pediatric oncologists in the Philippines and those subspecialists must rely heavily on residents and nurses as physician extenders. We expect this standardized algorithm to aid residents and nurses while providing a timely, cost-efficient means of diagnosing leukemia.

PUB-0239

SIGNIFICANCE OF MINIMAL RESIDUAL DISEASE AT END OF INDUCTION CHEMOTHERAPY TO PREDICT ADVERSE OUTCOME IN CHILDHOOD ACUTE LYLPHOBLASIC LEUKEMIA: REPORT FROM INDIA

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Purpose/Objective: Purpose: Acute lymphoblastic leukemia continues to have a relapse rate of 25% and half of these succumb. Studies have shown that the presence or absence of residual disease, as assessed by PCR or Flow cytometry is a prognostic factor in patients with ALL and threshold levels of residual leukemic cells have been proposed for predicting relapse.

The objectives of the study were to determine the presence (prevalence) of MRD in B- cell lineage ALL by flowcytometry at end of induction,follow up and correlation of MRD with subsequent relapse and correlation of MRD with other known risk factors for ALL relapse. (Age, sex, TLC at onset of induction, CNS disease, absence of blasts from peripheral smear at 2 weeks of initiation of chemotherapy).
Materials and Methods: Method: Clinical details were noted in B lineage ALL patients. Induction chemotherapy was given to all. MRD assessment was done at end of induction chemotherapy using flowcytometry. Patients were followed for relapse
Results: Results: 45 patients completed first induction therapy. Of the 45 patients studied, MRD was present in 26.7% (n = 12). On follow up adverse events were seen in 11 (24.4%) in the form of relapse and/or mortality. The predictors for adverse outcome (relapse& mortality)were older age group($p = 0.007$) and a high baseline TLC ($p = 0.04$) .MRD was also more (45.5% vs 20.6%) though this was not statistically significant ($p = 0.1$).
Conclusions: Conclusions: MRD positivity was not very good in predicting adverse outcome, but absence of MRD predicted good outcome in 79% of the patients. Therefore absence of MRD seemed a more useful parameter to predict better outcome and high TLC and Higher age predicted worse outcome. Thus risk stratification of patients for intensity of treatment may be done taking into consideration predictors like TLC, age at presentation and presence/absence of MRD at end of first induction

PUB-0240

INCREASING INCIDENCE OF CARBAPENEM-RESISTANT GRAM NEGATIVE BACTEREMIA AMONG PEDIATRIC CANCER PATIENTS

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Purpose/Objective: Increasing multidrug resistance Gram-negative bacteria, in particular *Carbapenemases* presents a serious infectious problem, especially in the setting of the immuncompromised host. There is a strong correlation between broad spectrum antimicrobials misuse and emerging multidrug resistant organism.
Materials and Methods: Patients with documented carbapenem-resistant bacteremias were investigated from January 2012 through December 2012. Demographic and clinical data of the patients were collected. A number of key risk factors for recovering carbapenemases in Gram-negative pathogens were reported; prolonged hospitalization, hematological malignancies, as well as use of carbapenems in previous febrile episodes. Evaluation of the association between carbapenem resistance and in-hospital mortality was reported.
Results: Throughout 2012 total number of blood cultures was 16,385 .Positive blood cultures, 1,355 (8%). Gram negative blood stream infections were 330 (24%) of the positive blood culture. Multidrug resistant (MDR) cultures were 234 out of 330 cultures (71%). Carbapenem - resistant were detected in about 60 cultures out of the MDR cultures (18%) of which 36 (60%) were *Enterobactrecae*. All of the patients were cultured during febrile, neutropenic episodes, with prolonged hospital stay. About 60% of cases were patients with hematological malignancies receiving intensive chemotherapy.When dividing the whole year in to two time frames each of six months duration according to the cycling policy of the first line empiric antibiotic therapy, there was an obvious increase in number of carbapenem-resistant infections within the second time frame B (June to December). Mortality was higher among patients with hematological malignancies (60%) of the total mortalities.
Conclusions: There is an increasing incidence of carbapenem resistant gram-negative infection isolated from febrile and neutropenic cancer patients at our hospital although this group of organisms was rarely detected at our hospital. Implementing a stewardship program is highly recommended to reduce emerging MDR organisms.

PUB-0241

OUTCOME OF CENTRAL NERVOUS SYSTEM (CNS) PRIMITIVE NEUROECTODERMAL TUMORS (PNETS) IN CHILDREN: FIFTEEN YEARS EXPERIENCE FROM A SINGLE CENTER IN TURKEY

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Purpose/Objective: Purpose: Childhood PNETs in CNS is one of the most important concerns in pediatric oncology and its outcome has significantly improved recently. This study aimed to investigate the outcome of children with PNETs located in CNS in our institution.
Materials and Methods: Method: This is a retrospective review of 40 children with PNETs located in CNS up to 18 years old treated in between 1996 to 2012. Survival analysis was performed using log rank test and Kaplan-Meier method.
Results: Results: The median age of diagnosis was 8 years old (range 0.3 to 17 years) with male to female ratio 1. Thirteen patients were at 5 years old or younger at the time of diagnosis. Among the patients, 33 had infratentorial PNETs. Only one had tumor in spinal cord. All patients underwent surgery; complete resection in 25, partial resection in 14 and only biopsy in 1. According to Chang staging system, 21 patients were in high-risk. Disease status was M0 in 32, M1 in 2 and M3 in six patients. While 33 patients received combined chemotherapy and radiotherapy, three were given only adjuvant chemotherapy and only radiotherapy, each. In one patient did not receive any treatment following surgery. Of these 40 patients, 17 developed relapsed or progressive disease. Overall (OS) and progression free survival (PFS) at 3 years were $70.6 \pm 7.9\%$ and $57.3 \pm 8.2\%$, respectively. For metastatic PNETs cases OS and PFS at 3 years were $20.8 \pm 17.9\%$ and $16.7 \pm 14.8\%$, respectively. However in case of standard risk PNETs older than 5 years old; OS and PFS at 3 years were $76.3 \pm 8.6\%$ and $64.6 \pm 9.1\%$, respectively.
Conclusions: Conclusion: The results of our institution are consistent with those in literature. However metastatic cases have still poor prognosis.

PUB-0242

LONG-TERM CONSEQUENCES OF ANTICANCER TREATMENT IN PEDIATRIC CANCER SURVIVORS

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Purpose/Objective: Aim of this study is to assess the rate and severity of long-term complications in pediatric cancer survivors.
Materials and Methods: From September 2009 to April 2012 133 patients receiving in 1995-2010 treatment for Hodgkin lymphoma (n = 38), non-Hodgkin lymphoma (n = 23), nephroblastoma (n = 26), neuroblastoma (n = 17), germ cell tumors (n = 10), osteogenic sarcoma (n = 10), Ewing sarcoma (n = 9). All patients underwent a routine follow-up study consisting of physical examination and anthropometry, functional and clinical status evaluation, thyroid and sex hormones tests.
Results: Nine (24%) of Hodgkin lymphoma patients developed hypothyroidism after cervical or clavicular lymph nodes irradiation (25-40 Gr). Four (17.4%) female patients with history of pelvic irradiation (35-40 Gr) developed hypogonadism. Among the patients with non-Hodgkin lymphoma (n = 23) only one (4.34%) developed hypothyroidism and 3(13.04%) subclinical hypothyroidism, 2 patients developed thyroid tumors (adenoma and papillary carcinoma), 1 female patient developed ovarian hypoplasia and amenorrheawith after pelvic irradiation (38 Gr). Patients treated for nephroblastoma (n-26) had tendency for higher serum glucose and, if older, than 5 years at the time of treatment tendency for hypogonadism and higher BMI. Neuroblastoma patients display no significant endocrinal status changes. One (10%) of the patients with central germ cell tumors developed hypopituitarism (10%). Eight (80%) of patients with osteogenic sarcoma (n - 10) have an increased BMI in spite of having fully functional limbs (MSTS 78-95%). Patients receiving treatment for Ewing sarcoma (n-9) have normal metabolic status, one patient with history of pelvic irradiation (54 Gr) and high-dose chemotherapy developed amenorrhea. Limb functional defects and growth impairment were found in 4 (44.4%) patients.
Conclusions: The most severe functional and cosmetic defects developed in patients receiving combined treatment with total irradiation dose of more, than 30-35 Gr. Patients with history of lymphoma treatment have most evident endocrinal status changes. Patients with nephroblastoma have higher risk of hypogonadism if treated at the age of 5 or later.

PUB-0243

PARAPARESIS AS A PRESENTING FEATURE IN PEDIATRIC ONCOLOGY: A SINGLE CENTER EXPERIENCE

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Purpose/Objective: Paraparesis is an uncommon but striking presentation among children with oncologic disorders. This oncologic emergency heralds serious morbidity and requires rapid intervention to prevent permanent disability. We studied the incidence, presentation, interventions and outcomes in pediatric oncology patients presenting with paraparesis at a single center in a developing country.
Materials and Methods: A prospective study of data for paraparesis in pediatric oncology patients at our institution between March 2010 and February 2013 was performed.
Results: Nine (2.5%) children out of a total of 355 pediatric patients with oncologic disorders presented with paraparesis during the study period. Four (11.1%) were diagnosed with neuroblastoma, 1 (11.1%) had a ganglioneuroblastoma and a further one patient (11.1%) each was diagnosed with metastatic primitive neuro-ectodermal tumor (PNET), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and Hodgkin lymphoma (HL) respectively. The onset of paraparesis was 3 days or less in 3 patients (33.3%) and more than 3 days in the other 6 (66.6%). Six (66.6%) children had bowel and/or bladder involvement at diagnosis. One (11.1%) patient each with metastatic neuroblastoma and ganglioneuroblastoma underwent emergency decompressive surgery and urgent local radiotherapy respectively to attempt rapid relief of the neurologic deficit. The other 7 (77.7%) patients received appropriate disease specific chemotherapy to relieve their paraparesis. All patients received immediate therapy with corticosteroids to reduce the spinal cord compression and attempt neurologic recovery. Complete/near complete recovery from neurologic deficit was noted in the 3 (33.3%) patients with paraparesis of less than 3 days duration and recovery was poorest in 3 (33.3%) patients with the longest duration of deficit.
Conclusions: Paraparesis is a rare but often defining symptom in pediatric oncology, seen in a variety of malignancies. Urgent intervention, most commonly in the form of local radiotherapy or emergency surgery, as early from onset as possible is essential to maximize neurologic outcomes.

PUB-0244

CLINICAL PROFILE AND CHEMOTHERAPY RESPONSE IN CHILDREN WITH HODGKIN LYMPHOMA AT A TERTIARY CENTRE IN INDIA

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Purpose/Objective: Purpose: Optimal treatment strategy in children with Hodgkin Lymphoma (HL) still remains controversial especially in advanced disease (combined chemo*radiotherapy (CMT) or chemotherapy (CT) alone), Our objective was to review the clinical profile and to evaluate the efficacy of chemotherapy alone as a therapeutic modality in pediatric HL.
Materials and Methods: Methods: Retrospective record review for 35 patients treated for HL at our centre was done
Results: Results: 31 males and 4 females with a median age of 8 years (range 3.5 to 13years) were studied. 24 patients (68.6%) were $<$ 10 years old, and 23 (65.7%) had advanced stage disease (IIB*IV). B-symptoms were present in 21(60%) cases, bulky mediastinal disease in 9(25.7%), spleen involvement in 21(60%), and bone marrow involvement in none. The histological types were equally represented * nodular sclerosis in 10 patients(28.6%), mixed cellularity in 9(25.7%), lymphocyte predominant in 9(25.7%), and lymphocyte depleted in 7(20%) patients. Most patients received ABVD-COPP or ABVD. 2 patients needed BEACOPP due to progressive disease. 4 patients needed low-dose involved field radiotherapy (RT). During CT, 5 patients (14.3%) showed persistent or progressive disease. At an extended event-free follow-up median duration of 42months (range 8-72 months), 4 patients relapsed. One was lost to follow-up, while 3 were treated by CT. No child died due to disease. There was no association of adverse prognostic factors with outcome or event-free survival.
Conclusions: Chemotherapy alone is an effective therapy in childhood HL, irrespective of stage and subtype of disease. Radiotherapy may be used as a second line salvage therapy.

PUB-0245

LITERATURE TRENDS IN END-OF-LIFE (EOL) CARE IN PAEDIATRIC ONCOLOGY

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Purpose/Objective: Increasing attention has been given to the development of EoL care for children with cancer over the last few decades, exploring patient and family needs during palliation, and transition to this phase. This review aims to explore how current literature reflects this growth in our experience and knowledge of EoL care for children with cancer, and changing trends in research from 2002 to 2012
Materials and Methods: AMED, EMBASE, MEDLINE, PsycINFO, BNI and CINAHL were searched via NHS Evidence using the search terms 'palliative care, palliative therapy, end of life care or terminal care' and 'cancer or oncology'. Searches were limited to children (0-18), and results published in 2002 or 2012
Results: Non-paediatric, non-cancer or non-palliative care results, and duplicates were excluded. Non-English results were included were an English abstract was available. 8 results from 2002, and 37 from 2012 were included.

In 2002, 4/8 results (vs 3/37 for 2012) related to clinical practice guidelines (all related to pain management), while 2/8 (vs 10/37 for 2012) described the development of palliative care programmes or services.

2012 results included 8 (vs 0/8 in 2002) qualitative studies (all of which explored parental perspectives on EoL care) and 5 systematic reviews (vs 0/8 in 2002).

Of the 37 studies from 2012, 7 were from low or middle income countries (vs 0 in 2012)
Conclusions: EoL care in paediatric oncology has received increasing coverage in clinical and scientific literature over the last decade, especially with regard to service development and improvement, and reporting from low and middle-income countries. Research is increasingly qualitative, predominantly exploring parent and family experiences of palliative care. Alongside this, systematic reviews and meta-analyses in specific areas of EoL care will continue to generate evidence and inform clinical developments.

PUB-0246

RETROSPECTIVE DRUG USE EVALUATION OF APREPITANT IN PAEDIATRICS AND ADOLESCENTS

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Purpose/Objective: To identify the prescribing patterns and evaluate the appropriate use of aprepitant in paediatric oncology patients and identify any potential problems in the use of aprepitant that may necessitate intervention to optimize its usage.
Materials and Methods: A single centre, retrospective drug use evaluation of aprepitant in the paediatric oncology population was conducted at KK Women's and Children's Hospital (KKH). All patients below 18 years old and prescribed with aprepitant between 1 January 2002 and 31 December 2010 were included. Vomiting was graded according to the Common Terminology Criteria for Adverse Events v4.0.
Results: Twenty-four patients and 227 chemotherapy cycles were reviewed. Chemo-na●ve patients have better control of emesis when aprepitant was given appropriately. Fifteen of the 21 chemo-na●ve patients had highly emetogenic chemotherapy (HEC) cycles. Out of the 15 patients, 7 patients received aprepitant and 3/7 were patients given aprepitant appropriately. One did not vomit while 2 had vomit grading of 2. Four patients that were not given aprepitant appropriately, 2/4 had vomit grading of 1 and another 2/4 with vomit grading of 3. The 8/15 patients who did not receive aprepitant, had poorer control of emesis than patients that received; 1 did not vomit while 7/8 had poor control. There were 83 HEC cycles and 50/83 cycles received aprepitant. Outcomes were comparable between cycles that received aprepitant and those did not. For cycles that received aprepitant, 27/50(54%) did not vomit; 10/50(20%) had poor control of emesis. Cycles that were not given aprepitant, 15/33(45.5%) did not vomit; 5/33(15.2%) had poor control of emesis.
Conclusions: Aprepitant should be prescribed to chemo-na●ve patients especially in HEC cycles in order to improve outcome of chemotherapy induced nausea and vomiting (CINV). There is a need to review our guidelines and processes to ensure patients are receiving optimal medication regimen to help reduce CINV.

PUB-0247

LANGERHANS CELL HISTIOCYTOSIS: STILL A MISSED DIAGNOSIS

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Purpose/Objective: Purpose: Langerhans Cell Histiocytosis (LCH),an enigmatic disease, has varied presentations, possibly resulting in misdiagnosis, delay in diagnosis and delay in starting therapy. This leads to progression of disease and consequent irreversible damage to affected organs. This analysis was done to study the varied presentations, identification of referral diagnosis and time lag in achieving the diagnosis.
Materials and Methods: Method: Prospective evaluation of children diagnosed as LCH was done at our Oncology clinic. A complete history and physical examination was undertaken followed by laboratory and radiological evaluation. Biopsy of the appropriate specimen was done. The referral diagnosis, time lag since initiation of therapy and cause for delay in diagnosis ascertained. Extent of the disease documented, accordingly treated and followed up after appropriate classification (Single system/ multisystem, risk organ involvement. They were followed up for remission/progressive disease and sequelae.
Results: Results: 49 children with LCH were diagnosed during the study period. Age at presentation ranged from 8 to 72 months. Duration of symptoms ranged from 2 months-4.5

years. Mean time to arrive at diagnosis was 9.9 months. Common presenting symptoms were fever, abdominal distension, bony/soft tissue involvement and skin lesions. Signs most commonly seen were hepatomegaly, splenomegaly and tacyhpnea. Most common system affected was skeleton (77%). Risk organ most affected was liver. 11 children had pulmonary involvement. Common referral diagnosis included immune deficiency, skin/dental problems, recurrent pneumonia and malignancy. LCH as initial diagnosis was made in 5/49 patients only. Sequela seen in 42% cases comprised of short stature, bony defects and chronic liver disease.
Conclusions: Conclusion: LCH remains a versatile mimicker; Diagnosis is often difficult and delayed. Misdiagnosis is common. Sequela are significant. There is need for high index of suspicion for diagnosis of LCH for better outcomes

PUB-0248

NECESSITY OF BLOOD COMPONENTS AND GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA DURING INTENSIVE CHEMOTHERAPY

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Purpose/Objective: Acute lymphoblastic leukemia (ALL) is most common malignant disease in childhood-representing 30% of all malignancies in children. The survival rate for children younger than 15 years of age reaches about 75% and this great success is attributed in part to improvements in supportive care with blood components and GCSF during periods of morbidity due to therapeutic interventions.
Our purpose was to evaluate the needs for blood components and GCSF per patient during intensive chemotherapy in children with ALL treated after ALL BFM 2000 protocol.
Materials and Methods: Retrospective analysis of 45 records of children with ALL for amounts of transfused blood derivatives and applied GCSF during protocol I, protocol M and protocol II
Results: : During protocol I all patient 45(100%) received filtered red blood cell transfusion (6.5 transfusions per patient), 34(75%) patient received platelet transfusion (5.7 per patient), 21(46%) received plasma transfusion (1.8 per patient), 41(91%) received GCSF (8.0 per patient) and 9(20%) received albumin transfusion (1.9 unit per patient). In protocol M 18(40%) patients received blood transfusion (1.7 per patient), 23(51%) received platelet transfusion (1.6 per patient), 5 (11%) children received plasma (0.8 per patient) 18(40%) received GCSF (3.0 per patient) and none of the patients needed albumins. In protocol II 40(88%) patients received blood transfusion (2.8 per patient), 23(51%) received platelet transfusion (3,2 per patient), 16(35%) received plasma transfusion (0.7 per patient) 42 (93%)received GCSF (10 per patient) and 15(33.3%) received albumins (5.8 per patient)
Conclusions: The most commonly applied blood components during the treatment were filtered red blood cells (average 11.4 $\pm$ 6.3 units per patient) and platelet mass (9.35 $\pm$ 6.2 units). The need for red cell transfusion and platelets are grater in the first three months of therapy (during protocol I) despite the grater need for transfusion of albumins and application of GCSF in protocol II.

PUB-0249

NEUROLOGICAL MANIFESTATIONS OF PEDIATRIC MALIGNANCIES - CASE SERIES FROM INDIA

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Purpose/Objective: To describe varied neurological manifestations in children with malignancy managed between October 2008 to December 2012 at tertiary care Children's Hospital either directly related to disease or secondary to treatment.
Materials and Methods: Data of 29 children with neurological problems in childhood malignancies between 3 months to 15 years of age, were identified and reviewed.

Children with preexisting neurological problems or post chemotherapy isolated cognitive dysfunctions were excluded.

Type of Study: Retrospective chart review
Results: Twenty nine children with neurological manifestsations were identified. Acute lymphoblastic leukemia (ALL) was the most common malignancy11/29, followed by neuroblastoma(NBL)8/29. 4/8 neuroblastomas presented with Opsoclonus Myoclonus syndrome. Four were Ewings sarcoma /PNET, presented with spinal cord compression. Histiocytic disorder with Diffuse Central Nervous System(CNS) involvement was seen in 2. Acute myeloid leukemia, Diffuse Large B cell lymphoma, Rhabdomyosarcoma(RMS) and germcell tumors(GCT), one each.

Disease related neurological problems seen in 20 children,16 were directly related to disease and 4 part of paraneoplastic syndrome. 10/ 16 had focal weakness with cord compression or CNS deposits. 2 had facial nerve palsy with tumor infiltration in CNS/into nerve.One each had ptosis, seizures. Intense head ache and vomitings secondary to CNS deposits noted in one and one was with combination of hemiparesis and facial nerve palsy.

Treatment related problems noticed in 9.Stroke like presentation was seen in three. Seizures post methotrexate therapy in four 4. One had ventriculitis with hydrocephlaus while on Induction and subsequent neurocognitive problems. One had vincristine induced neuropathy.
Conclusions: Neurological manifestations are varied, early recognition is essential to reduce mortality and morbidity. Knowledge of different neurological manifestations with these disorders or secondary to medications is essential for optimal management.

PUB-0250

ACUTE SIDE EFFECTS OF ABDOMINAL RADIATION THERAPY IN WILMS TUMOR- SINGLE CENTER EXPERIENCE

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Purpose/Objective: Radiation therapy (RT) has a well established role in treatment of Wilms tumor (WT). However its use has been limited to advanced stage local tumors or metastatic disease because of its immediate and long term adverse effects. Purpose of this study was to assess the acute side effects of abdominal RT administered in WT patients in our hospital.
Materials and Methods: Out of 78 WT patients treated in Shaukat Khanum Memorial Cancer Hospital & Research Center Lahore during January 2007 and December 2011, 28 received abdominal RT. We retrospectively reviewed the medical records of these children during and 4 weeks after completion of RT. Chemotherapy was continued in all patients during RT as per treatment protocol. Findings of serial CBCs done within four weeks before RT were also recorded to assess the trend of platelet and absolute neutrophil counts.
Results: Median age at presentation was 4 years; with a male to female ratio of 1.3:1. Total abdominal radiation dose ranged from 11-35 Gy. Eighty nine percent (n = 25) children suffered from acute diarrhea for a duration of 3.6 $\pm$ 2.2 days; with 20 patients recovering with symptomatic treatment and ORS. However five patients had severe dehydration with or without electrolyte imbalance. Severe neutropenia was recorded in 82% (n = 23) and 54% (n = 15) required platelet transfusions for life threatening thrombocytopenia. Eighteen patients developed febrile neutropenia and half of them needed inpatient admission for close monitoring and management. Three patients had cultures proven infections and one of those having candidemia died within one week of completion of RT. Treatment had to be interrupted in three septic patients and one patient who had profuse watery diarrhea.
Conclusions: Diarrhea was the most common acute side effect of abdominal RT followed by severe neutropenia and thrombocytopenia. Dietary modifications and neutropenic precautions during RT can reduce the morbidity and mortality.

PUB-0251

DEFORMABLE IMAGE REGISTRATION AND DOSE MAPPING TO OBTAIN COMPOSITE DOSE-VOLUME STATISTICS FOR RE-IRRADIATION OF A CASE OF RECURRENT PEDIATRIC INFRATENTORIAL EPENDYMOMA

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Purpose/Objective: Retrospective studies of re-irradiation for recurrent pediatric ependymoma demonstrate improvement in local control. However, uncertainty about normal tissue tolerance may lead to increased toxicity and long-term effects. Treatment planning with dose-volume data may mitigate these toxicities. Deformable image registration and dose mapping has not been applied to re-irradiation of pediatric tumors.
Materials and Methods: A patient was diagnosed at 10 months of age with a posterior fossa ependymoma and had gross total resection followed by chemotherapy to delay radiotherapy. Due to poor tolerance to chemotherapy, the patient was treated 5.5 months later with focal IMRT (59.4Gy). Five years later, local recurrence was confirmed by maximal safe resection leaving residual gross tumor. The patient was re-irradiated with IMRT (54-59.4Gy). Re-irradiation PTV (PTV2) was smaller than initial PTV1 (16.8 versus 76.4cm3). Treatment planning incorporated post-operative MRI images rigidly registered with the planning CT. Plan optimization utilized manual dose accumulation for target and normal structures. The patient tolerated treatment well with minimal acute toxicities.

The plans were retrospectively registered with a constrained, intensity-based deformable registration algorithm (MIM). Brain volume increased from 1082 to 1400cm3. The accuracy of the deformation was assessed visually and quantitatively. The initial dose distribution was mapped onto the re-irradiation CT dataset. Dose-volume histograms were generated for the plan summation.

Results: All structures increased in volume over time (irradiated volume surrounding PTV1 increased 13%). Deformable dose summation of minimum, mean, and maximum doses was compared to manual summation. Mean-dose agreement for PTV2 was within 3%, but ranged from -31% to 2.3% for organs at risk. Structures near steep high dose gradients had larger discrepancies.
Conclusions: This technique is feasible for re-irradiation treatment planning for locally recurrent pediatric ependymoma. Altered time-dose fractionation may be possible without exceeding constraints for organs at risk. Further quality assurance testing and validation is needed with a larger cohort.

PUB-0252

INVASIVE FUNGAL INFECTIONS IN CHILDREN TREATED FOR ADVANCED EWING SARCOMA – UNDERESTIMATED CLINICAL PROBLEM

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Purpose/Objective: To assess the scale of the problem of invasive fungal infections (IFIs) in children treated for advanced Ewing sarcoma (ES).
Materials and Methods: A retrospective case series study was performed in 12 children with stage III and IV ES (F/M = 7/5, median age 12y) treated with chemotherapy, radiotherapy and surgery (all) and autologous hematopoietic stem cell transplantation (auto-HSCT * 2 patients) between 1992 and 2012.
Results: 16 IFI episodes were stated in six patients, in four children three and more episodes occurred. Severe symptoms from digestive tract (typhlitis, diarrhea and paralytic ileus) and FUO predominated. Urinary tract IFIs were components of multiorgan infections. Lung IFIs were detected in routine CT in 3 patients. 81% of episodes were associated with elevated CRP. Only one IFI episode was diagnosed as definite (multiorgan *Candida glabrata* infection of peritoneum, digestive and urinary tracts in a girl after auto-HSCT). Simultaneously a probable lung aspergillosis was found in this patient. 81% of episodes were diagnosed as possible IFIs. Apart from central vein catheters, wide spectrum antibiotics and neutropenia, main risk factors for IFIs comprised: cachexia, immobilization after surgery, active cancer phase (soon after diagnosis and/or at progression), implantation of intestinal stoma and/or bladder catheters and parenteral nutrition. Therapy of IFIs included: caspofungin (9 episodes), liposomal Amfotericin B (8), voriconazole (5), micafungin (1), posaconazole (1). Secondary prophylaxis with voriconazole seemed effective in most patients. 88% of IFIs were curable. One patient died of ES progression with active IFI (FUO). Another child died due to multiorgan *Candida glabrata* and *Aspergillus* IFI soon after auto-HSCT in ES remission.
Conclusions: Incidence of IFIs in advanced childhood ES is underestimated. Highly aggressive combined multimodal therapy of ES predisposes to IFI. Although in most cases diagnoses are only possible, IFIs cause delays of oncologic therapy, increase mobidity and mortality. Early empirical anti-fungal therapy followed by secondary prophylaxis should be recommended for childhood ES.

PUB-0253

STUDY OF MORTALITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED AT A TERTIARY CARE CENTER IN SOUTH INDIA

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Purpose/Objective: Although the outcome of ALL has improved significantly in developed world, it is still poor in developing countries. The published data on treatments and outcome are lacking in India. We designed this study to understand the causes of mortality of children with ALL in a Tertiary Government hospital in south India which cover a populations of.more than 10 million
Materials and Methods: This is retrospective study of mortality in 67 children with Acute lympmpho blastic leukaemia (ALL) in a major Government paediatric institute in Kerala,India over 4 years period between 2008and 2012
Results: Mortality of 67 children treated between 2008 and 2012 were analyzed. Male (38) to Female (29) was 1.3. 57. (87%) of children were in the age group 1-9 years. 20(29.8%) cases were ALL L1. 44(64.6%) cases were ALL L2.3 cases were not specified.40(59.7%) cases belonged to B cell lineage.8 (11.9%) belonged to Tcell.One case of mixed lineage and in 18 cases immune phenotyping could not be done. 41 (61%) were high risk and 26 (38.8%) were standard risk. 31 cases (11 in high risk and 20 in standard risk) died during induction and 26 cases (15 in high risk and 11 in standard risk) died during maintenance phase. Others were in the interim maintenance and in relapse treatment. Of the causes of mortality 36(53.7%) were due to febrile neutropenia,17 (25.3%) were due to relapse and 7 (10.4%) were due to intracranial bleed. Of the relapse in 17 cases 14 cases (87.5%) were in the high risk group.Analysis of bacteriological profile in febrile neutropenia showed 7 cases of klebsiella 4 cases of Pseudomonas aerugenosa
Conclusions: Most common case of mortality was due to febrile neutrpenia relapse and intracranial bleed.Death due to relapse occurred more in high risk groups. Induction mortality was high which needs to be reduced by intense supportive care and further risk categorization

PUB-0254

GLIOMATOSIS CEREBRI MIMICKING ENCEPHALITIS: A CASE REPORT

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Purpose/Objective: Background and Aim: Gliomatosis cerebri (GC) is an uncommon, diffusely infiltrating glial neoplazm of the brain. It is extremely rare in children, have variable infection-like presentations, and typically very poor outcome. In this report, we describe here a teenage that initially considered as encephalitis, but diagnosed as GC in the clinical follow up.
Materials and Methods: Case report: A 13 year old boy referred to our hospital with complaints of right facial paralysis, right hemiparesis and cognitive difficulties. From his medical history it was learned that he had been hospitalized, and cephtriaxone and acycylovir were started for suspected encephalitis. MRI of the brain revealed midline shift and diffuse white matter changes involving all of the brain, particularlly left hemisphere. On T2-weighted images, there was a diffuse hyperintensity. Stereotaxic brain biopsy was performed, and reported as diffuse grade II astrocytoma. The patient received radiotherapy and temazolomide based chemotherapy.
Results: Approximately 11 months after initial presentation, his condition had significantly improved and radiological response was also observed. He is still alive at the time of writing this presentation
Conclusions: In conclusion, the misdiagnosis of GC cause delay for the optimal treatment in children with GC, which is still not clear. This report highlights the importance of suspicion in patients, who presents neurological deterioration and imaging findings of diffuse brain involvement.

PUB-0255

NON-WILMS RENAL TUMORS IN CHILDREN ARE STILL A CHALLENGE

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Purpose/Objective: The Wilms tumor is the most common pediatric renal tumor and cover about 6-7% of all pediatric malignancies. Although, pediatric non-Wilms renal tumors can be seen less than 10% of the renal tumors, they have dramatically notable mortality. Currently, controversies still persist for optimal management, due to their rarity and heterogenity. Most of them have very good prognosis such as cystic lesions, on the other hand clinicians must be vigilant about very aggressive neoplasms like malign rhabdoid tumors. We would like to share our experience of Non-Wilms renal tumors in children who have been followed at Erciyes University, Kayseri, Turkey.
Materials and Methods: Between 2000-2013, 11 patients were followed for non-Wilms renal tumor in our center (4 mesoblastic nephroma, 2 clear cell carcinoma, 2 rhabdoid tumor, 1 inflamatory myofibroblastic tumor, 1 multicystic nephroma, 1 cystic partially diferentiated nephroma).
Results: We report here all the patients' demographics, pathologically reports, radiologic findings, treatment regimens, and other characteristics. Radiologic imaginations showed 4 cystic and 7 solid tumors, all of them underwent nephrectomy. 5 patient (3 mesoblastic nephroma 2 rhabdoid tumor) received chemotherapy, and 2 mesoblastic tumors received concomitant radiotherapy. 2 patients died (1 mesoblastic nephroma and 1 rhabdoid), due to relapse and lung metastasis. Remaining is still alive.
Conclusions: The prognosis of pediatric non-Wilms renal tumors may improve with suitable management and multidiciplinary colloborative treatment. Surgery is fundamental, but response of the chemotherapy is extremely variable from case to case.
Key words: non-Wilms renal tumors, childhood, rhabdoid tumor

PUB-0256

PULMONARY LANGERHANS CELL HISTIOCYTOSIS MIMICKING BRONCHIAL ASTHMA

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Purpose/Objective: Pulmonary Langerhans cell histiocytosis (PLCH) in children usually occurs in patients with multisystemic involvement Isolated pulmonary compromise is more

frequent in adults than in children. Respiratory symptoms are the cardinal clinical features. Early in the disease, the most common radiographic manifestation is that small nodules, which exhibit characteristic irregular borders. As the disease progresses, reticulonodular abnormalities may result in a predominance of cystic changes, and then progress to honeycomb lung. Pneumothorax is a recognized complication of PLCH. In this presentation we present an adolescent boy with PLCH mimicking bronchial asthma.
Materials and Methods: Case report: a 17-year-old boy was referred to our hospital with complaints of dyspnea induced by simple effort. From his medical history it was been learned that he was smoking for 11 packet year, diagnosed as bronchial asthma for two years. He was using irregular medications and his symptoms were worsened during the last month. Echocardiography showed pulmonary hypertension, and the thorax tomography revealed multiple cystic lesions. Biopsy from the pulmonary lesion showed PLCH and diagnostic studies were normal.
Results: He was diagnosed as isolated PLCH and we advised to stop smoking and started prednisolon treatment.
Conclusions: Recently many children with respiratory complaints are misdiagnosed with bronchial asthma. PLCH may cause a diagnostic challenge for inexperienced clinicians who are unfamiliar of this rare disease. Patients with respiratory complications must be evaluated carefully and PLCH must be considered as differential diagnosis in patients with specific radiological findings.
Keywords: Adolescent, bronchial asthma, pulmonary Langerhans cell histiocytosis

PUB-0257

PROFILE OF MALIGNANCIES IN INFANTS: A SINGLE CENTRE EXPERIENCE FROM A DEVELOPING COUNTRY

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Purpose/Objective: Malignancies in infants represent a special subset in pediatric oncology due to diagnoses unique to this age-group, variability in clinical behaviour and pharmacokinetics. Age less than 1 year is a poor prognostic factor for most pediatric cancers. Here we describe our centre's experience over the years with respect to infantile neoplasia.
Materials and Methods: A retrospective review of medical records of all pediatric oncology cases diagnosed between 2004 to 2013 was performed to identify children younger than 12 months of age.
Results: Of 928 malignacies diagnosed at our centre in the study period, we identified 40 (4.3%) infants. The median age at diagnosis was 7 months (range 1 to 12 months) and male-female ratio was 2:1. The most common neoplasm in this age group was neuroblastoma accounting for 10 cases (25%). The next most frequent diagnosis was Wilms tumor (WT) and acute lymphoblastic leukemia (ALL) seen in 7 patients (17.5%) patients each. Others include 4 patients (10%) of juvenile myelomonocytic leukemia (JMML), 3 each of acute myeloid leukemia (AML), rhabdomyosarcoma (RMS) and langerhans cell histiocytosis (LCH), 2 of hepatoblastoma and a solitary patient of unilateral retinoblastoma. The proportion of infants out of total number of cases diagnosed for each malignancy was 18% for neuroblastoma, 20% for WT, 1.6% for ALL, 4% for AML, 50% for JMML, 10.75% for LCH, 13.6% for RMS, 22.2% for hepatoblastoma and 11.1% for retinoblastoma. Twenty-seven patients (67.5%) opted for treatment. The rest abandoned treatment and their outcomes are unknown. The overall survival rate of the cohort was 42.5% and for 63% for patients who took treatment.
Conclusions: Malignancies in infants account for a small but significant proportion of cases. The variety of oncologic diagnoses in this special group is noteworthy. Treatment abandonment rates were found to be high in the cohort.

PUB-0258

IMAGING STUDIES DURING LAST PHASE OF LIFE IN PEDIATRIC ONCOLOGY

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Purpose/Objective: Evaluate current practice of performance of various imaging studies (IS) among children with various solid tumors during last 3 months of their life.
Materials and Methods: Retrospective analysis of medical charts of 48 (25 males and 23 females, with median age of 12.5 years, range 0.5-28y) pts who died between 1.1.2003 and 1.10.2007 was performed. 21 pt suffered from brain tumors, 19 pts * sarcomas, 6 pts * neuroblastoma and 2 pts * carcinoma.
Results: During the final period of pts' life were performed 173 various imaging studies (X-ray, US, CT, MRI, bone scan and other scans with various isotopes).Every pt underwent at average 3.60 IS (range, 0-10).70% of IS were performed in pts with sarcomas. One pt with carcinoma and 9 pts with brain tumors underwent no IS at all. 34.7% of all IS were performed due to emergency conditions. 58.4% of IS * for evaluation of disease status, 6.9% - as follow-up after some kind of surgical intervention (pleural puncture, central line insertion, etc).
Conclusions: 1. Complexity of final phase of life of pts with various extracranial solid tumors necessitates relatively frequent performance of various IS. 2. Earlier clarification of incurable status of pts' disease may potentially decrease the need for performance IS and thus to diminish discomfort of such pts during last months of their life.

PUB-0259

RADIOTHERAPY IN CHILDHOOD AGGRESSIVE FIBROMATOZIS

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Purpose/Objective: Aggressive fibromatozis (AF) is a local aggressive soft tissue tumor in childhood. It usually recurs despite surgical excisions. Irradiation and chemotherapy may also be effective in controlling recurrent tumors. In this study we aimed to analyse treatment results of AF patients.
Materials and Methods: Between January 2000 and June 2011 we treated 12 patients with AF. Median age was 9.5 years (5-17). There were 9 males (75%) and 3 females. Tumor location was gluteus in 4 patients whereas lower extremity in 2, upper extremity in 3, trunk in 2, head and neck in one.
Results: Before irradiation, the patients had median 3 recurrences (1-15). All patients were given external irradiation at a dose of 45-54 Gy in local sites. Five patients were also given methotrexate-vinblastine combination.
Median follow-up time was 51 months (19-120), and 6 patients relapsed after irradiation. We calculated 5-year-event free survival rate as 46% by irradiation. Among the side effects of radiotherapy and surgery, local growth retardation was striking in 10 out of 12 patients.
Conclusions: In conclusion, childhood aggressive fibromatozis is a rare soft tissue tumor. Recurrences are common despite multiple surgeries. Irradiation is an effective local control measure in half of the patients.

PUB-0260

BOTRYOID EMBRYONAL RHABDOMYOSARCOMA OF THE RENAL PELVIS. A CASE REPORT.

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Purpose/Objective: Botryoid embryonal rhabdomyosarcoma is an extremely rare entity and can thus be difficult to identify. Only two cases have been reported in the pediatric literature, although more cases have been recorded in tumor registries. We aim to highlight this unusual entity.
Materials and Methods: A 12 year old female presented with a two year history of flank pain, hematuria and hydronephrosis. An open biopsy was performed at the referring hospital, and gelatinous tissue was observed in the renal pelvis. She was referred with a presumptive diagnosis of teratoid nephroblastoma. CT scan showed hydronephrosis, thinning of the renal cortex and a mass in the renal pelvis. At laparotomy a nephrectomy was performed and the macroscopic appearance was that of a cystic mass reminiscent of a duplicated cystic renal upper pole. The specimen was sent for histological examination.
Results: Macroscopically, a botryoid tumor was found in the renal pelvis, and the kidney parenchyma was uninvolved. The polypoid lesion was lined with intact urothelium, superior to neoplastic spindled cells. Nodules of small, round, blue cells showed rhabdomyoblastic features. Immunohistochemistry stains were negative for AE1/AE3, confirming the absence of an epithelial component, and negative for WT1. Positive stains included desmin in the cambium layer and cellular nodules, myogenin in the nuclei and MyoD1 focal staining, demonstrating rhabdomyoblastic differentiation. Metastatic work up was negative. The tumor was completely excised and the patient received six cycles of vincristine, ifosfamide, carboplatinum and etoposide, followed by 16 cycles of vincristine, actinomycin D and cyclophosphamide. She is currently in remission and well 30 months from diagnosis.
Conclusions: Botryoid embryonal rhabdomyosarcoma of the renal pelvis is an exceedingly rare tumor in childhood.
Favorable prognostic factors included complete surgical excision, botryoid embryonal subtype and tumor size less than 5cm.

PUB-0261

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PEDIATRIC PATIENTS WITH SOLID TUMORS: AN EXPERIENCE FROM TURKEY

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Purpose/Objective: Limited information is available from developing countries about long-term outcome of pediatric patients following high-dose chemotherapy (HDCT) and hematopoietic stem cell transplantation (HSCT). Aim of this study was to report the results of HSCT performed in a single center from Turkey.
Materials and Methods: Medical records of patients with solid tumors who underwent HSCT were reviewed retrospectively. Survival analysis was done using Kaplan-Meier method.
Results: Between 1998 to 2012 forty three pediatric patients underwent HSCT, 41 autologous and 5 allogeneic. Patient's median age was 72 months (range 4- 240 months). There were 17 females and 29 males. Indications for transplant included neuroblastoma (n: 26), relapsed lymphomas (n: 10), relapsed Ewing sarcoma (n: 5) and others (n: 5). Disease status before transplantation was complete remission in 25 patients and very good partial response in 20 and overt disease in one. All but one were chemosensitive disease before transplantation. Mucositis and veno-occlusive disease were major non-hematological complications, 4.3% of patients died of regimen-related toxicities. Of these patients 73.9% developed febrile neutropenia. At a median follow-up of 88 months (range 20-442 months), overall survival and event free survival (EFS) at 5 years were 71.0 $\pm$ 7.1% and 60.9 $\pm$ 8.0%, respectively. OS and EFS at 5 years were 71.6 $\pm$ 9.2% and 60.2 $\pm$ 10.5% for patients with neuroblastoma, 77.8 $\pm$ 13.9% and 77.8 $\pm$ 13.9% for lymphoma and 58.3 $\pm$ 18.6% and 41.7 $\pm$ 20.5% for other solid tumors, respectively.
Conclusions: Our analysis demonstrates that such procedure can be successfully performed in a developing country with results comparable to developed countries.

PUB-0262

MEDULLOBLASTOMA IN A 14-YEAR-OLD GIRL WITH FAMILIAL ADENOMATOUS POLYPOSIS

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Purpose/Objective: Several well-characterized hereditary syndromes predispose to the development of nervous system's tumors and result from germline mutations in high-penetrance genes. Signaling pathways involved in these syndromes include RAS, WNT, RB1, TP53, PTCH. Mutations of the APC gene is responsible for familial adenomatous polyposis (FAP) with elevated risk of colon cancer. This gene encodes a tumor suppressor protein that acts as antagonist of the Wnt signaling pathway which is disrupted in sporadic cancers. FAP may be associated with various extracolonic manifestations such as desmoid fibromatosis, osteomas and brain tumors.
Materials and Methods: Case report. DNA was extracted from fresh blood samples from family members and analysed for APC mutation.
Results: A 14 year-old girl presented with a hIstory of right VII cranial nerve palsy and ipoacusia. MRI study revealed a lesion involving the ponto-cerebellar angle. Family history was positive for colorectal cancer on paternal lineage. Analysis of DNA from affected family members revealed an inherited germline mutation at codon 4448 of APC gene. She underwent surgical removal of lesion which was confirmed as classic medulloblastoma. Metastatic work up was negative. Post-operative course was complicated by severe neurological impairment that required tracheostomy and gastrostomy for several months. Chemotherapy was initiated with carboplatin and etoposide following which she received craniospinal irradiation and maintainance chemotherapy according to SIOP PNET4. Chemoterapy was complicated by vincristine induced neuropathy. She remains with stable disease and partial recovery of neurotoxicity. Colonscopy performed at the end of treatment (16 years-age) was negative.
Conclusions: Tumor predisposition in children is rare, accounting for approximately 10% of all cancers in childhood. In our case, the central nervous system tumour represents an extracolonic manifestation of FAP. The identification of these predispositions is important for improved management for both the child and relatives and has been the basis for target identification and drug development.

PUB-0263

OSTEOSARCOMA AFTER BONE MARROW TRANSPLANTATION FOR DIAMOND-BLACKFAN ANEMIA

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Purpose/Objective: Diamond-Blackfan anemia (DBA) is a rare disease characterized by aplasia or hypoplasia of erythroid lineage, associated congenital malformation and an increased risk of hematopoietic malignancy. Several cases are trasfusion-dependent. Hematopoietic stem cell transplantation (HSCT) may be a curative option for patients affected by DBA. Recently, solid tumors such as hepatocellular carcinoma and osteosarcoma have been reported in DBA patients, some attributable to hemosiderosis and/or androgen therapy malignancy. We describe a young boy who had Diamond-Blackfan anemia and who developed an osteogenic sarcoma, after HSCT. This case highlights chemotherapy treatment considerations in patients who have underlying cancer predisposition syndrome.
Materials and Methods: Medical records and radiological studies from the referring hospital and from our institution were reviewed.
Results: A 21-year-old boy who had transfusion-dependent Diamond-Blackfan anemia underwent HSCT from familiar donor at age of ten years. The conditioning regimen included busulphan fludarabine, thiotepa. Nine years after trasplantation he developed an osteoblastic/condroblastic sarcoma of the right tibia. The patient had an initial response with Methotrexate-Adriamycin-Cisplatinum containing chemotherapy regimen but developed multiple pulmonary metastases during course of treatment. At last follow-up he has stable disease after eight cycles of ifosfamide containing chemoterapy.
Conclusions: Osteosarcoma should be included among the secondary malignancies that can arise following HSCT in selected patients with cancer predisposition syndrome such as DBA.

PUB-0264

DOWN SYNDROME PATIENT WITH SEVERE HEMOPHILIA AND ACUTE MYELOID LEUKEMIA: CASE REPORT

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Purpose/Objective: Case report
Materials and Methods: Retrospective analysis on record of Patient with Down Syndrome, Hemophilia A severe transient myeloproliferative syndrome and subsequent AML-M7
Results: Male patient, twenty four month old with Down syndrome, who is diagnosed at birth with severe hemophilia. At birth the patient presented transient myeloproliferative syndrome too, wich healed spontaneusly. At the age of fourteen months old he is diagnosed with AML FAB M7. He begins his treatment with Protocol GATLA 8-LMA-07. The patient is prescribed with recombinant human Factor VIII , with a dose accorded to the platelet count (platelet count: less than 50000 he recived FVIIIr 25U/kg every 12 hours and more than 50000 platelets FVIIIr 25U/kg three times a week). During the profuse bleeding episodes and/or invasive procedures he received an extra dose of recombinant human Factor VIII of 50 U/kg. The patient did not developed inhibitor throughout the rest of the treatment, nor platelet refractoriness. Currently he is under maintenance process in complete remission.
Conclusions: The association of severe hemophilia and AML is rare, there are few cases described in literature and the management of factor VIII is not standardized. The treatment administered rFVIII was well tolerated by the patient and he didn«t present any complications associated with severe bleeding nor with the management of implantable catheter. It«s worth to ask ourselves whether the fact that the patient didn«t develop the FVIII inhibitor for the treatment, would be related to his immunosuppression secondary to chemotherapy or to his base condition.

PUB-0265

OUTCOME OF CHILDREN WITH OSTEOSARCOMA IN SOLCA HOSPITAL, QUITO

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Purpose/Objective: Purpose: Treating patients with osteosarcoma remains a challenge, especially if they have high-risk features. This study describes the clinical characteristics of our patients.
Materials and Methods: Methods: We analyzed the medical records of children, aged less than 18 years, with osteosarcoma, diagnosed from January 2000 to December 2012.
Results: Results: Ninety-three patients were included. The median age was 13.4 (4-18). Fifty-eight were male. The predominant symptoms were pain (74.2%) and presence of a tumor (25.8%). The interval between first symptoms and definitive medical care was in average 3 months. The predominant histopathology was osteoblastic osteosarcoma in 53 (56.9%), followed by fibroblastic 14 (15.5%) chondroblastic 11 (11.8%) and pleomorphic 10 (10.7%). Alkaline phosphatase was significantly elevated and related to tumor size. In 65 patients (69.8%) the tumor size was greater than 8 cm (average 17.05 cm). Of note, 45

patients (48.3%) had metastases at diagnosis; the predominat site was lung followed by bone. We had three multiostotict osteosarcomas. Forty patients (43%) were amputated, and 53 (57%) underwent limb-sparing procedures. In average the percentage of tumor necrosis was 52%. Only 9 patients (9.6%) had over 90% necrosis. Thirty-five patients relapsed (37.6%). The average time was one year after diagnosis. Our overall survival is 29% (27 patients). Sixty-one patients are dead and 5 lost to follow-up. The causes of death were progression in 31 patients (50.8%), abandonment or refusal to treatment in 16 patients (26.2%), very advanced disease at diagnosis in 7 (11.4%) and infections in 5 (8.1%). If we censored the abandonment, the cure rate will be around 46%.
Conclusions: Conclusion: The outcome is low in our hospital. We encountered patients with very high-risk features and poor response to initial chemotherapy. We have to make efforts in order to decrease the rate of abandonment especially before surgery.

PUB-0266

PLEUROPULMONARY BLASTOMA. CASE REPORT IN A LOW INCOME COUNTRY AND LITERATURE REVIEW.

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Purpose/Objective: Pleuropulmonary blastoma (PPB) is a rare primary intrathoracic mesenchymal malignancy that occurs exclusively in early childhood. It is extremely uncommon, and it is well known to have a very poor prognosis, especially in not industrialized countries
Materials and Methods: We present the case of a 6 year old boy, admitted in a hospital with a history of chest pain and respiratory distress, treated initially in Oaxaca as 'pneumonia'. After several studies, a left intrathoracic tumor was discovered, and underwent a left thoracothomy. The tumor was completely removed, and started chemotherapy courses using dactinomycin, vincristine and doxorrubicin for 5 courses., but after 5 months, there was tumor progression and the patient was referred to Centro Medico Nacional '20 de Noviembre' ISSSTE, where a new tumor resection was performed. We started again polychemotherapy and radiotherapy, using Ifofamide, Carboplatine and Etoposide. After 1 year, he had tumor progression so we started a third line of chemotherapy used in refractory solid tumors with Irinotecan, Vincristine and Erlotinib
Results: The boy is now disease-free, 2 years after the surgical operation, with good quality of life.
Conclusions: The biologic behavior of the tumor is considered unpredictable, and for this reason much effort has been expended in trying to identify prognostic factors and its treatment, with is primarily surgical, although, combination chemotherapy has been reported to result in objective responses in inoperable tumors or after incomplete resections. In this case, we also used radiotherapy and chemotherapy, including target therapy. The literature on the treatment of PB is reviewed in this work.

PUB-0267

LEFT VENTRICULAR HEART FUNCTION IN CHILDREN WITH OSTEOSARCOMA DURING CHEMOTHERAPY

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Functional Diagnostics, Belarusian Research Center for Pediatric Oncology Hematology and Immunolog, Minsk region, Belarus

Purpose/Objective: Characterization of contractile and pumping of left ventricular (LV) heart in children with osteosarcoma initially and at the end of therapy containing anthracycline antibiotics.
Materials and Methods: There were examined 21 children age are 5 to 16 years old (13.19 + 2.58 years), median 14 years with osteosarcoma. Males were predominated (57.14%). No there were risk factors systolic dysfunction from patients (congenital heart diseases). Treatment of the main disease (osteogenic sarcoma) was conducted on the protocol OS Minsk-98, including a 48-hours infusions of doxorubicin in a doses of 90 mg/m2. The cumulative dose of doxorubicin was 360 mg/m2. Echocardiography was performed to all patients. Were determined: stroke volume (SV), cardiac output (CO), fraction shortening (FS), ejection fraction (EF).
Results: In the group of patients with osteosarcoma before the start of polychemotherapy LV myocardial systolic function was normal (SV - 58.93 $\pm$ 15.71 ml, CO - 5.10 $\pm$ 1.40 l/min, FS - 36.35 $\pm$ 3.70% and EF - 66.22 $\pm$ 4.95%). After carrying out chemotherapy in patients with osteosarcoma the systolic and pumping functions of hearts underwent no statistically significant changes (SV - 60.55 $\pm$ 15.22 ml, CO - 4.85 $\pm$ 0.92 l/min, FS - 34.65 $\pm$ 4.16% and EF - 63.73 $\pm$ 5.57%).
Conclusions: In the near term after carrying out chemotherapy the applied dose anthracycline in the regimes of prolonged introducing of doxorubicin in patients with osteosarcoma do not have a significant impact on the pumping and retractive function of the myocardium LV.

PUB-0268

TWO CASES OF SUCCESSFUL LIVER TRANSPLANTATION FOR ANGIOSARCOMA IN CHILDHOOD

F. Gauthier[1], O. Ackermann[2], V. Fouquet[1], E. Gonzales[2], S. Franchi-Abella[3], M. Fabre[4], C. Guettier[4], S. Branchereau[1], E. Jacquemin[2], H. Martelli[1]

[1]Pediatric Surgery, Bicetre hospital, Le Kremlin Bicetre, France; [2]Pediatric Hepatology, Bicetre hospital, Le Kremlin Bicetre, France; [3]Pediatric Radiology, Bicetre hospital, Le Kremlin Bicetre, France; [4]Pathology, Bicetre hospital, Le Kremlin Bicetre, France

Purpose/Objective: Version:1.0 StartHTML:0000000201 EndHTML:0000003276 StartFragment:0000002455 EndFragment:0000003240 SourceURL:file://localhost/Users/fredericgauthier/.Trash/abstract%20SIOP%20angiosarcoma%20.doc Liver hemangioma (HE) occurring in infancy is regarded as a benign tumor because of it absence of metastastic progression. In a preliminary study (Ackermann O, 2011) we reported about a subtype of liver HE akin to angiosarcoma (AS). These AS, presenting as a new tumor arising after infancy, or as the relapse of a previous infantile regressive multiple HE, lead constantly to death after attempt at conservative management. Therefore prompt liver transplantation (LT) was proposed to treat them. We report here history and outcome of 2 children treated for AS by primary LT
Materials and Methods: Version:1.0 StartHTML:0000000201 EndHTML:0000002765 StartFragment:0000002455 EndFragment:0000002729 SourceURL:file://localhost/Users/fredericgauthier/.Trash/abstract%20SIOP%20angiosarcoma%20.doc Retrospective review of cases #1 and #2 focused on diagnosis of AS, assessment of absence of metastases, pathology of explanted liver and outcome after LT.
Results: Version:1.0 StartHTML:0000000201 EndHTML:0000003353 StartFragment:0000002456 EndFragment:0000003317 SourceURL:file://localhost/Users/fredericgauthier/.Trash/abstract%20SIOP%20angiosarcoma%20.doc A girl of 4.5 and a boy of 3.8 years presented with huge multifocal PRETEXT IV non-secreting liver tumors. In case #1 imaging and fine needle biopsy features were concordant with the diagnosis of AS. In case #2 imaging and age were suggestive of AS and biopsy of atypical HE. Absence of distant metastases was assessed by total body MRI. Both children could have prompt LT 15 and 13 days after registration. Main tumor was in right lobe in case #1, in left lobe in case #2, and both had scattered nodules in opposite lobe. None had liver hilum or node involvement. Phenotype of tumor cells was consistent with AS in both cases. With follow-up of 5.5 and 2 years both patients are alive without sign of recurrence.
Conclusions: Version:1.0 StartHTML:0000000201 EndHTML:0000002876 StartFragment:0000002455 EndFragment:0000002840 SourceURL:file://localhost/Users/fredericgauthier/.Trash/abstract%20SIOP%20angiosarcoma%20.doc To our knowledge, this is the first report of long tumor-free survival after LT for AS developed beyond infancy. These results advocate the policy of prompt LT for non metastatic chilhood AS.

PUB-0269

EWING SARCOMA FAMILY OF TUMORS IN CHILDREN FROM SOLCA HOSPITAL, QUITO - ECUADOR

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Purpose/Objective: In the pediatric population, Ewing sarcoma family of tumors (ESFT) constitute the second most frequent bone malignancy but may arise in soft tissues. We describe the clinical characteristics and outcome in our patients.
Materials and Methods: We analyzed the medical records of our patients younger than 18 years of age with ESFT, diagnosed from January 2000 to December 2012.
Results: Thirty-five consecutive patients treated at our institution were included. The median age was 10,5 years (range 1.2 -18). The male to female ratio was 1:1.06. The size of the primary tumor ranged from 2.5 to 25 cm in diameter. Pain, a tumor mass and fever were the presenting symptoms. Eight patients had localized disease, 17 had regional extension and 10 had metastatic disease at diagnosis. The tumor was located in the pelvis in 8 patients, lower extremities in 6, upper extremities 6, mandible 4, extraosseous 4, vertebral 3, polyostotic 3 and thorax 1.

Treatment included surgery and intense chemotherapy. Radiation therapy was given to 16 patients.

Two patients abandoned therapy. One patient died of secondary acute myeloid leukemia. Fourteen patients (40%) are alive with a mean follow up of 5.8 years (range 0.3-13).
Conclusions: Due to the nature of these tumors, curative treatment is intense and toxic. We will continue our efforts in order to improve survival by controlling infections, decreasing abandonment and optimizing treatment strategies.

Author/Abstract Index
(Number + *: Author is main author of this abstract)

A
A.A.Doumit, M., PUB-0005
Aalbers, A.M., P-0088, P-0101
Abad Calvo, P., P-0299
Abass, H., P-0192
Abate, M., O-0170
Abbas, N., O-0125
Abbott, L., P-0035
Abboud, M., PUB-0051
Abdalla, A., P-0280
Abdallah, F.K., O-0114
Abdel Khalek, E.R., P-0396
Abdel Rahman, H., PUB-0182
Abdel-Sayed, A., P-0234
Abdelghany, W., PUB-0185
Abdelkhalek, A., P-0416, P-0362
Ablin, A., P-0466
Abou Ghalia, A.H., P-0319
Abramovitz, L.Z., P-0565
Abramson, D.H., P-0310
Absalon, M., P-0447, P-0083
Abu-Shanab, M., PUB-0156, PUB-0201
Abuabed, J., PUB-0103
Acebo, J., PUB-0269, PUB-0265
Acevska, A., PUB-0248
Acha, T., O-0080, O-0079
Acharya, S., O-0196
Acharya, S.K., P-0301
Acipayam, C., P-0528
Acker, S., O-0177, O-0174
Ackermann, O., PUB-0268
Acord, M., P-0160, P-0182
Adachi, J., P-0328
Adachi, N., P-0462
Adachi, S., P-0531, O-0015
Adakl Aksoy, b., PUB-0218, PUB-0217
Adakli Aksoy, b., PUB-0217
Adaletli, I., PUB-0095
Adamaki, M., P-0368, PUB-0159
Adamkiewicz-Drozynska, E., PUB-0252, P-0179
Adams, D., P-0447
Adamson, L., O-0187
Adel, N., PUB-0240
Adiguzel, H., P-0440
Adu, C.A., P-0547
Afanasiev, B.V., PUB-0234
Afanasyev, B., P-0369
Affinita, M.C., P-0016
Agaoglu, F., PUB-0065
Agaoglu, F.Y., P-0311, P-0202
Agaoglu, L., PUB-0178, P-0055, P-0033, PUB-0033
Agarwal, D.B., O-0153
Agarwala, S., O-0189, P-0293, O-0164, O-0136, P-0156, O-0193, P-0292, O-0169
Agasoy, T., P-0491
Aggarwal, M., P-0413
Aggarwal, R., PUB-0131, P-0498
Agodi, A., O-0074
Agrawal, S., P-0052
Aguiar, S., P-0354, P-0348
Aguilar, D., PUB-0227
Ahmad, A., P-0111, PUB-0211, O-0125
Ahmed, A., P-0040
Ahmed, E.M., PUB-0057
Ahmed, H., PUB-0240
Ahn, H.S., P-0314, P-0183, P-0245, P-0149, P-0258, PUB-0110
Ahn, Y.J., P-0224
Ai, Y., P-0109, P-0010
Aida, N., PUB-0209
Aigrain, y., O-0081
Ajala-Agbo, T., P-0476
Ajith kumar, v.t., PUB-0253
Akaihata, M., P-0067
Akasaka, Y., PUB-0153
Akbari Moqadam, F., P-0021, P-0020
Akcay, A., PUB-0190, PUB-0175, PUB-0065
Akcoren, Z., P-0216
Akdemir, O., P-0181
Akdemir, U.O., P-0178
Aki, H., PUB-0095
Akici, F., PUB-0190, PUB-0175, PUB-0065
Akiyama, K., P-0237
Aksoy, B., P-0159, P-0139
Aksoylar, S., PUB-0259, PUB-0219, P-0047
Aksu, N., P-0311
Aktas, S., P-0440, O-0065
Akyuz, C., P-0118, P-0114, PUB-0056, P-0315, P-0216, PUB-0054, P-0126, P-0213, PUB-0016, PUB-0055
Al -Mahallawy, H., PUB-0240
Al- Musa, A., PUB-0156
Al- Nassan, A., PUB-0202
Al-Ahmari, A., PUB-0185
Al-Bohaisi, M., P-0147
Al-Hebshi, A., P-0147
Al-Hussaini, M., P-0358
Al-Jumaily, U., PUB-0156, P-0145, P-0147
Al-Musa, A., PUB-0185
Al-Sakkaf, K., P-0457
Al-Seraihy, A., PUB-0185
Al-Shawabkeh, N., P-0147
Al-Yamani, Y., PUB-0156, P-0147
Alaggio, R., P-0236
Alam, M.M., P-0308, PUB-0038, PUB-0039
Alapetite, C., O-0066, P-0324
Alba, F., P-0564
Albert, D., O-0028
Alberto de Sousa Martins, C., P-0458, P-0294
Albritton, K., O-0166
Alcaraz, E., O-0031, P-0048
Alcasabas, A., P-0477
Alcasabas, A.P., P-0212
Alchek, Y., PUB-0052
Alebouyeh, M., PUB-0149, P-0373
Aleinikova, O., PUB-0232, P-0038
Alenikova, O.V., P-0036
Aleynikova, O., PUB-0012
Alfaro, E., P-0061, P-0090
Algar, E., O-0025
Ali, A., P-0192
Ali, A.S., PUB-0211
Ali, S., P-0292
Aliev, M., P-0162, P-0173
Aljumaily, U., PUB-0111
Alkayed, K., P-0040
Allen, J., O-0068
Almazán Castro, F., P-0299
Aloi, I., P-0298
Alon, N., P-0465
Alonso García de la Rosa, F.J., P-0318
Alonzo, T., O-0013
Alonzo, T.A., O-0014
Alpaslan Pinarli, F., P-0367
Alston, R., P-0526, O-0007
Altun, Z., P-0440, O-0065
Altvater, B., P-0436
Aluoch, L., O-0020
Alvarez, C., P-0546
Am Zehnhoff-Dinnesen, A., P-0474
Amayiri, N., P-0358
Ambdekar, D.Y.K., O-0153
Amiel, J., P-0274
Amireh, A., P-0145
Amstutz, U., O-0100
An, J., P-0465
An, S., P-0266
Anacak, Y., PUB-0259
Anak, S., PUB-0178, P-0055, P-0033, PUB-0033
Anand, S., O-0041
Anastasiou, A., PUB-0220
Anastasiou, K., P-0368
Andersen, N.H., P-0479
Anderson, P., P-0305, P-0445, P-0136, O-0151
Andion, M., PUB-0073
Andrade, A., P-0343
Andrade, A.F., P-0438
Andre, N., O-0027, P-0511
Andreoli, G., P-0190
Ang, L.C., P-0177
Anjos-Afonso, F., O-0106
Anoun, S., PUB-0205, P-0206, PUB-0037
Antonelli, A., P-0209, O-0029
Antonini, S.R.R., O-0026
Anurathapan, U., P-0144
Anwar, S., P-0111, O-0125
Aoi, S., O-0173
AP Tahir, R., O-0199
Apak, H., PUB-0095, P-0491, PUB-0019
Aponte, S., P-0048
Ara, Z., P-0031, PUB-0101, P-0388, PUB-0060, P-0085, PUB-0042
Arakawa, H., O-0018, O-0015
Arakawa, Y., P-0237
Arakkal, R., PUB-0253
Araujo, A., P-0354, P-0348, P-0019
Archer, G., O-0045
Areemithr, S., PUB-0143
Arentsen-Peters, S.T., O-0014
Arentsen-Peters, S.T.C.J.M., O-0016
Arias, D., PUB-0264
Aries, I.M., P-0020
Arigela, R.S., PUB-0228, P-0411
Arinç, E., P-0005
Aristizabal, M.P., O-0054
Aristizabal, P., P-0410, P-0408
Arjmandi Rafsanjani, K., PUB-0014, PUB-0009
Armeanu-Ebinger, S., O-0181
Armstrong, G., P-0466
Arnaiz Peña, S., O-0030
Aronow, B., P-0417
Aronson, D., O-0052
Aronson, D.C., O-0188
Arora, B., P-0152, P-0125, O-0122, P-0331, P-0051, P-0110, P-0129, P-0123
Arora, R., P-0307
Arora, R.S., O-0058, P-0526, P-0424, P-0331, P-0146, P-0423, P-0110
Arreguin, F., PUB-0266
Arrieta, M., PUB-0264
Arroyo-Acosta, B., P-0151
Artac, H., P-0122
Arun, S., PUB-0259
Arvidson, J., PUB-0077
Arvidsson, D., P-0480
Arya, l.S., PUB-0109
Asanuma, S., P-0462
Asghar, N., P-0111, PUB-0211, O-0125
Ash, S., P-0277, P-0148
Ashley, D., O-0025
Ashraf, M., P-0059
Ashraf, M.S., P-0308
Ashraf, S., P-0150, P-0374, P-0071
Aslam, S., PUB-0039
Assanasen, C., P-0455
Astuto, M., O-0074
Atas, E., P-0118, P-0114, P-0213
Athale, U.H., O-0036
Athanasiadou, A., P-0368, PUB-0159
Atra, A., O-0125
Attarbaschi, A., P-0103
Attinà, G., PUB-0236
Aubert, D., O-0165
Auvrignon, A., O-0013
Avar, O., PUB-0096
Aveh, F., O-0198
Avigad, S., P-0277
Awadi, S., PUB-0202
Ayan, I., P-0311, P-0202
Ayarzabal, V., P-0227
Aydin, B., P-0118, P-0114, PUB-0056, P-0315, P-0216, PUB-0054, P-0126, P-0213, PUB-0055
Aydogan, G., PUB-0190, PUB-0175, PUB-0065, P-0047
Ayello, J., P-0428, O-0120
Ayllon, L., PUB-0073

AYOUB, I., PUB-0233, PUB-0235
Ayoujil, A., PUB-0141
Aysev, d., PUB-0218
Aysha, J., P-0042
Aytac, S., P-0068
Azad, R.V., P-0306
Azizi, A., PUB-0084
Azizi, A.A., P-0334

B
Ba Saleem, H., P-0457
Babelyan, S., P-0332
Bachir, J., PUB-0084
Badaro, N., PUB-0051
Bader, P., O-0105
Badhiwala, J., O-0036, P-0376
Badot, I., PUB-0132
Badr, L., PUB-0051
Badran, H., PUB-0202
Baek, H.J., P-0011
Baek, M., P-0395
Baek, M.K., P-0203, P-0189
Bagga, D., P-0301, O-0196
Baggott, C., O-0155, P-0497
Bagolan, P., P-0298
Bagriyanik, A., P-0440
Bahkshi, S., P-0310
Bahl, A., PUB-0187
Bahnassy, A., P-0234
Bahoush Mehdiabadi, G., PUB-0009
Bai, D., P-0312
Baidildina, D., P-0091
Baizakova, D., PUB-0215
Bajpai, M., P-0293, O-0164, O-0193, O-0169
Baka, M., PUB-0230
Bakan, M., P-0515
Baker, J.N., P-0504
Bakhshi, S., P-0307, O-0189, P-0509, O-0164, O-0136, P-0157, P-0156, O-0193, O-0169
Bakiratharajan, D., P-0222
Bakshi, A., P-0417
Bakshi, G., O-0041
Bal, C., P-0293
Balagade, J., P-0187
Balakrishanan, N., P-0513
Balcerska, A., P-0179
Balsamo, L., O-0038, O-0037
Banavali, S., P-0152, P-0125, O-0122, P-0129, P-0123
Bandopadhayay, P., O-0069, O-0131, P-0350, O-0025, P-0352
Bansal, D., P-0027, P-0521, PUB-0131, P-0501, P-0498
Bao, P., P-0456
Baothman, A., PUB-0097
Barbar, M., P-0358
Barchitta, M., O-0074
Barone, C., P-0016
Barr, R., PUB-0177, O-0021
Barr, R.D., P-0494
Barredo, J., P-0013, O-0103
Barrera, M., PUB-0080
Barron, M., P-0353
Barrow, L., P-0568
Bartelheim, K., P-0342
Bartels, U., P-0351, O-0067, P-0353, P-0325, P-0465, PUB-0080
Barth, M., P-0419
Barth, T.F., P-0024
Bartholdson, C., P-0492
Barton, C., PUB-0245
Bartzeliotou, A., P-0368
Baruchel, A., O-0014, O-0016
Baruchel, S., P-0437
Basharova, E., O-0043, PUB-0032
Basso, M.E., P-0236
Basta, N., P-0452, P-0451
Basta, N.O., P-0453, P-0454
Basu, M., P-0083
Basu, M.X., P-0417
Bate, J., P-0197, P-0516
Baumann, I., P-0088
Bauters, T., P-0265, O-0158
Bayes, F., PUB-0101, P-0085
Baykaner, K., P-0367
Bayram, I., P-0528, P-0276
Baytan, B., PUB-0066, P-0054
Bazzeh, F., PUB-0112
Beck, L., P-0436
Becker, K., P-0503
Beckwith, B., O-0083
Bedir, R., PUB-0125, PUB-0093
Begg, C.B., O-0042
Begum, F., PUB-0101, P-0388, P-0085, PUB-0042
Begum, M., P-0031, PUB-0101, P-0388, PUB-0060, P-0085, PUB-0042
Begun, I., PUB-0267, PUB-0232, PUB-0226, P-0238, PUB-0012
Beilhack, A., P-0336
Beishuizen, A., P-0115, P-0103
Bekkering, P., P-0249
Belaid, I., PUB-0169
Belgaumi, A., PUB-0185, P-0071
Belmore, J., P-0556
Belogurova, M., O-0043
Beltinger, C., P-0024
Ben -Hrush, M., PUB-0103
Ben Ahmed, S., PUB-0169
Ben Fatma, L., PUB-0169
Ben-Gal, Y., PUB-0052
Benchekroun, S., PUB-0205, P-0206, PUB-0037
Bender, S., O-0087
Benesch, M., P-0342, O-0127, O-0047
Benhamou, E., O-0001
Benitez Carabante, M., P-0309, P-0318
Benner, A., O-0087
Bennett, J., O-0126
Bennett, K., PUB-0162, PUB-0114
Bennett, K.G., PUB-0260
Benoit, Y., P-0574, O-0143, P-0265, O-0158
Benso, V., PUB-0210, PUB-0197
Berberoglu, M., P-0210
Berger, C., PUB-0044
Bergeron, C., O-0180, O-0111, P-0185, O-0080, O-0132, O-0079
Bergthold, G., O-0069, O-0131, P-0350, P-0352
Bernier, V., O-0111, PUB-0044
Bernier-Chastagner, V., P-0349
Beroukhim, R., O-0069, O-0131, P-0352
Berstein, L.M., PUB-0242
Berthold, F., P-0242, O-0002, P-0253, P-0392
Bessho, F., P-0449
Beverloo, H.B., P-0088, O-0014, P-0427
Bevilacqua Macaroni, G.E., P-0566
Beyene, J., O-0098
Bezerra, S.M., P-0344
Bhadoo, D., O-0193
Bhadri, V., P-0134
Bhakta, N., P-0412, PUB-0238
Bhalla, A.K., P-0501
Bhalla, R., O-0204
Bhalla, S., P-0221, P-0384
Bhambhani, K., PUB-0145
Bharatiya, s., PUB-0249
Bhartiya, D., O-0041
Bhat, A., P-0113
Bhatia, S., P-0466, O-0042
Bhatnagar, S., O-0175, P-0303
Bhatnagar, V., P-0293, O-0164, O-0193, P-0292, O-0169
Bhatt, A., P-0175
Bhattacharjee, K., P-0306
Bhattacharya, A., PUB-0187
Bhutta, A., O-0097
Biagi, E., O-0106, P-0429, P-0430
Bidadi, B., O-0011
Bielack, S., O-0116
Bielorai, B., P-0510
Bien, E., PUB-0252, P-0172, P-0179, O-0064
Bigner, D.D., O-0045
Bilbao-Aldaiturriaga, N., P-0133, O-0092
Bilska, K., P-0300, O-0168
Biondi, A., O-0051, O-0106, P-0429, P-0430
Birch, J., O-0007
Bisogno, G., P-0209, P-0163, O-0170, P-0236, O-0064
Biswas, B., P-0509, O-0136, P-0157, P-0156, O-0169
Biyikli, Z., PUB-0193, P-0159, P-0393
Blackburn, L., PUB-0260
Blackmon, J., O-0077
Blanco Dominguez, J., P-0299
Blanco-Morales Limones, M.J., P-0309
Blay, J.Y., O-0117
Blijdorp, K., P-0464, P-0461
Blom, T., P-0249
Blomgren, K., P-0480, P-0492
Blouin, P., P-0330
Bluebond-Langner, M., O-0142
Blum, R.R., P-0217
Bobb, D., P-0434
Bobeková, A., O-0127
Boddy, A., P-0281
Boer, J.M., P-0021
Boichenko, E., P-0038
Bojagieva, S., PUB-0248
Bokkerink, J., O-0035
Boklan, J., O-0068
Boldrini, R., P-0298
Bolle, S., O-0066, O-0111, P-0324
Boman, K., O-0072
Boman, K.K., O-0023
Bomanji, J., P-0364
Bonaldo, M.d.F., P-0344, P-0343
Bonanni, C., P-0282
Bonnet, D., O-0106, P-0430
Boodhan, S., O-0099
Boonkerd, A., PUB-0035
Boop, F.A., P-0356
Boot, A.M., P-0472, O-0150
Bor, O., P-0047
Bora, H., P-0178
Borello, E., P-0568
Borgstein, E., P-0187, PUB-0049
Borker, A., PUB-0041
Borkhardt, A., O-0105
Borodina, I., P-0341, O-0043
Borowitz, M.J., O-0034
Bosaleh, A., P-0227, PUB-0207
Bosch, V., P-0313
Bosomprah, E., O-0138
Bosumprah, E., O-0139
Botana, C., PUB-0207
Bothra, M., PUB-0247
Bottigliero, G., P-0016
Boubnova, J., O-0182
Bouffet, E., P-0351, O-0067, O-0044, P-0377, P-0347, P-0358, P-0353, P-0325, PUB-0084, P-0465, O-0129
Bouhoutsou, D., PUB-0230
Boulamery, A., P-0511
Bourdeaut, F., P-0407, P-0274, P-0324
Bouts, a., O-0179
Bove, K., P-0447
Bowes, L., O-0098
Boyd, T., P-0447
Boys, R., P-0520
Boyunaga, O., P-0181
Bozkurt, C., P-0239, P-0240, PUB-0214
Bracken, M.B., O-0037
Bradley, K., P-0459
Bradner, J.E., O-0131
Brady, B., P-0112
Bramer, J., P-0249
Branchereau, S., PUB-0268, P-0228
Brandalise, S., P-0354, P-0348, P-0019
Brandalise, S.R., O-0026, O-0009
Brasme, J.F., O-0096
Brassesco, M.S., P-0340, P-0438
Braun, M., P-0379
Braun, Y., P-0406
Bravo, L.E., O-0054
Brenann, B., O-0132
Brennan, B., O-0064
Brennan, L., O-0104
Breslow, N., O-0083
Briere, T., P-0305
Brinksma, A., P-0533, O-0147, O-0150
Brisse, H., PUB-0113, PUB-0090, P-0324, O-0081
Brock, P., P-0486
Brocknäs, A., O-0207
Broeren, J., P-0480

Bronowicki, K., O-0171
Brossard, J., O-0098
Brown, C.A., PUB-0138
Brown, J., P-0357
Bruce, F., O-0139
Bruce, J., O-0184
Brugiere, L., O-0027
Brugières, L., O-0091
Bruin, M., O-0035
Bruny, J., O-0177, O-0174
Bryan, G., O-0142
Bryant, R., P-0538
Bubala, H., O-0121, P-0470, P-0469, PUB-0133
Bubuteishvili-Pacaud, L., PUB-0084
Buchner, A., PUB-0183
Budanova, M.V., PUB-0213
Buettner, S., PUB-0128
Buffa, P., O-0170, O-0195, O-0113
Bui Thi Thanh, H., PUB-0160
Buke, E., P-0460
Burdach, S., O-0095, O-0093
Burgerhof, J.G.M., O-0150
Burkhardt, B., P-0103
Burns, K., P-0447
Buxi, T., P-0221, PUB-0050
Buyukavci, M., P-0239, P-0240, P-0047
Buyukpamukcu, M., P-0118, P-0114, PUB-0056, P-0216, PUB-0054, P-0126, P-0213, PUB-0017, PUB-0055
Buziba, G., O-0020
Bydanov, O.I., P-0036

C

Cabrera Roldan, P., P-0333
Cacciavillano, W., P-0227, PUB-0207, P-0168
Cai, F., PUB-0123
Cai, r., P-0165
Cai, R.Q., P-0269
Cai, Y., P-0046
Caicedo, W., PUB-0269, PUB-0265
Cairney, E., P-0177
Cairo, M.S., P-0428, O-0120
Cakir, B., P-0515, PUB-0180
Cakir, F.B., P-0239, P-0311, P-0202
Caliskan, U., P-0122, P-0047
Campbell, L., P-0431
Campos, B., P-0333
Canale, S., P-0166
Canavera, K.E., O-0075, P-0530
Cañete, A., PUB-0084
Caniza, M., O-0031, PUB-0222, P-0048
Caniza, M.A., PUB-0227
Canoz, O., PUB-0256
Cao, L., P-0006, P-0100, PUB-0137, P-0022
Cao, M., PUB-0251
Capasso, M., O-0086
Capsomidis, A., P-0516
Caraglia, M., P-0016
Carboné Bañeres, A., P-0018
Carceller, F., P-0048
Card, C., P-0476
Cárdenas-Cardós, R., P-0174
Cardinalli, I., O-0009
Cardoso, L.C.A., P-0271
Carleton, B., O-0100
Carli, M., P-0163
Carlos Gilberto Carlotti Jr, C.C.G.Jr., P-0339
Carlotti Jr, C., P-0354, P-0348
Carlotti Jr, C.G., P-0438
Caroline, H., O-0103
Caron, H., P-0493, P-0283, O-0003, P-0249
Carotenuto, M., P-0266
Carpine, A., P-0219, PUB-0130, PUB-0129
Carret, A., O-0067
Carrie, C., O-0111, P-0327
Carroll, A.J., O-0034
Carroll, W., O-0032, O-0103
Carroll, W.L., O-0034
Carson, K., O-0151
Carter, B., P-0526
Caruso Brown, A.E., P-0504, PUB-0138
Carvalho, r., P-0458
Carvalho, T.V., P-0271
Casale, F., PUB-0172, P-0016
Casanova, M., P-0164
Castel, V., O-0113
Castellanos-Toledo, A., P-0151, P-0142
Castellvi Gil, A., P-0299
Castillo-Deluao, C.M., PUB-0227
Castro, A., P-0044
Castro, M.X., P-0044
Cataudella, D., PUB-0080
Cavaliere, E., P-0163, P-0236
Cavalli, F., O-0048, O-0050
Cavé, H., O-0051
Cave, J., O-0008
Cazzaniga, G., O-0051
Ceccanti, S., P-0190, P-0194
Cecchetto, G., O-0170, P-0236, O-0195, O-0064, O-0113
Cecen, E., P-0239, P-0240
Celia, m., P-0112
Celkan, T., PUB-0096, PUB-0095, P-0491, PUB-0019, P-0047
Cellot, C., O-0098
Cernvall, M., O-0022
Cervio, G., P-0227
Cetin, M., P-0068, P-0098, P-0047
Cetingul, N., PUB-0259
Chabchoub, I., PUB-0169
Chaber, R., O-0168
Chafai, R., PUB-0169
Chai, Y., P-0094, P-0006, PUB-0001, P-0065, P-0022
Chakarbarti, A., P-0521
Challinor, J., O-0138, P-0565
Chalumeau, M., O-0096
Chan, C.F.G., P-0243, P-0442, P-0372, P-0371, PUB-0151, P-0199
Chan, C.K.Y., P-0542
Chan, C.W., PUB-0186, P-0552
Chan, C.W.H., P-0508
Chan, G., P-0078, P-0478, P-0070, P-0074, P-0102, P-0066
Chan, G.C., P-0229, P-0329, P-0121, P-0323
Chan, G.C.F., P-0560, P-0559
Chan, H.Y., PUB-0186, P-0560, P-0559
Chan, J., O-0069
Chan, K., P-0264
Chan, K.E., PUB-0146
Chan, K.W., P-0204, O-0194
Chan, M.Y., P-0261, P-0212
Chan, S., PUB-0151
Chan, Y.K.W., P-0199
Chang, G., O-0077
Chang, H.H., O-0110
Chang, J., O-0124, P-0232
Chang, K., P-0486
Chang, K.T.E., P-0273, P-0270
Chang, X., PUB-0147
Chang, Y., P-0364
Chantada, G., PUB-0207, P-0310
Chao, L., P-0094
Chao, Y., PUB-0076, P-0360, P-0359
Charron, B., PUB-0090
Charron, E., O-0089
Chasnis, J., O-0151
Chastagner, P., O-0167, P-0349, PUB-0008
Chattapadhyay, P.P., O-0189
Chau Van, H., P-0058
Chaudhary, N., P-0424
Chaudry, G., P-0160, P-0182
Chavez, E., PUB-0043
Chawla, B., P-0317
Che, L., PUB-0001, P-0065
Chekmeneva, J.J., P-0036
Chen, B., PUB-0036
Chen, C., P-0053
Chen, J., P-0076, P-0049, P-0089, P-0108, P-0381, P-0012, P-0158
Chen, J.j., P-0127
Chen, k., PUB-0018
Chen, L., O-0126, P-0251, PUB-0087
Chen, Q., P-0380
Chen, R.p., PUB-0018
Chen, S., PUB-0085
Chen, T., O-0059
Chen, Y., O-0059, P-0137, P-0414, P-0273, P-0270, O-0123, PUB-0126, P-0422, P-0009, P-0176, PUB-0047, P-0107, P-0269, P-0165
Chen, Z.m., O-0010
Cheng, F., P-0478, P-0473, P-0489
Cheng, F.W.T., P-0246
Cheng, K., P-0572, P-0523, PUB-0010, P-0487
Cheng, K.K.F., P-0508
Cheng, S., O-0107
Cheng, W.T.F., P-0199
Cheng, Y., PUB-0126, P-0089, P-0081
Chenkai, M., P-0365
Cherkaoui, S., PUB-0205, P-0206, PUB-0037
Cheshire, S., O-0131
Cheuk, D., P-0078, P-0478, P-0070, P-0074, P-0102, P-0066
Cheuk, D.K., P-0235, P-0473, P-0121, PUB-0107, P-0116, P-0106
Cheuk, D.K.L., P-0229, P-0141, P-0560, P-0559
Cheuk, K.L., P-0084
Cheuk, K.L.D., P-0372, P-0371, P-0199
Cheung, J., P-0572
Cheung, J.S.S., P-0246
Cheung, N.K., O-0088
Cheung, W., PUB-0087, PUB-0086
Chevez-Barrios, P., O-0028
Chi, S., P-0350, O-0068, P-0352
Chi, T.L., P-0362
Chiang, A., P-0078, P-0542, P-0102, P-0066, P-0103
Chiang, A.K., P-0235, P-0121, PUB-0107, P-0116, P-0106, PUB-0029
Chiang, A.K.S., P-0229, P-0141, P-0560, PUB-0098, P-0559
Chiang, K.S.A., P-0372, P-0371
Chichra, A., PUB-0109, PUB-0119, PUB-0118
Chien, W.T., P-0508
Chin, M., P-0263, P-0188
Chinnabhandar, V., PUB-0257, PUB-0243, P-0519, PUB-0196, PUB-0195, P-0077, P-0029
Chinnaswamy, G., P-0152, O-0133, P-0125, O-0122, P-0051, P-0281, P-0252, P-0222
Chintagumpala, M., O-0028, P-0304
Chisholm, J., O-0132, P-0164
Chiu, S.Y., P-0560, P-0559
Chiuri, R., PUB-0263
Cho, B., P-0382
Cho, K.A., P-0389
Cho, W., P-0203, P-0189
Cho, Y., PUB-0122
Cho, Y.J., O-0131, O-0049
Chocholous, M., P-0334
Choi, E.S., P-0421
Choi, K.C., P-0508
Choi, Y.M., P-0314, P-0183, P-0245, P-0149, P-0421, PUB-0110
Choneska Jovanova, B., PUB-0248
Chong, C., P-0302
Chopra, A., PUB-0239
Chopra, P., PUB-0195
Chopra, S., PUB-0050
Chotsampanchareon, T., O-0152, P-0402
Chou, J.F., O-0042
Chou, P.M., P-0344
Chow, L., P-0447
Chowdhury, Y.J., PUB-0042
Christensen, P.B., PUB-0015
Christine, D., O-0132
Christofferson, R., PUB-0191
Chu, R., PUB-0145
Chu, Y., P-0478
Chua, J., P-0302
Chua, J.H.Y., P-0273, P-0270
Chua, Y.W., P-0273, P-0270
Chuang, J., P-0233
Chuang, J.H., PUB-0022
Chuansumrit, A., P-0144
Chui, C.H., O-0183
Chumber, S., P-0293
Chunfu, L., P-0404
Chung, J., P-0203, P-0189, PUB-0080
Chung, L.W., O-0145
Chung, N.G., P-0382
Chung, S.W., P-0138

Chusovitin, D., P-0259
Ciarimboli, G., P-0474
Ciarlini, P., P-0350
Ciftci, e., PUB-0218
Cimmino, F., O-0086
Cinalli, G., P-0266
Citti, A., P-0298
Claerhout, B., P-0406
Clark, C., P-0361
Clark, C.A., P-0363
Clarkin, A., P-0556
Classen, C.F., P-0207
Claude, L., O-0111
Clayden, J.D., P-0363
Clerico, A., P-0282
Clifford, S., O-0046
Close, P., O-0152
Cocciolo, A., PUB-0262
Coco, S., O-0086
Codispoti, K., O-0044
Coenen, E., O-0013
Coenen, E.A., O-0016
Cohen, I.J., P-0148
Cohen, J., PUB-0188, P-0471
Cohen, K., O-0068
Cohen, M., P-0536
Cohn, R., P-0538
Cohn, R.J., O-0162, P-0471
Cohn, S., O-0004
Collins, V.P., P-0335
Conde Cuevas, N., P-0318, P-0309
Conklin, H.M., P-0356
Contet, A., PUB-0008
Cooper, L.J.N., P-0429
Cooper, S.E., PUB-0138
Cooper, T.M., O-0105
Corapcioglu, F., P-0240
Corby, A., P-0419
Corn, T., P-0034
Cornelissen, L., O-0145
Correa, P., PUB-0264
Cost, C., P-0447
Costa, F.D., P-0344
Coulombe, A., O-0080
Couturier, J., P-0272
Cowie, F., P-0357
Coze, C., O-0167, P-0274, O-0111, O-0165, P-0272
Cozzi, D., P-0190, P-0194
Cozzi, F., P-0194
Craft, A., P-0452
Craig-Barnes, H., P-0481
Craigie, R., O-0184
Crane, S., P-0439, P-0248
Cribioli, E., P-0430
Crocoli, A., P-0298
Cropet, C., P-0185
Croul, S., O-0129
Crowne, E., P-0459
Cruz-Medina, C., P-0023
Csagoly, E., P-0135
Csoka, M., P-0103
Csordas, K., P-0135, P-0004
Cui, J., P-0312
Cui, L., P-0008, P-0046
Cui, Y., P-0312, P-0056
Cummins, M., P-0291
Curbelo Rodriguez, M., P-0299
Cyprova, S., P-0184, P-0241
Czauderna, P., O-0052
Czech, T., P-0334

D

D'Angelo, P., P-0236, O-0195
D'Angelo, V., PUB-0172, P-0016
D'Angio, G., O-0083
Dabbah, K., PUB-0052, P-0554
Dahl, G., P-0034
Dai, y., PUB-0091
Dall'Igna, P., O-0170, P-0236, O-0195
Dalvi, N., O-0209
Damodaran, S., P-0281
Dana, H., PUB-0230
Dana, Z., P-0554
Dang, A., P-0564
Dantonello, T., O-0116, O-0115
Darendeliler, E., PUB-0190, P-0311, P-0202
Darlington, A.S., P-0495, O-0102
Darmawikarta, D., P-0483
Darrigo Jr, L., P-0354, P-0348
Darrigo Jr, L.G., P-0339
Das, B., P-0501
Das, P., PUB-0168
Das, R., PUB-0244
Das, S., P-0177, P-0306
Datta-Gupta, S., O-0189
Dave, A., P-0529
Davidson, A., PUB-0200, P-0119
Davidson, A.ne., P-0476
Davies, P.S., PUB-0134
Dávila, M.T.G.d., P-0227
Dbucoider, A., PUB-0103
de Antonellis, P., P-0266
de Araujo, A.G., P-0339
de Camargo, B., O-0080, O-0079
de Campos, C., P-0539
De Carli, E., P-0419
de Castro, M., O-0026, O-0009
De Corti, F., O-0170
De Diego Suárez, M., P-0299
De Graaff, L., O-0072
De Grazia, A., P-0282, P-0517
de Groot-Kruseman, H., O-0035
de Haas, V., P-0101, O-0016, O-0013
de Jong, A.X., P-0101
de Jong, M., P-0493
de Kraker, J., O-0080, O-0079
de Kraker, J., O-0003
de Lambert, G., O-0167
De Lorenzo, P., O-0051
De Moerloose, B., P-0088, P-0101, P-0265
De Napoli, L., O-0029
de Pernillo, M., O-0021
de Rooij, J.D., O-0014
De Rossi, A., P-0132
de Sant'Ana, V.K.S., P-0438
De Strooper, E., O-0143
De Vita, G., P-0266
Deavers, M., P-0134
Debatin, K., P-0024
Deebajah, R., PUB-0112
Defachelles, A., O-0111
Defachelles, A.S., P-0407
Del Toro, N., PUB-0073
Delai, A., P-0219, PUB-0130, PUB-0129
Delattre, O., P-0407, P-0274, P-0272
Dell, S., P-0481
Deluao, C.M., P-0563
Demarche, M., O-0165, P-0228
Demarzi, L., O-0066
Dembowska - Baginska, B., P-0484
Demirkaya, E., PUB-0017
Demirkaya, M., PUB-0190, PUB-0175, PUB-0065
DeMoerloose, B., O-0013
Demoor-Goldschmidt, C., PUB-0044
Den Boer, M., O-0051
Den Boer, M.L., P-0427, P-0021, P-0020
den Hoed, M., P-0472
Dendale, R., O-0066
Deo, S., O-0136, P-0156
Deodhar, D.J., O-0211
Deodhar, J., P-0544
Deparis, M., O-0091
Depei, W., P-0401, P-0400
Derache, A., O-0027
Derla, E., PUB-0043
Dertmann, T., O-0017
Dervisoglu, S., PUB-0065
Desai, S., O-0133, O-0133, P-0222, PUB-0075
Deuster, D., P-0474
Devalck, C., O-0111
Devecioglu, O., PUB-0178, P-0055, P-0033, PUB-0033
Devidas, M., O-0034, P-0048, O-0032, O-0103
Deville, A., O-0027, P-0274
DeWire, M., P-0447
Dhalluin, C., P-0164
Dhamankar, V., O-0041, O-0209
Dhanachai, M., PUB-0035
Dhanya, M., O-0184
Dhingra, N., PUB-0257, PUB-0243, P-0519, PUB-0196, PUB-0195, P-0029, PUB-0050
Dhooge, C., O-0143
Di Carlo, D., P-0163
Di Cataldo, A., P-0236, O-0074
Di Giannatale, A., O-0117
Di Pinto, D., P-0016
Di Rocco, C., PUB-0262
Dias, N., O-0117
Didumarti, R., PUB-0216
Dieckmann, K., P-0334
Dierkes, C., P-0436
Dietl, S., P-0336
Diez, C., P-0412
Diez, C.L., PUB-0238
Digumarti, R., PUB-0228, P-0411
Diller, L.R., O-0042
Dinand, V., P-0413, P-0057, P-0029, P-0384
Dincarslan, h., PUB-0218, PUB-0217
Dincaslan, H., PUB-0193, P-0159, P-0393, P-0210
Dinda, A.K., O-0189
Dindar, h., PUB-0218
Ding, X., P-0278
Ding, X.h., O-0010
DiRenzo, J., O-0068
Dirks, P., P-0465
Dirksen, U., O-0094, P-0201
Divane, A., PUB-0230, PUB-0159
Diver, J., PUB-0145
Dix, D., O-0098
Dizdar, Y., P-0311
Do Nascimento, C., PUB-0044
Dogan, I., P-0367
Dogan, O., PUB-0190, PUB-0180
Doganis, D., PUB-0230
Dolendo, M., P-0412, PUB-0238, PUB-0227
Dolendo, M.C., P-0563, PUB-0043
Dolgopolov, I., P-0366, P-0332
Dolgushin, B., P-0316
Dollman, K., O-0201
Dome, J., P-0434, O-0083
Dommange-Romero, F., O-0064
Dommett, R., O-0006
Donadieu, J., P-0419
Dong, K., P-0251, O-0061, P-0211, P-0267, PUB-0025
Dong, R., O-0061
Dong, W., PUB-0139, P-0099
Dongre, A., O-0122, P-0123
Doolan, E.L., O-0162
Doria, A.S., P-0426
Dou, J., P-0226
Dourthe, M.E., O-0001, P-0166
Downie, A., PUB-0080
Doyle, J., P-0483, P-0481
Doz, F., O-0046, O-0167, P-0310, P-0324, O-0049
Drekov, A., PUB-0267
Dresse, M.F., PUB-0132
Drew, D., O-0162
Drew, S., P-0522
Dreyer, Z., P-0034
Driscoll, T., O-0045
Druy, A., O-0109, P-0259
Dua, V., PUB-0257
Dubali, M., P-0550, P-0549
Dubb, M., PUB-0260
Dube, M., O-0100
DuBois, S., O-0004
Dubuc, A., O-0129
Ducassou, A., O-0111
Duckworth, J., PUB-0177
Dufour, C., O-0001, O-0091, P-0330, P-0166
Dunn, S., O-0044
Dunt, D., P-0522
Dupuis, L.L., P-0035, O-0099, P-0497
Dupuy, A., O-0129
Dursun, D., O-0065
Duyu, M., PUB-0219
Dwivedi, P., P-0152, O-0122, P-0123

Dworzak, M., P-0088, P-0101, O-0016, O-0013
Dylewska, K., O-0121, P-0172
Dzampaev, A., P-0162, P-0173

E
Eagle, R., O-0028
Eaves, D., P-0447
Ebinger, M., P-0063
Eche, I.J., PUB-0171
Echebarria, A., P-0007
Eckhoff, S., P-0024
Edan, C., P-0330
Eden, T., P-0187
Edgar, A., P-0378
Efrat, R., PUB-0052
Egas Bejar, D., P-0445
Egeler, M., P-0483, P-0481
Eguiguren Leon, J., PUB-0269
Eguiguren, J., PUB-0265
Eguiguren, M., PUB-0269
Einberg, E., O-0163
Eipel, O., P-0135
Eipel, O.T., P-0004
Eker, N., PUB-0241
Ekermans, P., PUB-0162
Ekert, P., O-0025
Ekmekci, A., P-0367
El Kiki, H., P-0362
El Sharkawy, N., PUB-0182
El-Haddad, A., P-0280
El-Safy, H.M., PUB-0057
El-Shakankiry, N., P-0280
El-Solh, H., PUB-0185, PUB-0051
El-Wakil, M., P-0234
Elayyan, M., P-0358
Elhasid, R., P-0510
Elia, E., PUB-0031
Elias, D., O-0165
Elias, E., P-0437
Elisa, C., P-0169
Elliott, M., O-0113
Elliott, S., PUB-0134
Ellis, S.J., O-0162
Ellison, D., O-0126, O-0046
Elmadi, A., PUB-0113
Elsayed, E.K., P-0319
Elshafy, m., P-0507
Elson, R., P-0459
Elvis Terci Valera, V.E.T., P-0339
Elwakeel, M., P-0507
Emanuelson, I., P-0480, P-0375
Eminoglu, t., PUB-0217
Emir, S., P-0239, P-0240
Emmrich, S., P-0095, O-0017
Ensabella, E., PUB-0264
Enskär, K., O-0163
Epari, S., P-0129
Epie, N., P-0453
Epstein, J., P-0487
Ercetin, P., O-0065
Erdelyi, D.J., P-0135, P-0004
Erden, E., P-0210
Erginoz, E., PUB-0019
Eroglu Ertugrul, N., PUB-0056
Errington, S., P-0452, P-0451
Ertem, A.U., PUB-0214
Escherich, G., P-0427
Escobosa Sanchez, O., O-0030
Espejo Arjona, F., P-0318, P-0309
Estefan, A., PUB-0004
Ethier, M., O-0098
Eun Seok, C., O-0203, PUB-0083, P-0448
Evans, A., O-0083
Eveslage, M., P-0474
Eyles, D., P-0534
Eyrich, M., P-0379, P-0336
Ezz Eldeen, N., PUB-0182

F
F, V., P-0337
F.Semsei, A., P-0135
Faber, C., P-0436
Fabre, M., PUB-0268
Fadoo, Z., P-0071, PUB-0038, PUB-0039
Faizan, M., P-0111, O-0125
Falchook, G., P-0445
Faldum, A., P-0345, O-0047
Falkenburg, N., P-0495
Fan, Q., O-0071
Fang, J., PUB-0104, PUB-0102, P-0053, PUB-0047, PUB-0027, PUB-0021, P-0130
Faqih, N., P-0358, PUB-0111
Faranoush, M., PUB-0149, P-0373
Färemo, A., O-0205
Faria, C., O-0044
Farol, H., PUB-0079
Farrag, A., P-0392
Farrelly, P., O-0184
Fasola, S., P-0272
Fatema, L., P-0388
Faulkner, L., P-0255
Faure Conter, C., P-0327
Faure-Conter, C., O-0165
Favara-Scacco, C., O-0074
Fawzy, M., PUB-0182, P-0234
Fazeli, M.A., PUB-0149, P-0373
Fechina, L., P-0039, P-0043, O-0109, P-0038, P-0259
Fedato, P., P-0019
Fedatto, P., P-0354, P-0348
Fedatto, P.F., P-0339, O-0026
Fei, Z., P-0105
Feifei, S., P-0105
Feinberg-Gorenshtein, G., P-0277
Feinmesser, M., P-0277
Feldman, I., O-0022
Felice, M., P-0030, P-0061, P-0090
Felizzia, G., PUB-0207, P-0061
Feltbower, R., O-0005
Feng, J., P-0422, P-0064
Feng, m., PUB-0091
Feng, X., PUB-0167, PUB-0166
Feng, Y., O-0052
Ferdouse, Z., PUB-0042, P-0031, PUB-0101
Ferdousi, Z., P-0388
Fernanda Fedatto, P., O-0009
Fernandez Pineda, I., O-0030
Fernandez, J., P-0546
Fernandez, R., P-0256
Fernandez-Delgado Cerda, R., O-0030
Fernandez-Pineda, I., O-0190
Fernandez-Teijeiro, A., P-0318, P-0309
Fernando Corrales, M., P-0445
Feroz Zada, Y., O-0100
Ferrand, S., P-0272
Ferrari, A., P-0163, O-0170, P-0236, O-0064
Ferrer-Luna, R., O-0069
Ferro Leal, L., O-0009
Festus, N., P-0397
Fiamoli, V., P-0446
Fiano, P., PUB-0172
Figarella-Branger, D., O-0046
Figueredo, D., O-0031, P-0048
Figueroa-Carbajal, J., PUB-0223, P-0151, P-0142
Filipovich, A., P-0425
Finegold, M., O-0059
Finlay, J., PUB-0251
Finset, A., P-0537, O-0076
Fiori, C., P-0219, PUB-0130, PUB-0129, PUB-0128
Fischer, A., P-0088, O-0105
Fiser, K., P-0001
Fisher, R., P-0505
Fisker, N., PUB-0015
Fitoz, S., P-0139
Fleer, J., P-0533
Fleischhack, G., P-0342
Fleischman, E., P-0039
Fleming, C., PUB-0188, O-0148
Fleming, C.A., P-0494
Floeth, M., P-0503, P-0502
Florkin, B., PUB-0132
Fonseca, A., P-0370
Foo, K.M., PUB-0246
Foreman, N., O-0126
Forget, P., PUB-0132
Forgó, N., P-0406
Formisano, S., P-0256
Forns Guzman, M., P-0299
Fouladi, M., P-0447, O-0044
Fouquet, V., PUB-0268
Fourcade, L., O-0167
Fournier Bidoz, N., P-0324
Franchi-Abella, S., PUB-0268, P-0228
Francisco, K., PUB-0224
François-Fiquet, C., O-0167
Fraoli, F., P-0364
Frappaz, D., O-0027, P-0324, P-0327
Frazier, L., P-0218
Frediani, S., P-0190, P-0194
Freeman, B., O-0128
Freidank, C., O-0138
French, C.A., P-0214
Freneaux, P., P-0272
Frezza, A.M., O-0117
Fried, I., P-0465
Friedman, D.L., O-0114
Friedman, D.N., O-0042
Friedman, H.S., O-0045
Friedrich, C., O-0047
Friedrich-Medina, P., P-0218
Frimpong, N.P., PUB-0068
Frobisher, C., O-0008
Frühwald, M., P-0214
Frühwald, M.C., P-0342, P-0342
Fu, A.C.C., P-0329
Fu, J., P-0015, PUB-0082
Fu, l., P-0297
Fu, R., P-0268, P-0014
Fu, R.Y., P-0010
Fuchimoto, Y., P-0171
Fuchs, J., O-0181, O-0176
Fuentes, L., O-0021
Fujimaki, T., P-0328
Fujimura, J., P-0050
Fukuda, K., PUB-0209, P-0171
Fukuda, M., PUB-0105
Fukuoka, K., P-0328
Fukushima, H., PUB-0148
Fukushima, T., O-0085, P-0167, P-0279, PUB-0148, PUB-0071
Fukuzawa, M., O-0108, O-0084, PUB-0140, P-0188
Fults, D., O-0129
Fumino, S., O-0173, P-0254
Furlong, W., PUB-0177
Furtwaengler, R., O-0080, O-0079
Furukawa, T., O-0173
Fusco, C., PUB-0172
Fuster Soler, J.L., O-0030
Fynn, A., P-0256

G
G, V., PUB-0187
Gaash, D., P-0277
Gajda, D., O-0001
Gajjar, A., O-0126
Galifer, R.B., O-0165
Galimberti, S., P-0430
Gallego, M., P-0090
Gallelo, S., O-0132
Galloy, M.A., O-0165
Galmiche-Rolland, L., O-0165
Galunova, T.Y., P-0527
Gambart, M., O-0111
Ganta, R.R., PUB-0228, P-0411
Gao, C., P-0008, P-0046, P-0009
Gao, J., P-0079, P-0109, P-0268, P-0010, P-0014
Gao, Y., P-0046, P-0108
Gao, Y.h., PUB-0061, P-0127
Gao, Z., PUB-0100
Garami, M., P-0355
Garaventa, A., P-0236
García Aldana, D., P-0318, P-0309
García de Andoin, N., P-0007
Garcia Lombardi, M., PUB-0210, PUB-0197
Garcia, G., P-0219, PUB-0130
Garcia-Abos, M., PUB-0073
Garcia-Espinoza, A., PUB-0223, P-0151

García-Miguel, P., P-0018, P-0007
Garcia-Orad, A., P-0018, P-0133, P-0007, O-0092
Garín, M., PUB-0073
Garrington, T., O-0177, O-0174
Gaspar, I., P-0045
Gaspar, N., O-0096, O-0117, O-0091
Gaspari, S., PUB-0263
Gassas, A., P-0483, P-0481
Gastier-Foster, J., O-0034
Gattari, P., PUB-0210, PUB-0197
Gauthier, F., PUB-0268, P-0228
Gaze, M., O-0132
Gaze, M.N., P-0364
Ge, L., P-0523
Ge, Y., P-0286
Geel, J., PUB-0162, PUB-0114
Geel, J.A., PUB-0260
Geladari, A., PUB-0221
Gelfand, M., P-0439, P-0248
Geller, J., P-0447, P-0248
Geludkova, O., P-0341, O-0043
Geoerger, B., P-0164
Georgantzi, K., PUB-0191
Gerber, N.U., O-0127, O-0047
Gevaert, K., P-0266
Gevorgian, A., P-0369
Gevorgyan, A., P-0341
Gevorgyan, A.G., P-0527, PUB-0234
Geyer, R., O-0068
Ghandour, K., PUB-0111
Gharbi, O., PUB-0169
Ghazaly, M.H., P-0392
Gholami, R., PUB-0149
Gholamin, S., O-0131
Gibson, F., O-0142, O-0146
Gibson, P., O-0099, P-0497
Gidding, C.E., P-0347
Gigante, C., O-0170
Gilbertson, R.J., O-0128
Gillenstrand, J., P-0480
Gillmeister, B., O-0098
Gindina, T., P-0039
Giordano Attianese, G.M.P., P-0429, P-0430
Giorgiani, G., PUB-0263
Githang'a, J.N., O-0114
Glade Bender, J., P-0529
Glamocanin, S., PUB-0248
Glosli, H., P-0479
Gnekow, A., P-0345
Goda, T., O-0108, PUB-0140
Godzinski, J., O-0171, P-0300, P-0172, O-0079, O-0168, O-0064
Goehring, G., P-0088
Goethals, K., P-0574
Goggins, W., P-0508
Goh, X.N., PUB-0246
Gokce, M., PUB-0190, PUB-0175, PUB-0065, PUB-0033
Gokcora, N., P-0178, P-0181
Goldberg, J., P-0013
Goldman, S., O-0101
Goldman, W., P-0256
Goldsby, R., P-0466
Goletz, G., P-0503, P-0502
Gollu, g., PUB-0218
Golub, T., O-0069
Gomez Plaza, M., P-0299
Gomez Storniolo, S., PUB-0264
Gomez, S., PUB-0222, P-0256
Gong, Y., P-0456
Gonzales, E., PUB-0268
González, C., P-0546
Gonzalez, M., PUB-0222
Gonzalez-Garay, A., P-0023, P-0174
Goodwin, B., PUB-0114
Gooskens, S.L., O-0080, O-0079
Gorbatykh, S., P-0341, O-0043
Gordon, L., O-0025
Gordu, Z., PUB-0193, P-0159, PUB-0218
Gore, L., O-0068, O-0151, O-0105
Gorelyshev, S., P-0332, O-0043
Gorgun, O., PUB-0175, P-0311, P-0202
Gorovtzova, O., P-0316
Gorr, T., P-0153
Goshen, Y., P-0467, P-0148
Goswami, S., O-0211, O-0209, P-0544
Gota, V., P-0281
Goteke, V.K.R., PUB-0228, P-0411
Goto, H., PUB-0209, P-0230
Goto, K., P-0037
Gotoh, C., P-0220
Goumberi, S., PUB-0221
Goumnerova, L., P-0352
Goumnerova, L.C., P-0350
Graf, N., P-0406, O-0080, O-0079, P-0345
Granger, M., O-0004
Grant, G.A., O-0045
Grecco, C., P-0019
Grech-Sollars, M., P-0363
Greeen, H., O-0166
Green, D., O-0083
Green, M., P-0335
Greenberg, M., P-0465
Greenberg, M.L., P-0483, P-0482
Grigoriy, K., O-0135
Grill, J., O-0066, O-0069, PUB-0084, P-0330
Grohs, E., P-0219, PUB-0130, PUB-0129
Groll, A.H., P-0503, P-0502
Gronych, J., O-0070
Grootenhuis, M., P-0249
Groshen, S., O-0004
Gross, C.P., P-0543
Gruhn, B., P-0342
Grundy, P., O-0083
Grupp, S., P-0069
Gryaznov, S., P-0434
Grynszpancholc, E., O-0201
Gu, C., P-0557
Gu, L., P-0049
Gu, W., PUB-0100
Gualdiero, G., P-0016
Guan, X., P-0072, PUB-0081, P-0383
Gucer, S., PUB-0055
Gudmundsdottir, E., O-0212, O-0023
Guérin, F., P-0228
Guerrini, L., P-0330
Guettier, C., PUB-0268, P-0228
Guilhaumou, R., P-0511
Guillemot, D., P-0407
Guimier, A., P-0272
Guinan, E., O-0104
Guitter, M., P-0030, P-0061, P-0090
Gujral, S., O-0122, P-0051, P-0129, P-0123
Gulati, R., P-0029
Guler, E., PUB-0261, PUB-0241, P-0047
Gulia, A., O-0133
Gulia, s., P-0051
Gullipalli, M., PUB-0228, P-0411
Gumruk, F., P-0068
Gunawan, S., P-0548
Gundeti, S., PUB-0228, P-0411, PUB-0216
Gunhar, S., P-0033
Guo, D., PUB-0001, P-0065
Guo, H., P-0130, PUB-0047, PUB-0027
Guo, X., P-0109, P-0010
Guo, Z.h., O-0010
Gupta, A., P-0447, PUB-0243, P-0519, PUB-0164
Gupta, A.K., P-0519, PUB-0196, P-0057, P-0221, O-0164, PUB-0050, O-0193
Gupta, D.K., P-0293, O-0164, O-0193, P-0292
Gupta, R., P-0301, O-0196
Gupta, S., P-0450
Gupta, V., P-0032
Gurgey, A., P-0068
Gurjar, M., P-0281
Gurman, C., P-0393
Gurses, S., P-0005
Guru, f., PUB-0109
Guru, F.R., PUB-0118, PUB-0119
Gururangan, S., O-0044, O-0045
Gustafson, W., O-0089
Gustafsson, G., O-0072, O-0046
Gutierrez-Camino, A., P-0018, P-0133, O-0092
Guttmann, A., P-0450
Guy, R.K., O-0128
Gwarzo, A.K., PUB-0040
Gwarzo, D., PUB-0040
Gylling, H., O-0100
Gyokova, E., P-0290
Gyurina, K., P-0045

H

Ha, C., PUB-0184
HA, S., P-0070, P-0078, P-0329, P-0121, P-0323
HA, S.Y., P-0084, P-0229, P-0060, P-0243, P-0560, PUB-0098, P-0559, P-0074, P-0102, P-0066
Haas, O., O-0013
Haas-Kogan, D., O-0004
Häberle, B., P-0253
Haberler, C., P-0334
Habib, F., PUB-0141
Habrand, J., O-0066, O-0111
Habrand, J.L., P-0324
Hadley, L., PUB-0049
Hadley, L.G.P., O-0188
Haeberle, B., O-0052
Hafiz, G., PUB-0101, P-0388, PUB-0060, PUB-0042
Hafiz, M., P-0085
Hah, J.O., PUB-0110
Hahashi, Y., O-0062
Haie-Meder, C., O-0182
Hailong, H., P-0401, P-0400
Hain, R., O-0099
Halac, E., P-0227
Halalshah, H., PUB-0156, P-0145, P-0147
Halalsheh, H., PUB-0111, P-0040
Hale, J., P-0451
Hales, P., P-0361
Halili, I., P-0545
Hall, A., P-0556
Hallaç, M., PUB-0095
Hallahan, A., PUB-0134
Hallmen, E., O-0115
Halpern, A.L., P-0344, P-0343
Hamanoue, S., PUB-0209
Hamazaki, M., O-0118
Hambir, t., PUB-0249
Hami, H., PUB-0163, PUB-0141
Hamid, S., P-0374
Hamilton, W., O-0006
Hamm, C.A., P-0344
Hammill, A., P-0447
Hammond, S., O-0042
Han, D.K., P-0011
Han, w., PUB-0053
Han, Y., P-0444
Hanada, R., P-0237, P-0050, P-0462
Hancock, K., PUB-0080
Handgretinger, R., P-0063, O-0105, O-0176
Hanif, G., O-0125
Hänold, S., P-0406
Hansen, G., O-0017
Hao, L., P-0082
Haq, A.U., PUB-0039
Hara, J., P-0531, O-0112
Hara, T., PUB-0208, O-0178
Hara, Y., O-0015
Harada, K., O-0160
Hargrave, D., P-0347, PUB-0084
Hariono, S., O-0071
Harnos, A., P-0004
Harrison, C., O-0051, O-0013
Hartman, A., O-0156
Hartung, S., P-0355
Haruta, M., O-0084
Hasan, T., PUB-0031
Hasanain, O., PUB-0240
Hasdiraz, L., PUB-0256
Hasegawa, D., P-0287, P-0037, PUB-0153, P-0540, O-0154
Hashem, S., P-0358
Hashii, K., PUB-0070
Hashii, Y., P-0531, P-0441, P-0433, P-0432
Hashizume, M., O-0178
Hashizume, R., O-0071
Hasiloglu, Z., PUB-0096
Hasle, H., P-0088, P-0101, P-0479, P-0084, O-0013
Hasselblatt, M., P-0355

Hatzidimitriou, V., P-0117
Hatzipantelis, E., P-0117
Hauch, H., P-0342
Hauser, P., P-0338
Hawkins, C., O-0067, O-0044, P-0353, P-0465
Hawkins, M., O-0008
Hayakawa, A., P-0531
Hayashi, M., P-0237
Hayashi, Y., O-0063, O-0018, O-0015, P-0170
Hayden, M., O-0100
Hayes Jordan, A., O-0166
Hazar, V., P-0239, PUB-0261, PUB-0241, P-0047
Hazarika, N., P-0175
He, H., PUB-0001, P-0065
He, J., P-0434
He, X., O-0090, PUB-0154
He, x.l., PUB-0135, PUB-0152
Hedayati ASL, A.A., PUB-0149, P-0373
Hedén, L., O-0159
Hegyi, M., P-0135, P-0004
Heide, S., P-0274
Heij, H., PUB-0049, O-0179
Heij, H.A., O-0172
Heim-Hall, J., P-0137
Heimburger, D.C., O-0114
Helfre, S., O-0066, O-0111
Henderson, T.O., O-0042
Hendricks, M., PUB-0200, P-0119
Hennessy, T., P-0273, P-0270
Hennig, C., O-0017
Hennig, M., PUB-0252
Henrich, K.O., O-0087
Henze, G., P-0038
Hereema, N.A., O-0034
Hermanova, I., P-0001
Hernandez, A., O-0053
Hernandez-Marques, C., PUB-0073
Herndon II, J.E., O-0045
Hero, B., P-0242, O-0002, P-0253, P-0392
Herrero, B., PUB-0073
Hertz, N., O-0089
Herzog, C., P-0445
Hess, K., P-0445
Hess, L., P-0083
Hesseling, P., P-0187, P-0558, PUB-0049
Hevessy, Z., P-0045
Heyman, M., P-0463
Hiddes, C.M., P-0347
Higuchi, K., O-0173
Hijiya, N., P-0034
Hilal, S., PUB-0054
Hinds, P., O-0146
Hinotsu, S., O-0084, P-0188
Hirai, M., P-0263
Hirano, K., O-0108, PUB-0140
Hirata Junior, R., P-0458, P-0294
Hirata, M., O-0154
Hiremath, S.C., P-0191
Hishiki, T., O-0060, O-0112
Hitzler, J., O-0017, O-0098
Hiyama, E., O-0060, PUB-0136, O-0052
Hiz, M., PUB-0095
Hjorth, L., P-0463
Hmood, A., PUB-0202
Ho Huu, S., PUB-0160
Ho Joon, I., PUB-0083, P-0448
Ho, K., P-0489
Ho, M., P-0273, P-0270
Ho, R., O-0114
Ho, S.M.Y., P-0542
Ho, S.S., P-0552
Hochlaf, M., PUB-0169
Hoefnagel, C., O-0003
Hoemberg, M., P-0242
Hogan, M., P-0485
Hojo, H., P-0279
Holdsworth, M., O-0099
Holdt, M., O-0040
Hollenberg, R., PUB-0177
Hollink, I.H., O-0014
Hollis, R., O-0138, O-0139
Holmes, K., O-0113
Holter, W., P-0342, P-0342
Honavar, S., O-0028, P-0306
Hong, C.R., P-0314, P-0183, P-0149
Hong, D., P-0445
Hong, L., P-0003, P-0080
Hong, Y.f., PUB-0151
Hongeng, S., P-0144, P-0499, PUB-0035
Hoogeveen, P.G., P-0427
Hop, W., O-0035
Hori, H., P-0531
HORIBE, K., P-0573, O-0015
Horie, H., O-0060, O-0084, P-0188
Hörnquist, L., O-0072
Horsnall, K., PUB-0245
Horstman, M., O-0142
Horstmann, M.A., P-0427
Hoshida, Y., O-0069
Hoshimo, N., P-0170
Hoshino, N., O-0063, O-0062
Hosoi, H., O-0173, P-0254, O-0137
Hosoya, R., P-0287, P-0037, P-0540, O-0154
Hosoya, Y., P-0287, P-0037
Hotchkin, T., P-0522
Hovén, E., O-0022
Howard, S., P-0048
Howard, S.C., P-0412, PUB-0238, P-0255, P-0504
Howell, L., O-0184
Hoyoux, C., PUB-0132
Hsiao, C., P-0233
Hsiao, C.C., PUB-0022
Hsiao, T.H., P-0414
Hsu, W.M., O-0110, PUB-0022
Hsueh, C., PUB-0085
Hu, L.M., P-0551
Hu, s., P-0022
Hu, W., P-0049
Hu, Y., P-0434
Hua, C., P-0356
Huang, A., O-0130, P-0353, P-0325, P-0465
Huang, C.C., P-0344, P-0343
Huang, J.D., P-0442
Huang, K., P-0130, PUB-0027
Huang, L., O-0033, PUB-0106
Huang, P., PUB-0072
Huang, S., P-0233, PUB-0104
Huang, S.G., PUB-0135, PUB-0152
Huang, X., P-0041, P-0012
Huang, Y., P-0414, O-0056, P-0130, PUB-0104, P-0198
Huang, Z., P-0456
Huchet, A., O-0111
Hudson, M.M., O-0042
Hughes, D., P-0529
Huh, W., P-0305, P-0136, O-0166
Hui, J., P-0017, PUB-0078, P-0391, P-0003, P-0080
Hui, Z., P-0180
Hukin, J., O-0100, O-0067, PUB-0080
Humayun, K., P-0357
Hume, L., O-0145
Hummel, T., P-0447
Hung, C.Y., P-0560
Hung, I., PUB-0085
Hung, J., O-0059
Hung, J.Y., P-0137, P-0414
Hunger, S., O-0032
Hunger, S.P., O-0034, O-0103
Hunt, L., P-0459
Hurley, M.L., O-0141
Hutsadol, S., P-0144
Hutter, B., O-0070
Hutter, S., O-0070
Hwang, J., O-0012
Hwang, T.J., P-0011

I

Iannotta, A., PUB-0172, P-0016
Ichikawa, M., PUB-0122
Ida, K., O-0060
Ideno, K., O-0160
Iehara, T., O-0173, P-0254, O-0137
Ieiri, S., O-0178
Igala, M., PUB-0037
Iguchi, A., PUB-0122
Ihara, S., PUB-0148
Iida, J., O-0154
Ijiri, R., O-0118
Ikeda, H., O-0085, P-0279, O-0112
Ikuta, K., P-0050
Ilhan, I., P-0161, P-0143
Ilhan, N.E., PUB-0261
Im, H., O-0203
Im, H.J., P-0421, P-0395
Imam, U., P-0071
Inada, H., P-0541
Ince, D., P-0440, O-0065, P-0460
Ince, e., PUB-0218
Indelicato, D.J., P-0356
Indolfi, C., PUB-0172, P-0016
Indolfi, P., P-0163, O-0170, PUB-0172, P-0016
Ingrosso, A., PUB-0262
Inoue, F., P-0561
Inoue, M., O-0108, PUB-0140
Inoue, R., P-0409
Inoue, T., O-0060, O-0118
Inserra, A., P-0209, P-0298
Iolascon, A., O-0086
Iosifidis, I., PUB-0221
Ip, W., PUB-0186, P-0487
Irga-Jaworska, N., PUB-0252
Irie, W., O-0154
Irken, G., P-0054
Irtan, S., PUB-0113, O-0165, PUB-0090, O-0081
Isa, N., P-0346, PUB-0173
Isaac, A., P-0378
Isaac, G., P-0313, P-0506
Ise, K., O-0112
Ishida, T., PUB-0153
Ishida, Y., P-0540
Ishii, T., O-0108, PUB-0140
Ishikawa, F., O-0160
Ishikawa, H., P-0167, PUB-0148, PUB-0071
Isik, B., PUB-0255, PUB-0254
Islam, A., P-0028, P-0031, PUB-0101, P-0388, PUB-0060, PUB-0042
Ismael, T., PUB-0156, P-0145, P-0147, PUB-0111
Ismail-zade, R., P-0193
Isnard Blanchar, R., P-0299
Israels, T., P-0310, P-0187, PUB-0049
Issakov, J., P-0148
Ito, E., O-0018
Ito, N., P-0561
Iukhta, T., P-0369
Ivan, m., P-0112
Ivanov, V., P-0341
Ivanova, N., PUB-0161, PUB-0115
Ivanyi, B., P-0249
Ivison, S., P-0069
Iwafuchi, H., O-0118
Iwanaka, T., O-0062
Iwasaki, F., PUB-0209
Iyer, K.K.V.K., PUB-0228, P-0411
Iyer, N., P-0485
Iyer, N.S., P-0543, O-0037
Iyer, P., P-0146
Iyer, V., PUB-0247
Iyer, V.K., O-0189
Izycka-Swieszewska, E., P-0179

J

Jabado, N., O-0067, O-0044
Jabbour, A., O-0025
Jacquemin, E., PUB-0268
Jacus, M., O-0128
Jaeger, N., O-0049
Jafri, S.R., PUB-0185
Jäger, N., O-0070, P-0337
Jahnukainen, K., P-0479
Jain, A., P-0525
Jain, P., P-0525
Jain, R., P-0532, PUB-0199
Jain, S., P-0154
Jaing, T., PUB-0085
Jakab, Z., P-0338
Jakobson, A., PUB-0191
Jakovljevic, G., P-0275

Jalali, R., P-0331
Jamal, C., P-0085
Jamal, C.Y., P-0031, PUB-0101, P-0388, PUB-0060
Jambhekar, N., O-0133
James Martin, J.X.S., P-0514, P-0513
James, B., P-0520
James, C., O-0071
James, P., P-0452, P-0451
Janardhanan, P., O-0008
Jang, H.I., P-0011
Janku, F., P-0134
Janoueix Lerosey, I., P-0272
Jansen, M.H., P-0347
Janssen, M., P-0493
Janssens, G.O., P-0347
Janzen, L., PUB-0080
Jarfelt, M., O-0039, P-0479
Jaroszewska, E., P-0172
Jaspan, T., PUB-0084
Jazbec, J., P-0275
Jazdon, M., P-0172
Jeha, S., P-0034
Jeison, M., P-0277, O-0013
Jenholt Nolbris, M., O-0146, P-0565
Jenney, M., O-0180, O-0132
Jenny, G., P-0112
Jerabkova, V., P-0184, P-0241
Jha, S., O-0209
Ji, C.Y., P-0443
Ji, X., P-0065
Ji, Z., PUB-0001, P-0065
Jia, C., P-0109, P-0268, P-0014
Jia, L., PUB-0058
Jia, Z., P-0105
Jian, P., PUB-0139, P-0099
Jiang, H., P-0076, P-0049, P-0381, PUB-0018
Jiang, L., PUB-0117
Jiang, Q., PUB-0072
Jiang, y., PUB-0120
Jianghua, z., P-0180
Jianguo, X., PUB-0076, P-0360, P-0359
JIashi, Z., P-0080
Jie, L., P-0401, P-0400
Jimbo, T., P-0220
JIN, M., P-0312, P-0262
Jin, R., P-0046
Jin, X., P-0278, P-0278, O-0010
Jin, X.q., O-0010
Jing, L., P-0087
Jing, Y., P-0104
Jingbo, S., P-0080
Jingwei, Y., P-0080
Jingyan, T., PUB-0078
Jirapradittha, J., PUB-0143
Jobe, C., O-0145
John, R.R., P-0398
Johnson, K., PUB-0222
Johnston, D., O-0098, P-0497, O-0013
Jolly, P., P-0286
Jones, C., PUB-0084
Jones, D., O-0070, P-0337, P-0335
Jones, D.T., O-0049
Jones, D.T.W., O-0130
Jones, R., P-0357
Jong Jin, S., PUB-0083, P-0448
Jónmundsson, G.K., P-0479
Jordan, M., P-0425
Jörschke, M., P-0153
José Andres Yunes, Y.J.A., P-0339
Joshi, R., PUB-0195
Jou, S.T., O-0110
Ju, H.Y., P-0314
Ju, X., P-0015, P-0041, P-0444, PUB-0082
Juan, W., P-0105
Judina, N.B., O-0078, PUB-0213
Jun, H., P-0401, P-0400
Jun, L., P-0401, P-0400, P-0099
Jun, P., PUB-0139
Jung, D.H., P-0223
Jung, H.L., P-0075
Jung, J., P-0217
Jung, S.E., P-0258, P-0223
Junqueira, V., P-0405
Jurgens, H., O-0094, P-0201, P-0474
Juvekar, S., O-0133

K

K, A.K., PUB-0243
K, H., O-0204
K.E, E., P-0042
Kabas, L., P-0562
Kabickova, E., P-0103
Kabyemera, R., P-0132
Kachanov, D., PUB-0092, P-0260
Kadan-Lottick, N., P-0485, O-0038, P-0543
Kadan-Lottick, N.S., O-0037
Kadioglu Demirag, B., PUB-0259
Kadyrov, S., O-0043
Kafadar, A., PUB-0096
Kagawa, N., P-0441
Kai, C., P-0391
Kailayangiri, S., P-0436
Kajdas, L., P-0172
Kalaldeh, S., P-0358
Kalapurakal, J., O-0083
Kale, G., P-0118, P-0114
Kalfa, N., O-0167
Kalinchenko, N., PUB-0115
Kalinina, I., P-0091
Kalkandelen, S., PUB-0178
Kalpathi, K., PUB-0216
Kalra, M., P-0505
Kam, M.K.M., P-0246
Kam, S.Y., P-0273, P-0270
Kamibeppu, K., P-0531
Kamijo, T., O-0085, P-0279, O-0112
Kamijyo, T., O-0060
Kamimatsuse, A., PUB-0136
Kampondeni, S., PUB-0049
Kamps, W.A., P-0533, O-0147, O-0150
Kamugisha, E., P-0132
Kanazawa, T., O-0018
Kaneko, M., P-0167, PUB-0071
Kaneko, Y., O-0084, P-0188
Kang, H.J., P-0314, P-0183, P-0245, P-0149, P-0258, PUB-0110
Kantar, M., PUB-0259, PUB-0219
Kao, Y., P-0233
Kapelushnik, J., PUB-0103
Kapoor, G., P-0154
Kapoor, R., P-0292
Kappelmayer, J., P-0045
Kapucu, O., P-0181
Karachunskiy, A.I., P-0036
Karachunsky, A., P-0038
Karacor Ziyanoglu, E., P-0276
Karadeniz, C., P-0178, P-0181, P-0367
Karakas, Z., PUB-0178, P-0055, P-0033, PUB-0033
Karakukcu, M., PUB-0255
Karaman, S., P-0033
Karapinar, B., PUB-0219
Karapinar, D.Y., P-0047
Karass, M., O-0082
Karhan, A., P-0126
Karim, A., PUB-0101, PUB-0060
Karim, M., P-0085
Karim, M.A., P-0031, PUB-0042
Kariminia, A., P-0069
Karns, R., P-0417
Karpelowsky, J., P-0231
Karytsky, A., P-0124
Kashyap, S., P-0317, P-0321, P-0320
Kaspers, G., P-0397, O-0020
Kaspers, G.J., P-0347
Kaspers, G.J.L., O-0016
Kaspers, J., P-0187
Katayama, A., O-0118
Katheria, D., O-0204
Kato, M., O-0018, P-0237, P-0462
Katou, M., P-0263
Katsumi, Y., P-0254
Katsumoto, S., O-0157
Katy, o., P-0112
Kaur, R., PUB-0195, P-0363, P-0361
Kawa, K., O-0108, PUB-0140
Kawahara, H., O-0108, PUB-0140
Kawakami, C., O-0160, P-0561
Kawano, T., P-0287
Kawasaki, H., P-0531
Kawasaki, K., PUB-0153
Kaya, Z., P-0047
Kaygusuz, G., P-0139
Kazakova, A., P-0091, P-0039, P-0260
Kazakova, A.N., P-0036
Kazancev, A., P-0289
Kazanowska, B., O-0171, O-0121, P-0172, P-0179, O-0116, O-0115
Kazantsev, A., PUB-0064
Kazantsev, I., P-0369
Kazantsev, I.V., PUB-0242, P-0527, PUB-0234
Ke, Z., O-0033, PUB-0106, P-0053
Kebudi, R., P-0515, PUB-0180, PUB-0175, P-0311, P-0202, P-0491
Kececi, B., PUB-0259
Kedrzycki, M., PUB-0252
Keino, d., PUB-0105
Keller, F., P-0034
Kelly, D., O-0142, O-0146
Kelly, K., P-0529
Kelly, P., O-0146
Kelsey, A., O-0180, O-0132, O-0007
Kembhavi, S., P-0252
Kemps, L., O-0020
Keogh, S., P-0291
Kerdraon, O., P-0274
Kerimo, P., PUB-0064
Kerimov, P., P-0289
Kesik, V., PUB-0017
Keys, C., P-0378
Khaleque, A., PUB-0101, P-0388, P-0085, PUB-0042
Khalifa, N., PUB-0125, PUB-0093
Khan, M., PUB-0250, P-0196
Khan, M.S., P-0128, PUB-0229
Khan, R., P-0150
Khan, S., O-0011
Khan, S.A., P-0156
Khan, Z.W., PUB-0038
Khandelwal, v., PUB-0189, O-0019
Khanna, N., O-0133, P-0129
Khanna, V., P-0293, O-0164
Khatoon, A., P-0570, P-0569, P-0571
Khattab, T., PUB-0097
Khattry, N., P-0125
Khedmat, H., PUB-0007
Khedr, R., PUB-0240
Khestanov, D., P-0162, P-0173
Khetan, V., O-0028, P-0306
Khlebnikova, O., P-0043, P-0038
Kholodov, B., O-0043
Khong, P.L., P-0229
Khoubila, N., PUB-0205, P-0206
Khranovska, N., P-0257
Kiatchoosakun, P., PUB-0143
Kibria, C.S.H., PUB-0101, PUB-0042
Kidenya, B., P-0132
Kieffer-Renaux, V., P-0330
Kieran, M., O-0069, P-0350, O-0068, P-0352
Kieran, M.W., O-0131, P-0334
Kigasawa, H., PUB-0209, O-0118
Kikuchi, A., P-0237, P-0050
Kikuta, A., P-0067
Kilday, J.P., P-0353, P-0325
Kilne, N., O-0146
Kim, B.J., P-0490
Kim, D., O-0012, P-0421
Kim, D.H., P-0140, P-0075
Kim, H., P-0314, P-0183, P-0149, O-0104
Kim, H.J., P-0075
Kim, H.K., P-0382
Kim, H.S., P-0149, P-0224, PUB-0108
Kim, H.Y., P-0245, P-0258, P-0223, PUB-0110
Kim, J.H., P-0314
Kim, J.Y., P-0224, PUB-0108
Kim, K., P-0203, P-0189
Kim, K.S., P-0395
Kim, M.S., P-0149

Kim, S., P-0245, O-0012
Kim, S.H., P-0258, P-0223, P-0075
Kim, U., P-0306
Kim, Y.J., P-0224
Kimura, O., O-0173
Kinghorn, A., P-0535
Kinoshita, A., PUB-0105
Kinoshita, Y., PUB-0208, O-0112, O-0178
Kinsey, S., O-0005
Kir, M., P-0210, P-0440
Kiratli, H., P-0315
Kiray, M., P-0440
Kirkim, G., P-0460
Kirov, I., P-0120
Kirsh, V., P-0482
Kishimoto, H., O-0118, P-0237
Kislyakov, A., P-0341
Kiss, C., P-0045
Kiss, G., P-0045
Kitagawa, H., PUB-0105
Kitagawa, N., PUB-0209, O-0118, P-0230
Kitagawa, Y., P-0171
Kitanovski, L., O-0127
Kladou, M., PUB-0220
Klap, B.C., P-0472
Kleinerman, E., P-0445
Kler, A., P-0384
Klimov, A.S., PUB-0234
Klingebiel, T., O-0002, O-0115
Klosky, J.L., O-0075, P-0530
Klusmann, J., P-0095, O-0017
Klymnyuk, G., P-0257
Knight, K., P-0486
Knijnenburg, S., O-0179
Knoll, J., P-0177
Kobayashi, H., PUB-0122
Kobayashi, K., P-0531
Kobayashi, S., P-0067
Koch, R., P-0436
Kocheva, S., PUB-0248
Kodet, R., P-0184
Koeck, R., P-0503
Koga, T., P-0328
Koga, Y., PUB-0208
Koh, K., O-0203, P-0237, P-0050, P-0462
Koh, K.N., P-0421
Koh, V., P-0212
Koh, Y.V., P-0261
Kohashi, K., PUB-0208, O-0178
Kohdera, U., P-0531
Koka, A., PUB-0019
Koksal, Y., P-0122
Kolatan, E., P-0440
Koliouskas, D., P-0117, PUB-0221, PUB-0220
Kollen, W., O-0035
Kollender, Y., P-0148
Kolygin, B., P-0124
Komvilaisak, P., PUB-0143, PUB-0142
Kon, A., O-0018
Kon, O.L., P-0273, P-0270
Kondo, A., PUB-0170
Kondo, S., O-0060
Kondoh, K., PUB-0105
Kondratchik, K., P-0038
Kong, M., P-0557
Kong, X., PUB-0158, PUB-0024
Kongjib, L., O-0152
Konovalov, A., O-0043
Konrad, B., P-0488
Kontny, U., P-0153
Koo, H.H., P-0075, P-0208
Kook, H., P-0011
Kool, M., O-0070, O-0048, O-0050, P-0337, O-0130, P-0335, O-0049
Kordes, U., P-0355
Korneeva, A., PUB-0116
Korshunov, A., O-0070, P-0341, O-0044, O-0130, O-0043
Korsvold, L., P-0537
Korten, I., P-0345
Kortmann, R., P-0345
Kortmann, R.D., O-0047
Korver, S., P-0535
Korzeniewska, J., P-0484
Kosaka, Y., PUB-0153
Koscielniak, E., O-0116
Kose, D., P-0122
Kose, M., PUB-0256
Koshinaga, T., O-0084, P-0263, P-0188
Kosmidis, H., PUB-0230
Kosztyla, D., O-0116, O-0115
Kota, R., PUB-0228, P-0411
Kotchawan, S., O-0152, P-0402
Kourti, M., P-0117, PUB-0221, PUB-0220
Kouya, F., P-0187
Kovacs, G.T., P-0135, P-0004
Kovalenko, S., P-0341, PUB-0032
Kozaki, A., PUB-0153
Kozlov, A.V., PUB-0234
Kraal, K., P-0283, O-0003, P-0249
Krailo, M., O-0052
Kramm, C., P-0345
Krasin, M., O-0190
Krasko, O., PUB-0012
Krawczyk, M., PUB-0252, P-0179
Kremens, B., O-0002
Kremer, A., P-0503
Kremer, L., P-0249, O-0179
Kremer, L.C.M., P-0500
Krenacs, T., P-0338
Krenova, Z., P-0103
Krieger, M., PUB-0251
Krivoy, N., P-0510
Kruger, M., P-0186, P-0310
Ku, T.L.D., P-0199
Kube, S., O-0116, O-0115
Kubota, A., O-0108, PUB-0140
Kucuk, O., P-0159
Kuczynski, S., P-0497
Kudo, K., O-0018, O-0015
Kuehl, J., P-0345
Kühl, J., O-0047
Kuhlen, M., P-0242
Kuijpers, T., P-0493
Kulej, D., O-0121, P-0172
Kulkarni, A.V., P-0377
Kulkarni, K.P., O-0058, P-0424, P-0331, P-0307, P-0146, P-0423, P-0110
Kulyova, S., P-0124
Kumagai, M., O-0085, O-0112
Kumamoto, T., P-0287
Kumar, A., P-0052, P-0525, P-0519, PUB-0196, PUB-0195, P-0083, P-0306
Kumar, D., P-0129, PUB-0086
Kumar, R., PUB-0239, O-0011, P-0293
Kumar, S., P-0437
Kumar, V., PUB-0038, PUB-0189, O-0019
Kumbhaj, P., PUB-0179
Kumirova, E., P-0341, O-0043
Kumpunen, S., O-0142
Kupeli, S., P-0528, P-0276, P-0240
Kupesiz, A., PUB-0261
Kuriyama, K., P-0531
Kurkure, D.P., O-0211
Kurkure, P., P-0152, O-0041, O-0209, P-0544, P-0281, P-0252
Kurkure, P.A., P-0051
Kuroda, T., P-0171, O-0112
Kurtzberg, J., O-0045
Kurucu, N., P-0161, P-0143
Kurzrock, R., P-0445
Kushel, Y., P-0341, O-0043
Kuskonmaz, B., P-0068
Kustanovich, A., P-0039
Kutluk, M.T., P-0118, P-0114
Kutluk, T., PUB-0056, P-0216, PUB-0054, P-0126, P-0213, PUB-0055
Kuwahara, Y., P-0254
Kwiecien, R., P-0345
Kwon, H.Y., P-0314, P-0183, P-0149
Kwon, M., P-0155
Kyncl, M., P-0184
Kyr, M., P-0446
Kyung Nam, K., PUB-0083, P-0448

L

Ladas, E., P-0529, O-0148
Ladas, E.J., P-0399, P-0494
Ladenstein, R., O-0116, O-0113
Lafay-Cousin, L., O-0067
Laffont, M., P-0313
Lagoiko, S.N., P-0036
Lai, D., P-0053
Lai, J.S., O-0101
Lai, S.H., P-0273, P-0270
Lai, X., P-0380
Lakshminarayanan, K., P-0513
Lall, M., P-0057
Lam, C., P-0572
Lam, C.G., P-0412, PUB-0238, P-0255, P-0504
LAM, E., PUB-0020
Lam, K., P-0473
Lambrou, G., P-0368, PUB-0159
Lancaster, D., O-0125, P-0516
Lang, P., P-0063
Langat, S., P-0397
Lange-Turenhout, E.A.M., P-0021, P-0020
Langer, T., P-0474
Langerak, A.W., P-0088
Langevin, A.M., P-0137
Langholz, B., O-0028, P-0069
Lannering, B., O-0072, O-0046, P-0480
Lanvers-Kaminsky, C., P-0474
Lapotentova, E., P-0038
Lapouble, E., P-0272
Lapperiere, N., P-0465
Laprie, A., O-0111
Larbcharoensub, N., PUB-0035
Larouche, V., O-0067
Larsen, E., O-0034
Laskar, S., O-0133, O-0122, P-0129, P-0252, P-0123
Laskov, M., P-0332
Lassailly, F., O-0106
Lassaletta, A., P-0048, PUB-0073
Lataifeh, I., PUB-0233, PUB-0235
Latha, M.S., PUB-0094
Latos- Grazynska, E., O-0121
Laughlin, S., P-0325
Laur, E., P-0467
Laurence, V., P-0324
Laureys, G., P-0574, O-0143, P-0265, O-0158
Lautner-Csorba, O., P-0004
Laven, J., P-0461, P-0115
Lazarte, T., O-0151
Lazzareschi, I., PUB-0236
Le Deley, M., O-0094
Le Deley, M.C., O-0117, PUB-0084
Leadley, M., P-0437
Leal-Leal, C., P-0205, P-0313, P-0310, P-0506
Lebenthal, Y., P-0467
Leblond, P., O-0027
Leclerc, G.M., P-0013
Leclercq, E., P-0500
Lee, A., P-0070
Lee, A.C., PUB-0107, P-0116, P-0106
Lee, C.W.A., P-0060, P-0372, P-0371
Lee, J.A., P-0140
Lee, J.M., PUB-0110
Lee, J.W., P-0245, PUB-0110, P-0382
Lee, K., P-0264
Lee, K.H., PUB-0146, P-0204
Lee, K.S., P-0314, P-0183, P-0245, P-0149, P-0421, PUB-0110
Lee, M., P-0473
Lee, N.H., P-0075
Lee, S., P-0203, P-0189, P-0428, O-0120
Lee, S.H., P-0075, P-0208
Lee, S.K., P-0208
Lee, S.W., PUB-0225
Lee, V., P-0246, P-0060, P-0141, PUB-0107, P-0070, P-0116, P-0106, P-0084, PUB-0098, P-0542, P-0489, P-0074, P-0487
Lee, W.S.V., P-0372, P-0371
Lee, Y., P-0302
Leeuw, J., O-0035
Legaszewski, T., P-0470
Lehmann, L., O-0104

Lehrnbecher, T., P-0488
Leisenring, W., P-0466
Leisenring, W.M., O-0042
Lemesheva, O., P-0259
Lervat, C., O-0027
Leseur, J., O-0111
Lethaby, c., O-0005
Leung, A., P-0070, P-0074
Leung, A.W.K., P-0141
Leung, D.Y., PUB-0186, P-0552
Leung, W., P-0489
Leung, W.K., P-0246, P-0060
Leung, Y., O-0033
Leuschner, I., O-0080, O-0116, O-0079, O-0052
Levine, D., P-0244
Levy, C.S., PUB-0260
Lewis, I., O-0094
Lewis, V., O-0098, P-0134
Lhekphet, K., P-0402
Li, A., P-0478
Li, B., P-0062, P-0012
Li, B.S., P-0381
Li, C., P-0235, P-0235, P-0235, P-0329, P-0478, P-0478, P-0473, P-0046, P-0435, PUB-0107, P-0070, P-0070, P-0116, P-0106, P-0053, P-0489, P-0323, P-0487, PUB-0024
Li, C.H., P-0141, P-0084, PUB-0098, P-0074
Li, C.H.R., P-0243, P-0372, P-0371
Li, C.K., P-0246, P-0060, P-0508, P-0508, P-0243, P-0372, P-0371, P-0084, PUB-0098
Li, D., P-0015, P-0444, PUB-0082
Li, f., PUB-0026
Li, G., PUB-0072, P-0268
Li, H., P-0078, P-0435
Li, J., P-0108, PUB-0091
Li, K., P-0251, P-0200, P-0267, P-0097, PUB-0025, P-0456
Li, L., P-0466
Li, m., P-0198
Li, M.J., O-0056
Li, P., O-0123
Li, Q., P-0109, P-0268, P-0014
Li, R.C., P-0329, PUB-0029, P-0323
Li, W., P-0008, P-0226, P-0086
Li, X., P-0041, PUB-0091
Li, X.r., PUB-0062
Li, Y., P-0322, PUB-0181, P-0226, PUB-0124, P-0130, PUB-0104, PUB-0102, PUB-0067, PUB-0047, PUB-0046, PUB-0045
Li, Z., P-0008, P-0046, P-0226
Lian, C., PUB-0010
Liang, R., O-0010
Liao, C., P-0496
Libes, J.M., O-0114
Lichter, P., O-0070, O-0130, O-0049
Lie, H., O-0076
Lie, H.C., P-0537
Liebsch, L., P-0436
Ligon, K., O-0069, O-0044
Ligon, K.L., P-0350
Liliana, v., P-0112
Lillo Lillo, M., O-0030
Lim Hsueh Yee, L., P-0477
Lim, D.H., P-0208
Lim, E., P-0523
Lin, D.T., O-0110
Lin, J., P-0435
Lin, K.H., O-0110
Lin, M., P-0529, P-0489
Lin, M.K., PUB-0186
Lin, S., O-0123
Lin, W., P-0086
Lin, y., PUB-0121
Linares, A., P-0044, P-0370
Lindahl Norberg, A., O-0022
Ling, J., P-0104
Ling, S., P-0235, P-0329, P-0478, P-0473, PUB-0107, P-0070, P-0116, P-0106, PUB-0029, P-0323
Ling, S.C., P-0060, P-0141, P-0243, P-0372, P-0371, P-0084, PUB-0098, P-0542, P-0074
Linga, V.G., PUB-0228, P-0411, P-0307, PUB-0216
Lingappa, l., PUB-0249
Linton, J., O-0174
Lirong, S., PUB-0078
Lissat, A., P-0153
Litvinov, D., P-0038
Liu, A., P-0435
Liu, G., P-0089
Liu, H., P-0014, PUB-0135, PUB-0152, PUB-0154
Liu, L., PUB-0124, PUB-0047, PUB-0046
Liu, W., P-0394, PUB-0100, P-0390
Liu, X., P-0226
Liu, y., PUB-0231
Liu, Y.L., O-0110
Liu, Z., O-0090, P-0097
Livio, V., P-0168
Ljungberg, C., P-0480
Ljungman, G., O-0116, O-0159
Lo Nigro, L., O-0016
Locatelli, F., P-0088, P-0101, O-0105
Lockwood, L., PUB-0134
Loge, J.H., P-0537, O-0076
Loh, A.H.P., P-0273, P-0270
Loh, J., P-0539
Loh, M., O-0032
Loh, M.L., O-0034
Loh, S.Y., PUB-0246
Lohmann, D.R., O-0040
Loisel, D., P-0419
Lombardi, A., P-0016
Lones, M., P-0120
Loo, T., O-0100
Lopez Almaraz, R., PUB-0144, O-0030
Lopez Guerra, J., P-0333
Lopez Gutierrez, J.C., O-0030
Lopez, A., P-0430
Lopez, J., P-0168, PUB-0207
Lopez-Lopez, E., P-0018, P-0133, P-0007, O-0092
Lopez-Ruiz, M., P-0151, P-0142
Lopez-Terrada, D., O-0059, O-0052
Lortat-jacob, s., O-0081
Losty, P., O-0184, O-0185
Lotero, V., P-0044
Louis, C., P-0247
Lovvorn III, H.N., O-0114
Lozano, D., PUB-0265
Lu, A., P-0002, P-0089, P-0081
Lu, C., PUB-0067
Lu, C.C., O-0110
Lu, F., P-0108
Lu, J., P-0226, P-0092, P-0022
Lu, M.Y., O-0110
Lu, S., P-0250, O-0123, P-0176, P-0165
Lu, S.Y., P-0107, P-0269
Lu, X., P-0079, P-0109, PUB-0072, O-0032, O-0103
Lu, Y., P-0015
Lu, z.h., PUB-0018
Lubritz, G., P-0503
Luciano Neder, N.L., P-0339
Ludick, A., PUB-0192
Lühl, N., P-0024
Luiza de Mattos Guaraldi, A., P-0458, P-0294
Luk, C., P-0070
Luk, C.W., P-0141, P-0243, P-0372, P-0371, P-0084, PUB-0098, P-0074
Luksch, R., O-0113
Luna-Fineman, S., P-0310
Lundquist, K., P-0475
Luo, C.J., P-0076, P-0381
Luo, C.Y., P-0076, P-0381
Luo, Q., O-0010
Luo, X., O-0033, P-0093, PUB-0106, P-0053
Luszawska- Kustrzeba, T., O-0121
Lutz, P., O-0027
Lützén, K., P-0492
Lv, Z.b., PUB-0018

M

M, d., PUB-0189, O-0019
M, R.P., P-0042
M.A.G.I.C., C., O-0048, O-0050
Ma, D.X., P-0443
Ma, J., P-0365
Ma, L., PUB-0102, PUB-0047, PUB-0046, PUB-0045, P-0380
Ma, X., P-0543, P-0284, PUB-0104, PUB-0102, P-0312, P-0262
Ma, Z., P-0079, P-0268, P-0014
Ma, Z.G., P-0010
Maaz, A., P-0196, P-0128
Mabbott, D.J., P-0377
Macartney, G., P-0497
MacDonald, T., O-0068
Maciejczyk, A., O-0171, P-0172
Maciejka- Kapuscinska, L., O-0121
MacIntyre, G., O-0142
Mackay, H., P-0378
Macy, M., O-0068
Madanat, F., P-0040
Madani, A., PUB-0205, P-0206, PUB-0037
Maddali, L.S., PUB-0228, P-0411
Maddi, R.N., PUB-0228, P-0411
Madero, L., O-0031, P-0048, PUB-0073
Madney, y., P-0507
Madni, M., P-0111
Maeda, R., O-0157
Magalhães Costa, A.M., P-0405
Magatha sneha, L., P-0514, P-0513
Magluta, C., P-0405
Magnani, C.F., P-0429, P-0430
Mahajan, A., P-0305, P-0136, O-0153, PUB-0119, PUB-0118, PUB-0109
Mahamadou Zaki, H., PUB-0163
Mahdi, H., PUB-0198
Mahé, M.A., PUB-0044
Mahfouz, Y., P-0416, P-0362
Mahmood, S., O-0125
Mahmoud, E., P-0362
Maibach, R., O-0052
Mairiang, D., PUB-0142
Majahan, A., O-0138
Makadia, d., PUB-0249
Makarova, I.V., PUB-0234
Makimoto, A., O-0112
Makwana, G., PUB-0164
Malath, I., P-0474
Maldyk, J., O-0121
Malhotra, J., O-0042
Malik, M., P-0376
Malinova, B., P-0184, P-0241
Malinowska, I., O-0121
Malis, J., P-0184, P-0241
Malkin, D., P-0465
Malmros, J., P-0479
Malogolowkin, M., O-0052, O-0083
Maloney, K.W., O-0034
Malric, A., P-0407
Maltese, F., P-0430
Mamoudou Garba, S., PUB-0163
Man, K.N., PUB-0151
Manabe, A., P-0287, P-0037, P-0050, P-0540, O-0154
Mandal, A., O-0196
Mandal, A.K., P-0301
Mandeles-Erez, R., P-0554
Manglani, M., PUB-0164, PUB-0165
Manjusha, A., PUB-0253
Manley, P., O-0068, P-0352
Manley, P.E., P-0350
Mann, G., P-0103
Mann, K.D., P-0453, P-0454
Mansuy, l., PUB-0008
Mantik, M., P-0548
Manzini, P.M.R., P-0340
Manzitti, C., P-0163
Marabelle, A., P-0272
Marachelian, A., O-0004
Marchante, J.R.M., P-0021
Marchioli, D., P-0219, PUB-0130, PUB-0129
Marco Antonio, D., P-0354, P-0348, P-0019
Marco Antonio, D.S., O-0026
Marcus, K., P-0352, O-0104
Marcus, K.J., P-0350
Marcus, R., O-0103
Marec Berard, P., O-0117
Maria Dias de Faria, L., P-0458, P-0294
Marin, V., P-0429, P-0430
Mark, A., P-0338

Markovic, S., O-0011
Maroz, A., O-0017
Marquez, C., P-0333
Marschalek, R., P-0039, O-0016
Marsh, R., P-0425
Marshall, K., P-0556
Marsot, A., P-0511
Martelli, H., PUB-0268, O-0180, O-0167, O-0182, O-0132, P-0228, P-0166
Martens, L., P-0266
Martin, R., O-0006
Martin-Guerrero, I., P-0018, P-0133, O-0092
Martinelli Jr, C.E., O-0026, O-0009
Martinelli, I., PUB-0172
Martinez Mechon, T., O-0030
Martinez, M., P-0256
Martinez, M.E., P-0410
Martinez-Avalos, A., P-0023
Martinez-Hernandez, C., P-0151
Martiniuk, A., P-0535
Martinova, K., PUB-0248
Martinsson, U., PUB-0077
Marton, L., P-0562
Martynenko, L., P-0039
Martynkevich, I., P-0039
Maru, M., O-0157
Marwa, B., PUB-0031
Marwaha, R., P-0027, P-0521
Marwaha, R.K., P-0532, PUB-0199, PUB-0187, P-0026, PUB-0131, P-0501, P-0498
Masako, T., O-0144, P-0567
Masalu, N., P-0132
Masarweh, M., PUB-0111
Maschan, A., P-0091
Maschan, M., P-0091
Masera, G., P-0048
Mashkov, A., P-0289
Maslak, K., O-0074
Masoud, S., O-0131
Masselli, G., P-0190
Massimino, M., P-0209, PUB-0084, O-0127
Mastellaro, M.J., O-0026, O-0009
Mastrangelo, S., PUB-0236
Masumoto, K., P-0220
Mateos Gonzalez, M.E., O-0030
Mathew, L.G., P-0398
Mathur, S.R., O-0189
Matsuishi, T., P-0541
Matsumoto, K., O-0085, O-0112
Matsutani, M., P-0328
Mattano, L., O-0034
Matthay, K., O-0089, O-0028, O-0004
Matthay, K.K., P-0255
Mattio, I., O-0031, P-0048
Matveeva, E., P-0091, P-0039, P-0260
Matveeva, E.A., P-0036
Matyar, S., P-0276
Maurage, C.A., P-0407
Maurin, S., O-0167
Maurizi, P., PUB-0236
Mavadati, O., P-0463
Mazal, A., P-0324
Mbah, G., P-0558
McAleer, M., P-0305, P-0136
McCabe, M., P-0335
McCarter, R., P-0434
McCarthy, M., P-0522, O-0073, P-0534
McCarthy, P., O-0099
McGowan, M., O-0202
McIntosh, D., P-0357
McLendon, R., O-0044
McLoone, J.K., O-0162
McMasters, R., P-0447, P-0083
McNally, R., P-0452, P-0451
McNally, R.J.Q., P-0453, P-0454
McShane, P., P-0516
Meadows, A., O-0028
Medaglia, C., P-0266
Medhi, B., P-0501
Medhi, S., O-0133, O-0122, P-0222, P-0123
Meena, L., PUB-0194
Megaro, G., P-0282, P-0517
Meghanathan, H.s., P-0513
Mehrvar, A., PUB-0149, P-0373
Mehrvar, N., PUB-0149, P-0373
Mehta, P., PUB-0165
Mehta, S., O-0057
Mehyar, M., P-0358
Meier, A., P-0153
Meiyin Qin, Q., O-0210
Mejri, N., PUB-0169
Melchionda, F., P-0163
Melikyan, A., P-0341, O-0043
Mellblom, A., O-0076
Meller, I., P-0148
Mellgren, K., P-0103
Melnikova, M., PUB-0092
Melo, M.I., PUB-0128
Menckes, O., P-0274
Meng, J., P-0108
Menon, H., P-0129
Menon, S., PUB-0075
Mentkevich, G., P-0332
Meral Gunes, A., PUB-0066, P-0054
Mercedes, T., P-0034
Merchant, T., O-0126
Merchant, T.E., P-0356
Merks, H., O-0132
Merks, J., P-0164
Merks, J.H.M., O-0172
Meshinchi, S., O-0014
Mestdagh, P., P-0266
Metwally, M., P-0362
Meyer, C., P-0039, O-0016
Meyer, L., P-0024
Meyerowitz, J., O-0089
Meyers, R., O-0052
Miakova, N., P-0038
Mian, A., O-0097
Miao, H., PUB-0089, P-0108
Miccoli, P., O-0029
Michelagnoli, M., P-0539
Michelagnoli, M.P., P-0364
Michiels, E., P-0495, O-0102
Michon, B., O-0098
Michon, J., P-0324, P-0272
Mignot, L., P-0324
Mihál, V., O-0013
Milano, G., P-0163
Milburn, M., P-0410
Milde, T., O-0049
Miles, L., P-0447
Millan, N., P-0030
Minard, V., PUB-0113, O-0081
Minard-Colin, V., O-0182, P-0228, P-0166
Minard-Collin, V., O-0132
Minckes, O., O-0091
Ming-ying, Z., PUB-0139, P-0099
Minkina, L., O-0043
Minz, R.W., P-0498
Miri Ali-Abad, G., PUB-0009
Mirsky, H., P-0277
Mishima, K., P-0328
Mishra, B., PUB-0199
Miskiewicz, P., O-0171
Misra, D., O-0057
Misra, R., O-0058
Missoten, P., PUB-0132
Mistry, M., P-0465
Mitchell, D., O-0098
Mitchell, D.A., O-0045
Mitchell, H., P-0485, P-0543
Mitra, S., O-0131
Mittal, R., PUB-0125, PUB-0093
Miyachi, M., P-0254, O-0137
Miyajima, M., PUB-0170
Miyamura, T., P-0441, PUB-0070
Miyano, S., O-0063, O-0018, O-0062, P-0170
Miyashita, E., P-0441
Miyata, K., PUB-0153
Miyoshi, K., PUB-0208
Mizia- Malarz, A., O-0121, P-0172
Mizia-Malarz, A., PUB-0176, PUB-0174
Mizukawa, B., P-0447
Mizumoto, M., P-0167, PUB-0148, PUB-0071
Mngomezulu, G., O-0149
Mngomezulu, S.G., O-0138
Mo, J., P-0447, P-0083
Moaed, B., PUB-0258
Mochizuki, K., P-0067, P-0230
Moens, K., P-0266
Moghaddamjou, A., PUB-0086
Mohammed, K., P-0392
Mohammed, R., PUB-0194
Mohanti, B., P-0156, O-0169
Moiseenko, R., PUB-0092, P-0260
Mokhtari, A., PUB-0141
Molinares, A.L., P-0494
Mollace, M.G., P-0282, P-0517
Mollah, L., P-0085
Mollah, L.R., P-0031, PUB-0101, P-0388, PUB-0060, PUB-0042
Molyneux, E., PUB-0049
Molynjeux, E., P-0187
Monclair, T., O-0113
Monges, S., P-0030
Monica, O., P-0112
Monnet, A., P-0164
Monoranu, C., P-0336
Moores, C., P-0526
Morales La Madrid, A., P-0350, P-0352
Morales, A.G., P-0340
Moreira, C., PUB-0049
Moreira-Ridsdale, D., P-0247
Moreno, L., P-0244
Morez, A., O-0143
Morgan, P., PUB-0084
Mori, M., P-0237
Mori, T., P-0103
Morimoto, M., PUB-0105
Morimoto, T., P-0441
Morini, F., P-0298
Morita, N., O-0160
Mornar, D., O-0197
Morozova, E., P-0369
Morozova, E.V., P-0527, PUB-0234
Morris, V., P-0439, P-0248
Mosby, T., O-0148
Mosby, T.T., P-0399, P-0494
Moschovi, M., P-0368, PUB-0159
Moser, A., PUB-0103
Moskowitz, C.S., O-0042
Mosseri, V., O-0132
Mostert, S., O-0020, P-0397
Mottadelli, F., O-0051
Mottolese, C., P-0327
Mou, J., P-0264
Mou, J.W.C., PUB-0146, P-0204, O-0194
Moules, N., PUB-0004, PUB-0003
Mridha, A.R., P-0157
Mubdi, N.Z., O-0042
Muckaden, M., O-0133, P-0129
Muftakhova, G., PUB-0092, P-0260
Mugishima, H., P-0263
Mukherjee, P., PUB-0164
Mukkada, S., PUB-0227
Mullassery, D., O-0185
Muller, C., O-0165
Munzer, C., O-0111
Muraji, T., O-0112
Murata, S., PUB-0105
Murphy, A., O-0148
Murphy, A.J., P-0399, PUB-0134, P-0494
Murphy, D., P-0357, P-0556
Murugan, V., P-0509
Musharbash, A., P-0358
Mushinskaya, M., P-0341, O-0043
Mushtaq, N., PUB-0038, PUB-0039
Musimbi, J., P-0397, O-0020
Musiol, K., PUB-0176, PUB-0174
Mussini, C., P-0228
Mustapha, M., PUB-0002
Mutafoglu, K., P-0440, O-0065, P-0460
Mutlu, F., PUB-0256, PUB-0255, PUB-0254
Muto, S., PUB-0105
Mwizamholya, D., P-0132

N
Na, Z., PUB-0078, P-0080
Nades, P., P-0481
Naeije, L., P-0500
Nagahara, N., O-0118
Nagao, A., P-0540
Nagarajan, R., P-0447, P-0248
Nagashima, T., PUB-0153
Nagata, Y., O-0018
Nageswara Rao, A., O-0011
Nagtegaal, M., P-0283
Naguib, M., O-0082
Nahar, K., PUB-0101, P-0388, PUB-0060, P-0085, PUB-0042
Naifeh Khoury, M., PUB-0005
Naing, A., P-0445
Nair, R., P-0042, P-0129, PUB-0028
Naka, N., P-0441
Nakadate, N., P-0188
Nakagaki, N., P-0573
Nakagami-Yamaguchi, E., P-0531
Nakagawara, A., O-0085, P-0279, O-0112
Nakamura, Y., O-0085
Nakayama, M., O-0108, O-0118, PUB-0140
Nakazawa, A., O-0085, P-0279
Nall, J., PUB-0079
Namgoong, J., O-0012
Naqvi, A., P-0071
Nara, K., PUB-0070
Narayana, A., P-0304
Narendran, A., O-0068
Naru, J., P-0498
Narula, G., P-0125, P-0051
Nasaka, S.V., PUB-0228, P-0411
Nasedkina, T.V., P-0036
Nathan, P., P-0465
Nathan, P.C., P-0483, P-0482
Natia Esiashvili, N., O-0082
Natrajan, S., P-0306
Navajas, A., P-0018, P-0007
Nayiager, T., O-0036, PUB-0177
Naz, F., PUB-0229
Nazemi, K., O-0068
Nazer, L., P-0145
Ncube, P., PUB-0183
Ndung'u, J.M., O-0114
Neder, L., P-0354, P-0348, O-0026, O-0009
Neggers, S., P-0464, P-0461
Neggers, S.J.C.M.M., P-0472
Negin, J., P-0535
Neglia, J., O-0038
Neglia, J.P., O-0042
Nekritz, E., O-0089
Neri, E., P-0406
Nerli, R., P-0191
Nerli, R.B., O-0055
Nesadeepam, N., P-0398
Neungton, C., PUB-0034
Neuwelt, E., P-0486
Ngo Thuy Minh, N., PUB-0160
Ngo, T., P-0455
Nguyen Dac, L., P-0058
Nguyen Nhu, A., PUB-0160
Nguyen, B., O-0131
Nicholls, J., PUB-0151
Nicolaides, T., O-0071
Nielsen Bech, E.S., P-0468
Niemeyer, C.M., P-0088, P-0101
Niggli, F., O-0116, P-0103
Nimmervoll, B., O-0128
Ning, B.T., P-0442
Ning, G., PUB-0099
NingLing, W., PUB-0078
Nisar, I., P-0071
Nishikawa, E., P-0263
Nishikawa, M., O-0108, PUB-0140
Nishikawa, R., P-0328
Nishimura, R., O-0063, O-0062, P-0170
Nishino, R., O-0154
Nisli, K., PUB-0033
Njamnshi, S.V., P-0558
Njoku, K., P-0454
Njuguna, F., P-0187, O-0020
Noboa, F., PUB-0269, PUB-0265
Noellke, P., P-0088
Noguchi, M., P-0541
Nomura, M., PUB-0070
Nonaka, J., P-0555, P-0553
Norman, P., P-0452, P-0451
Noronha, L., P-0217
Nortey, P., PUB-0068
Northcott, P., O-0048, O-0050, P-0337, O-0129
Northcott, P.A., O-0130, O-0049
Notz Carrere, A., P-0185
Nouhou, H., PUB-0163
Nozaki, M., P-0188
Nozaki, T., P-0287
Nozawa, K., PUB-0209, P-0230
Nunes, S., O-0044
Nunez, C., P-0445, PUB-0264
Nuskova, H., P-0001
Nuzynska- Flak, J., P-0172
Nwankwo, I., P-0406
Nwe, M., PUB-0184
Nygren, J., O-0163
Nysom, K., P-0479

O
O'Brien, J., O-0028
O'Brien, M., P-0447, P-0431, P-0083
O'Shaughnessy, E., O-0099
Oberbach, A., O-0186
Oberlin, O., O-0094, O-0096, O-0180, O-0182, O-0117, O-0132, P-0164, P-0166
Oberoi, S., P-0027, P-0521, P-0026
Oberthuer, A., O-0086
Ocak Yildirim, S., P-0315, P-0216, PUB-0055
Ocal, G., P-0210
Ochi, S., PUB-0153
Ochicha, O., PUB-0040
Oda, M., P-0531
Oda, Y., PUB-0208, O-0178
Oeffinger, K., P-0466
Oeffinger, K.C., O-0042
Ogawa, C., P-0287, P-0037
Ogawa, J., O-0160
Ogawa, S., O-0063, O-0018, O-0062, P-0170
Oguma, E., P-0237
Ogura, K., O-0060, PUB-0136
Oguz, A., P-0239, P-0178, P-0240, P-0181, P-0367
Ohara, A., P-0050
Ohba, U., PUB-0208
Ohira, M., O-0085
Ohki, K., O-0018
Ohshima, j., PUB-0122
Ohta, H., P-0531
Ohto, H., P-0067
Ohuchi, K., O-0137
Ohyama, R., PUB-0105
Oka, Y., P-0433, P-0432
Okamatsu, C., P-0279
Okascharoen, C., P-0499
Okita, H., P-0279, O-0084, P-0188
Okumura, T., P-0167, PUB-0148, PUB-0071
Okuno, Y., O-0063, O-0018, O-0062, P-0170
Okur, A., P-0178, P-0181
Olavides, J., P-0563
Olaya-Vargas, A., P-0418
Olbara, G., O-0020
Olch, A., PUB-0251
Olgun, a.N., P-0239, P-0240
Olgun, N., P-0440, O-0065, P-0460
Olgun, Y., P-0460
Oliveira, J., P-0019
Oliveira, J.C.D., P-0340
Oliveira, R., P-0354, P-0348
Olshanskaya, Y., P-0091, P-0039, P-0260
Olshanskaya, Y.V., P-0036
Omar, F., P-0186
Omar, S., P-0145, PUB-0125, PUB-0093
Omare, F., PUB-0183
Onder Sivis, Z., PUB-0219
Onitake, Y., O-0060, PUB-0136
Oniz, H., P-0239, PUB-0259, P-0240
Ookuma, H., P-0263
Orbach, D., O-0027, O-0132, PUB-0113, O-0165, PUB-0090, O-0064, O-0081
Oren, H., P-0054, P-0047
Oreste, M., PUB-0172
Orimo, H., O-0118
Orme, L., P-0522
Ortali, M., O-0052
Ortiz Gordillo, M.J., P-0333
Oruko, O.V., O-0114
Oshima, K., P-0050
Oshiro, Y., P-0167, PUB-0148, PUB-0071
Osorio, T., P-0296
Ottensmeier, H., O-0047
Ouchi, K., P-0254
Oue, T., O-0060, P-0441, P-0188, PUB-0070
Oulton, K., O-0142
Ovsepyan, V., P-0039
Owens Pickle, E., O-0126
Owusuaa, C., P-0115
Oyarce, V., P-0546
Ozawa, M., P-0540, O-0154
Ozbek, N., PUB-0016, P-0047
Ozbek, U., PUB-0019
Ozdemir, G.N., P-0491
Ozdemir, M., PUB-0256, PUB-0255, PUB-0254
Ozdemir, M.A., P-0047
Ozdemir, N., PUB-0096, PUB-0095, PUB-0019
Ozel, H., P-0393
Ozer, S., P-0055
Ozerov, S., O-0043
Ozerova, V., O-0043
Ozguven, A., P-0055, P-0033
Ozkan, A., P-0528, P-0276
Ozkan, E., P-0159
Ozkutlu, S., PUB-0055
Ozono, K., P-0441, P-0433, P-0432
Ozono, S., P-0541
Ozturk Goruroglu, O., P-0276
Ozturk, G., PUB-0178, P-0055, P-0033
Ozyoruk, D., PUB-0193
ÓBrien, M.M., O-0105

P
P, K., P-0042
P, R., PUB-0127
Packer, R., O-0044
Pacquement, H., PUB-0090
Padgaonkar, D.V., O-0211
Padgaonkar, V., P-0544
Padovani, L., O-0111
Padur Sivaraman, R., P-0514
Pagnier, A., O-0027
Paiano, M., P-0282, P-0517
Pakakasama, S., P-0144, P-0499, PUB-0035
Palacios, J., P-0205
Pan, C., P-0108, P-0158
Pan, J., P-0094, P-0022
Panagopoulou, P., PUB-0230
Panasiuk, A., P-0172
Panchal, H., P-0306
Pandey, R., P-0095, P-0306
Panepucci, R., P-0354, P-0348, P-0019
Panepucci, R.A., P-0339
Pang, K., P-0264
Pang, K.K., PUB-0146
Pang, K.K.Y., P-0204
Pang, L., P-0094, PUB-0001, P-0065
Panini, J.E., P-0219, PUB-0130, PUB-0129
Papassotiriou, I., P-0368
Papini, P., O-0029
Papkevich, I., PUB-0267, PUB-0232, P-0238
Pappo, A., O-0190
Parasuraman, V.P., P-0513
Parentelli, A.S., PUB-0008
Parikh, N.S., P-0255
Pariyar, J., O-0057
Park, B.K., P-0155
Park, E.S., PUB-0110
Park, H.J., P-0155
Park, J., PUB-0225, O-0004
Park, J.A., P-0490

Park, J.Y., P-0490
Park, K., P-0183
Park, K.D., P-0314, P-0183, P-0245, P-0149, P-0258, PUB-0110
Park, K.W., P-0245, P-0258, P-0223
Park, M., O-0018
Park, S., P-0140, P-0395
Parlak, S., P-0315
Parsons, D., O-0059
Parthak, P., O-0097
Partrick, D., O-0177, O-0174
Pastrana, A., P-0030
Pathy, S., P-0156
Patiño-García, A., P-0133, O-0092
Patiroglu, T., PUB-0255
Patte, C., P-0185, P-0324
Pau, B., O-0200, O-0208
Paulino, A., P-0304
Paulussen, M., O-0094
Pavelka, Z., P-0446
Pavlova, E., P-0341, O-0043
Pavlovskaya, A., PUB-0161
Pavlyk, S., O-0135, P-0257
Pearce, M., P-0451
Pearce, M.S., P-0453, P-0454
Pearson, A., P-0244
Pearson, D., P-0335
Pecinerli, S., P-0210
Pecoraro, G., PUB-0172
Pedone, C., P-0327
Peifang, X., P-0401, P-0400
Peinado, J., P-0333
Peixoto Lira, R.C., O-0009
Peksayar, G., P-0311
Pelidis, M., P-0516
Pellier, I., P-0185, P-0419
Peña, N., P-0205
Penelope, B., O-0113
Peng, P., P-0456
Pengfei, L., P-0105
Per, H., PUB-0254
Peralta, L., P-0061
Peregud- Pogorzelski, J., P-0172
Peregud-Pogorzelski, J., O-0171
Pereira, A., P-0296
Perek - Polnik, M., P-0484
Perel, Y., O-0111
Perentesis, J., P-0447, P-0248, O-0068, P-0431, P-0083, P-0096
Perentesis, J.P., P-0417
Perez Alonso, V., O-0030
Perez Garcia, m., P-0418
Pérez-Juárez, F., P-0174
Perez-Martinez, A., P-0048, PUB-0073
Pergert, P., P-0492
Perilongo, G., O-0052
Perin, C.A., P-0563
Perlman, E., O-0083
Peronace, G., P-0209, O-0029
Pession, A., O-0013
Petersen, C., P-0463
Peterson, S., O-0083
Petrara, M., P-0132
Petras, S., O-0066
Petrichenko, A., PUB-0115
Petricoin, E.F., P-0427
Petrosino, G., O-0086
Peuchmaur, M., P-0407, P-0274, P-0272
Peyrl, A., P-0334
Pezuk, J.A., P-0340, P-0438
Pfister, S., O-0070, O-0048, O-0050, O-0044, P-0335, O-0049
Pfister, S.M., O-0130, O-0087
Pham Hoang, H., P-0058
Phan Huy, T., P-0058
Philip, M., P-0467
Phillips, C., P-0447, P-0083
Phillips, R., P-0520, O-0099
Phipps, K., P-0361
Phipps, K.P., P-0363
Phulpin, A., PUB-0008
Pianovski, M., P-0217
Picard, D., O-0130
Picton, S., O-0005
Pieper, S., P-0502
Pierron, G., P-0274, P-0272
Pieters, R., P-0088, O-0051, P-0472, O-0014, P-0495, O-0102, O-0079, O-0035, P-0464, P-0021, P-0020, O-0156, P-0461, P-0427, O-0016, O-0013
Pietsch, T., O-0046, P-0345, O-0047
Piette, C., PUB-0132, O-0127
Piguet, C., P-0330
Pilar, Q., P-0112
Pillai, A., P-0423
Pimenov, R., P-0332
Piñan, M.A., P-0018
Pinargote, N., PUB-0265
Pinarli, F.G., P-0178, P-0181, P-0367
Pinches, N., O-0068
Pinel, S., P-0349
Piolat, C., O-0165
Piscione, P., P-0377
Pizer, B., P-0526, P-0331, O-0184, O-0127
Pizzitola, I., O-0106, P-0430
Plantaz, D., O-0111, P-0272
Plekhanova, O., P-0039
Ploszynska, A., PUB-0252
Plourde, P.V., P-0034
Plouvier, E., O-0111
Pluijm, S., P-0464
Pluijm, S.M.F., P-0472
Pobudejska-Pieniazek, A., P-0470, P-0469, PUB-0133
Pocza, T., P-0338
Pöder, U., O-0159
Podevin, G., O-0165
Podgornik, H., P-0275
Poetschger, U., O-0113
Pogudin, D., P-0038
Polczynska, K., PUB-0252, O-0168
Pole, J., O-0107, P-0465, P-0450
Pole, J.D., P-0483, P-0482
Pollock, B., O-0059
Polushkina, O., P-0225, PUB-0116
Polyacov, V., PUB-0074
Polyakov, V., PUB-0161, P-0316, P-0195, P-0215, P-0290
Pomeroy, S., O-0044
Pond, G., O-0067
Pongtanakul, B., PUB-0034
Poole, J., PUB-0162, PUB-0114
Poole, J.E., PUB-0260
Poon, T., O-0151
Popov, A., P-0039, P-0043, O-0109, P-0038, P-0259
Popov, V., P-0341, O-0043
Popova, O., P-0341, O-0043
Popova, T., P-0259
Popovski, D., O-0025
Porter, J.S., P-0530
Portilla, C.A., P-0044
Portwine, C., O-0098, O-0099, P-0497
Poskitt, K., O-0067
Postovsky, S., PUB-0258, P-0545
Pota, E., P-0016
Pourtsidis, A., PUB-0230
Powis, M., O-0187
Poyraz, A., P-0367
Pozdniakov, A.M., PUB-0213
Prabaharan, K., PUB-0094
Prabha, V., P-0191, O-0055
Prabhu, S., O-0068
Pradhan, N., P-0152
Praena-Fernandez, J.M., P-0333
Prasad, M., P-0152, P-0125, P-0051
Price, V., O-0098
Pritchard-Jones, K., P-0197, O-0080, PUB-0049
Prityko, A., O-0043, PUB-0115
Privalova, L., P-0341, O-0043
Proust, S., P-0419
Pucci, V., P-0209
Puget, S., P-0330
Pujar, V.C., P-0191
Pulsipher, M., P-0069
Punanov, Y., P-0369
Punanov, Y.A., PUB-0242, P-0527, PUB-0234
Pundy, T., P-0343
Punjwani, R., P-0571, P-0570, P-0569
Punnett, A., P-0035
Puri, A., O-0133
Puri, k., PUB-0244
Pushker, N., P-0317, P-0321, P-0320
Puttiaungkoon, N., P-0499
Pycha, K., P-0184, P-0241

Q

Qachouh, M., PUB-0037
Qaddoumi, I., P-0310
Qamar, F.N., PUB-0038
Qi, J., O-0131
Qi, X., P-0097
Qian, X., P-0108
Qiang, L., PUB-0076, P-0360, P-0359
Qiangya, M., P-0180
Qin, H., PUB-0147, O-0192, PUB-0053, P-0297, P-0262
Qin, L., P-0003
QIN, M., P-0262
Qin, R., P-0097
Qin, X., P-0381
Qin, Y., P-0089
Qin, Z., P-0401, P-0400
Qing, L., P-0017
Qu, Y., P-0130, PUB-0104
Quah, T., PUB-0224, P-0477
Quaye, A., PUB-0068
Quehenberger, F., P-0342, O-0127
Queiroz, R.d.P., P-0340
Quessar, A., PUB-0037
Queudeville, M., P-0024
Quintero, M., P-0044
Quiroga, E., P-0333
Qureshi, S., O-0133, O-0122, P-0252, P-0222
Quyou, A., PUB-0163, PUB-0141

R

Raber, S., P-0466
Rachkov, V., P-0260
Raciborska, A., P-0300, O-0168
Radhakrishnan, N., P-0413, P-0057
Raetz, E., O-0032
Raetz, E.A., O-0034
Raffoul, l., O-0081
Ragbaoui, Y., P-0206
Rahimian, J., PUB-0079
Rahman, A., P-0085
Rahman, A.A., PUB-0101, P-0388
Rahman, A.T.M., PUB-0060
Rahman, A.T.M.A., PUB-0042
Rahman, M., P-0028
Raj, r., PUB-0189, O-0019
Rajakumar, P.S., PUB-0094
Rajan, M., O-0153
Rajput, K., P-0486
Raju, D.S., P-0398
Ramadwar, M., P-0252, P-0222, PUB-0075
Ramaglia, M., PUB-0172, P-0016
Ramalho, L., O-0009
Ramaru, B., O-0141
Ramaswamy, V., O-0048, O-0050, O-0044
Rambau, P., P-0132
Ramirez Villar, G.L., O-0030
Ramirez, G., P-0333
Ramirez, M., P-0048
Ramirez, O., P-0044, O-0054
Ramzan, M., P-0077
Ranasinghe, N., O-0142
Ranft, A., O-0094, P-0201
Rangarajan, V., O-0122, P-0123
Rangaswami, A., O-0052
Rangrajan, V., P-0129
Rao, B., O-0190
Rapala, M., O-0171, O-0121, P-0172
Raquin, M., P-0330
Rashid, A., PUB-0250, PUB-0229
Raslawski, E., P-0168
Raspin, S., P-0534
Rassekh, S., O-0100
Rastogi, S., P-0156
Rathe, M., PUB-0015

Rathore, A.W., PUB-0211
Ratiu, T., P-0228
Rauber Antonini, S.R., O-0009
Ravi kumar parihar, r., PUB-0119, PUB-0118
Ravikanth, B., PUB-0212, P-0285
Rawat-Pawar, E., O-0209
Ray, P., P-0027, P-0026
Raza, M., P-0150
Rebecca, L., P-0488
Rechnitzer, C., O-0132
Recklitis, C., O-0077
Redaniel, T., O-0006
Reddy Marri, P., O-0011
Reddy, M.N., P-0191
Refaat, A., P-0416, P-0362
Refaat, T., P-0416
Regina, A., P-0488
Réguerre, Y., P-0419
Reifenberger, G., O-0070
Reinhardt, D., P-0095, O-0017, O-0014, O-0016, O-0013
Reinhardt, K., O-0017
Reis, G.P., PUB-0218, PUB-0217
Reis, P., P-0159, P-0139
Reisli, I., P-0122
Reiter, A., P-0103
Rekhi, B., O-0133
Remke, M., O-0048, O-0050, O-0044, P-0337
Renard, C., P-0185
Renner, L., PUB-0068, P-0547
Renner, L.A., P-0187
Rey, A., O-0180, O-0132, P-0166
Rey, G., PUB-0210, PUB-0197
Reyes Abreu, G., PUB-0144
Reyes, M., P-0346, PUB-0173
Reyes-Kattar, J., P-0296
Reynders, D., P-0186, PUB-0183
Rheingold, S.R., P-0034, O-0105
Rialland, X., P-0272, P-0330
Riaz, S., P-0196
Ribeiro, K., P-0218
Ribeiro, R., P-0218, P-0408, P-0048
Ribeiro, R.C., P-0504
Ricardo dos Santos Oliveira, O.R.S., P-0339
Riccardi, R., PUB-0236
Rice, M., O-0184, O-0185
Rich, B., O-0069
Richardson, K., P-0439
Richter, G., O-0095
Rickardsson, J., O-0072
Ridola, V., PUB-0236
Riedel, S., P-0336
Riffkin, C., O-0025
Rigby, L., O-0025
Riger, T., P-0039
Rihani, R., P-0415, PUB-0235, PUB-0233
Rikiishi, K., P-0531
Rinaldi, E., O-0052
Ring, J., P-0436
Ritchey, A.K., O-0103
Ritchey, M., O-0083
Rivas, S., O-0021
Rivera Gómez, R., P-0408
Rivera-Luna, R., P-0023, P-0174
Riziq, M., P-0040
Rizzi, A., P-0227
Rizzo, D., PUB-0236
Robays, H., P-0265, O-0158
Robert, K., P-0568
Roberts, I., O-0017
Roberts, S., O-0088
Roberts, W., P-0408
Robinson, P.R., O-0099
Robison, L., P-0466
Robison, L.L., O-0042
Robison, N., P-0350, O-0068, P-0352
Robles, C., P-0506
Robles, J., P-0205
Robles, R., PUB-0073
Robles-Aviña, J., P-0151
Rodgers, P.C., P-0399
Rodrigues, M., P-0218
Rodrigues, S., P-0219, PUB-0130, PUB-0129
Rodriguez Luis, J., PUB-0144
Rodriguez, K., PUB-0210, PUB-0197
Rodriguez, V., O-0011
Rodriguez-Galindo, C., P-0218
Rogers, P.C., P-0494
Rogers, T., O-0180, P-0291
Rogosic, S., P-0275
Rogowska, E., O-0168
Rohr, R., PUB-0210
Rohren, E., P-0305, P-0136, P-0134
Roilides, E., PUB-0221
Roman, A., O-0077
Rome, A., P-0511
Ronghe, M., P-0357, P-0556
Roodbol, P.F., P-0533, O-0147, O-0150
Roos, J., O-0035
Rosa, A., P-0219, PUB-0130, PUB-0129, PUB-0128
Roschina, N.V., PUB-0242, P-0527
Rose, A., P-0227, PUB-0207, P-0168
Roshan, T., P-0301
Rosolen, A., P-0103
Ross, C., O-0100
Rossell, N., O-0053, O-0024
Rossi, J., P-0061, P-0090
Rossig, C., P-0436
Rostovtsev, N., P-0195
Rouault-Pierre, K., O-0106
Roumyantsev, A., P-0038
Round, J., P-0516
Rousseau, R., P-0164, PUB-0084
Roy Moulik, N., P-0052, P-0525
Roy, S., PUB-0050
Ru, w., P-0198
Ruan, Y., PUB-0166
Ruano, D., PUB-0073
Rubansky, M., PUB-0064
Rubie, H., P-0272
Rubinstein, M., P-0536
Rubnitz, J., O-0013
Ruccione, K., O-0146
Ruffier-Loubiere, A., P-0324
Ruggiero, A., PUB-0236
Rui, Z., P-0104
Ruidong, Z., PUB-0204
Ruland, V., P-0355
Rumyantceva, J.V., P-0036
Rumyantsev, A., P-0341, O-0043
Runming, J., PUB-0123
Russell, K.M., O-0075, P-0530
Russo, G., O-0074
Russo, M., P-0346, PUB-0173
Rutka, J., O-0044
Rutkowski, S., O-0046, P-0345, O-0127, O-0047
Ruud, E., P-0537, O-0076
Ryabov, A., PUB-0064, P-0289, P-0215
Rybakova, D., P-0289
Rybka, B., O-0121
Rychlowska- Pruszynska, M., P-0172
Rychlowska-Pruszynska, M., P-0300, O-0168
Rykov, M., P-0366, P-0518, PUB-0006, P-0288, P-0215, P-0290
Ryu, J., P-0395
Ryu, K.H., P-0389, P-0245
Ryzhova, M., O-0070, P-0341, P-0337, O-0043

S

S Souza, M., P-0405
S, L., P-0042
Saab, R., PUB-0051
Saad-Eldin Sadek, Y., P-0295, PUB-0069
Saadati, M., O-0087
Saatci Cekirge, I., P-0315
Sabah, D., PUB-0259
Sabai, S., P-0477
Sabel, M., P-0480
Sachdeva, A., PUB-0257, P-0413, PUB-0243, P-0519, PUB-0196, PUB-0195, PUB-0194, P-0057, P-0221, P-0077, P-0029, PUB-0050, P-0384
Saeedipour, T., PUB-0014
Safonova, S., P-0369
Safonova, S.A., PUB-0242, P-0527, PUB-0234
Safronov, G., PUB-0032
Saglik, Y., P-0159, P-0139
Sah, K., PUB-0150, PUB-0013
Saha, V.H., O-0051
Sahin, g., PUB-0214
Said, A.M.A., P-0319, PUB-0057
Saikawa, Y., P-0171
Saini, N., P-0320
Sainte Rose, C., O-0066, P-0324, P-0330
Saito, A., PUB-0153
Saito, M., P-0188
Saito, T., P-0050
Saitou, T., P-0263
Sakamoto, K., P-0254, O-0137
Sakamoto, N., P-0220
Sakata, H., P-0462
Sakurada, R., PUB-0128
Sakurai, H., P-0167, PUB-0148, PUB-0071
Salami, K., P-0040
Salaria, M., PUB-0131, P-0498
Salaverria, C., O-0053
Salcioglu, Z., PUB-0190, PUB-0175, PUB-0065
Salem, M., P-0192
Salgado, C., P-0546
Salifu, N., O-0161
Salmanidis, M., O-0025
Salvador, L., O-0151
Samaan, C., P-0376
Sampson, J.H., O-0045
Samudio, A., O-0031, P-0048
Samy, M., P-0416
Sanada, M., O-0063, O-0018, P-0170
Sánchez de Toledo, J., O-0180
Sanchez La Rosa, C., P-0090
Sanchez, G., PUB-0269, PUB-0265
Sanchez-Diaz, P.C., P-0414
Sánchez-Toledo, J., P-0018
Sander, S., PUB-0190, PUB-0065
Sanderman, R., P-0533
Sands, S., P-0529
Sandstedt, B., O-0080, O-0079
Sankaranarayan, S., P-0514
Sano, H., P-0067
Sanpakit, K., PUB-0048
Sansom-Daly, U., P-0538
Santagata, S., O-0069
Santos Marco Antonio, D., P-0339
Santos, C., PUB-0128
Sarabia, M., P-0227
Sarac, A., P-0367
Saraceno, D., O-0052
Saran, F., PUB-0084
Sari, N., P-0161, P-0143
Sarialioglu, F., P-0239, P-0240
Sarin, Y., PUB-0206, PUB-0203
Sarin, Y.K., O-0058
Sarmiento, I., P-0044
Sarnacki, S., PUB-0113, O-0165, PUB-0090, O-0113, O-0081
Sarper, N., P-0047
Sarpong-Oduro, A., O-0161
Sasaki, T., P-0220
Sastry, J., P-0357, P-0556
Satheesha, S., P-0169
Sato, M., PUB-0140
Sato, Y., O-0062
Saud, B., PUB-0199
Sauerwein, W., O-0040
Saunders, D.E., P-0363
Saury, J., P-0480
Saury, J.M., P-0375
Sauvanet, A., O-0165
Sauvat, F., PUB-0113
Savasan, S., PUB-0145, O-0013
Saveliev, L., P-0039, P-0043, O-0109, P-0038, P-0259
Sawada, M., P-0531
Sawant, T., O-0153
Sawaya, D., O-0190
Sawhney, S., P-0413
Sawyer, S., P-0522
Saxena, A., P-0521
Sayitoglu, M., PUB-0019
Saylors, R., O-0097

Sayour, E.J., O-0045
Scalisi, R., O-0074
Scalzone, M., PUB-0236
Scanlan, T., P-0187, PUB-0049
Scarzello, G., O-0170
Schäfer, B., P-0169
Schechter, T., P-0483
Scheinemann, K., O-0067, P-0376, P-0370, P-0465
Schepke, E., O-0039
Scherbenko, O., P-0341
Schiavello, E., O-0127
Schieving, J., P-0347
Schiff, D.E., P-0410
Schlegel, P.G., P-0342, P-0379, P-0336
Schleiermacher, G., O-0111, O-0079, PUB-0090, P-0272, P-0185
Schlichting, N., O-0186
Schmid, D., O-0206
Schmid, I., O-0052
Schmidt, F., P-0095
Schmidt, R., O-0002
Schmugge, M., P-0088, P-0101
Schoeman, J., P-0186, PUB-0183
Schomerus, E., P-0468
Schrappe, M., O-0051
Schrey, D., P-0244
Schubert, S., O-0131
Schuck, A., O-0116
Schuller, U., O-0044
Schulte, F., PUB-0080, PUB-0004
Schultz, K., P-0069
Schuttemberg, V., P-0256
Schwartz-Atias, I., P-0554
Schwyzer, R., PUB-0114
Scianguetta, S., PUB-0172
Sciuk, J., P-0214
Scopinaro, M., P-0227, P-0168, O-0132
Scordo, L., O-0074
Scott, J.X., PUB-0094
Scott, R.M., P-0350
Scrideli, C., P-0354, P-0348, P-0019
Scrideli, C.A., P-0339, O-0026, P-0340, O-0009, P-0438, P-0438
Sebestyen, A., P-0338
Sedlacek, P., P-0241
Sefi, E., P-0486
Segers, H., P-0464
Seidinger, A.L., O-0026, O-0009
Seifu, A., O-0140
Seigneur, E., P-0324
Seitz, G., O-0181, O-0176
Seiwerth, S., P-0275
Seker-Cin, H., P-0337
Seki, M., O-0063, O-0062, P-0170
Sekitomi, A., O-0154
Sema, V.D., P-0239
Semsei, A.F., P-0004
Sen, H., PUB-0190, PUB-0175, PUB-0056, P-0315, P-0216, PUB-0055
Sen, S., P-0317, P-0321, P-0320
Senawong, S., PUB-0034
Sender, L., P-0120
Sengar, M., P-0129
Senzhapova, E., P-0173
Seo, J., O-0203
Seo, J.J., P-0421, P-0395
Seong Soo, J., P-0448
Sepang, F., P-0548
Serbetcioglu, B., P-0460
Serebryacova, I., PUB-0074
Serrasesumaga, L., P-0133, O-0092
Servin, J., P-0048
Servitzoglou, M., PUB-0230
Seth, R., PUB-0247, PUB-0244, PUB-0239
Seth, T., P-0424
Seuanez, H.N., P-0271
Sevinir, B., P-0239, P-0240
Sezgin Evim, M., PUB-0066, P-0054
Sezgin, A., PUB-0016
Sezgin, G., P-0528, P-0276
Shabbir Ali, A., P-0111, O-0125
Shabna, A., P-0362
Shah, N., PUB-0249, PUB-0164
Shah, S., O-0122
Shaheen, N., P-0128
Shahine, R., PUB-0051
Shahzad, M.K., PUB-0250
Shaida, E., O-0135
Shaikh, F., P-0035
Shaikh, G., P-0357
Shaikh, k., P-0059
Shaikh, R., P-0160, P-0182, P-0385
Shaker, S.S., PUB-0057
Shalaby, L., PUB-0240, P-0507
Shalitin, S., P-0467
Shamanskaya, T., PUB-0092, P-0260
Shamardina, A., P-0038
Shamasov, R., P-0341
Shamberger, R., O-0083
Shammasov, R., O-0043
Shams, I., P-0377
Shankar, A., P-0539, P-0364
Shanmugam, M., P-0306
Shao, X., PUB-0001
Shao-yan, H., P-0401, P-0400, P-0087, PUB-0139, P-0099
Sharma, A., P-0281, O-0189, P-0321, P-0320
Sharma, B., O-0190
Sharma, D., O-0136, P-0156, O-0169
Sharma, D.O.P., PUB-0179
Sharma, J., P-0413
Sharma, K.S., O-0057
Sharma, M., P-0157, P-0156
Sharma, R., P-0152, PUB-0179, PUB-0164
Sharma, S., PUB-0164, PUB-0165
Sharoev, T., P-0225, PUB-0116
Sharon, N.A., P-0277
Sharp, S., P-0248
Shats, L., P-0341
Shaw, P., P-0505
Shayda, E., P-0257
Shcherbenko, O., O-0043
Shea-Perry, M., P-0535
Shehadah, A., P-0147
Shehata, B.M., O-0082
Shehata, H.H., P-0319
Sheil, A., P-0447
Shelat, A., O-0128
Shelby, K., O-0059
Shen, G., P-0557
Shen, H., P-0131, P-0064
Shen, L., P-0477
Shen, S., P-0049, P-0158
Shen, S.h., P-0381
Shen, V., P-0120
Shen, X., PUB-0046
Shenton, G., P-0520
Sheridan, R., P-0447
Sherief, L., PUB-0031
Sherif, L.M., P-0396
Shet, T., O-0122, P-0129, P-0123
Shewaramani, N., P-0035
Shi, C., P-0226
Shi, Q., P-0015, P-0444
Shi, S., P-0496, P-0064
Shiba, N., O-0018, O-0015
Shichino, H., P-0263
Shih, D., O-0044, O-0129
Shimada, A., O-0015
Shimanski, A., P-0238
Shimizu, Y., PUB-0170
Shimozawa, K., P-0263
Shin, H., P-0421
Shin, H.J., PUB-0108
Shin, H.Y., P-0314, P-0183, P-0245, P-0149, P-0258, P-0223, PUB-0110
Shing, M., P-0329, P-0070, P-0489
Shing, M.K., P-0246, P-0243, P-0372, P-0371, P-0199, P-0074
Shing, M.M., PUB-0029, P-0323
Shing, M.M.K., P-0141, P-0084
Shinkai, M., PUB-0209, O-0118, P-0230
Shinkai, T., P-0220
Shirahata, M., P-0328
Shirahata, N., P-0555
Shiraishi, Y., O-0063, O-0018, O-0062, P-0170
Shiriaev, S.N., PUB-0234
Shishkina, L., P-0341, O-0043
Shishkov, R., PUB-0161
Shkalim-Zemer, V., P-0148
Shochat, S., P-0255
Shokat, K., O-0089
Shorikov, E., P-0039, P-0043, O-0109, P-0038, P-0259
Shrubsole, M.J., O-0114
Shu, Q., PUB-0100, PUB-0030, O-0191
Shu, Y., P-0097
Shuang, H., P-0104
Shuba, S., PUB-0094
Shui-yan, W., P-0099
Shukla, N., O-0136, P-0156
Shulkin, B.L., P-0356
Shum, S.K., P-0560, P-0559
Shun, A., P-0231
Shvetsov, A.N., PUB-0234
Siddaiahgari, S., PUB-0249
Siddiqi, F., P-0177
Siddique, R., P-0031, PUB-0101, P-0388, PUB-0060, P-0085, PUB-0042
Sidi, V., P-0117, PUB-0220
Siekerman, M., P-0431, P-0083, P-0083
Siklar, Z., P-0210
Silva, M., O-0098, P-0219, PUB-0130, PUB-0129
Silva, R., P-0218
Silveira, V., P-0354, P-0348
Silvera, V.M., P-0350
Silvia Regina Brandalise, B.S.R., P-0339
Simmons, C., P-0480
Simmons, J.L., O-0075, P-0530
Simon, N., P-0511
Simon, T., P-0242, O-0002, P-0253
Simone Aguiar, A.S., P-0339
Singer, J., P-0410
Singh, A., P-0032
Singh, L., P-0317, P-0321, P-0320
Singh, M.K., P-0320
Singh, P., PUB-0244
Singh, S., PUB-0239
Singh, U., P-0306
Sinha, S., PUB-0206, PUB-0127
Sint, K., O-0038
Sirachainan, N., P-0144, P-0499, PUB-0035
Siratesmi, M.N., P-0397
Sitaresmi, M., O-0020
Sitorus, R.S., P-0310
Siveira, A., P-0019
Sjöli, P., O-0039
Sjölund, A., P-0480
Skärsäter, I., P-0565
Skiles, J., P-0397, O-0020
Sklar, C., P-0466
Sköldenberg, E., PUB-0191
Slavakis, A., PUB-0221
Slavc, I., P-0345, P-0334
Slot, A., P-0397
Smets, A., P-0249
Smith, A., O-0126, O-0068
Smolarek, T., P-0083
So, H., P-0478
So, W.K.W., P-0508
Soanes, L., O-0146
Soares, F.A., P-0344
Sobol, G., O-0171, P-0172
Sobol- Milejska, G., O-0121
Sobol-Milejska, G., PUB-0176, PUB-0174
Soeastomo, R., O-0199
Soejima, T., O-0112
Soh, H., PUB-0070
Soh, S., P-0302, P-0477
Soh, S.Y., P-0273, P-0270, P-0261, P-0212
Sokolov, Y., P-0289
Sokova, O., P-0039
Solh, Z., PUB-0177
Soligo, E., P-0219, PUB-0130, PUB-0129
Song, A.Q., PUB-0061, P-0127
Song, E.S., P-0314, P-0183, P-0149
Song, H., P-0496, P-0064

Song, S.H., P-0395
Song, W.S., P-0140
Sonkusare, L., P-0544
Sonmez, C., P-0161
Sonneveld, E., O-0014
Sosa, F., PUB-0222
Soulaymani, A., PUB-0163, PUB-0141
Soulier, J., P-0407
Souzaki, R., PUB-0208, O-0178
Sperl, D., O-0127
Spicer, R., O-0180
Spichak, I., PUB-0032
Spiegler, B., P-0497
Spinelli, C., P-0209, O-0029
Spivakoski, C., P-0219, PUB-0130, PUB-0129
Spreafico, F., O-0079
Squire, R., O-0187
Sredni, S.T., P-0344, P-0343
Sri, k., PUB-0189
Srineevas, V., O-0136, P-0156
Srinivas, M., P-0293, O-0164, O-0193, O-0169
Srinivasan, A., P-0512, PUB-0168
Sripornsawan, P., P-0402
Sripronsawan, P., O-0152
Srirambhatla, J., PUB-0127, PUB-0011
St George, J., P-0357
Stachowicz-Stencel, T., PUB-0252
Stadel, D., P-0024
Stam, R.W., O-0016
Stanek, J., P-0447
Stanulla, M., O-0051
Starkova, J., P-0001
Stary, J., P-0184, P-0241, P-0088, P-0101, O-0016
Stefan, D.C., P-0386
Stefanowicz, J., PUB-0252
Stehlikova, O., P-0446
Stein, J., P-0510
Stein, K., P-0494
Stepan Giljevic, J., P-0275
Stepanova, T.V., O-0078, PUB-0213
Stepensky, P., P-0510
Sterba, J., P-0446
Stevens, M., O-0180, O-0132, O-0006, P-0459
Stewart, C., O-0128
Stewart, R.E., P-0533
Sticz, T.B., P-0338
Stiles, C., O-0069
Stobart, K., O-0098
Stoneham, S., P-0539, P-0364
Stones, D., O-0134
Stoppa Lyonnet, D., P-0407
Storck, S., P-0214
Stovall, M., O-0042
Stratton, K., P-0466
Streneva, O., P-0043, P-0038
Streng, I., O-0102
Stridsberg, M., PUB-0191
Strong, L., P-0466
Strother, D., PUB-0080
Strother, M., O-0020
Sturm, D., O-0130
Su, J., P-0304
Su, Y., P-0072, PUB-0081, P-0056, PUB-0036, P-0383
Subbiah, V., P-0305, P-0445, P-0136, P-0134
Subramaniam, P.G., P-0051
Sudour, H., P-0185, P-0349
Sugito, K., O-0112
Sugitou, K., P-0263
Sugiyama, H., P-0433, P-0432
Suh, J., O-0203
Sukhov, M., P-0260
Sulkers, E., P-0533, O-0147, O-0150
Sultan, I., PUB-0202, PUB-0201, PUB-0156, P-0145, PUB-0111
Sumboonnanonda, A., PUB-0048
Suminoe, A., PUB-0208, O-0178
Sun, B.P., O-0191
Sun, F., P-0250, O-0123, P-0176, P-0420
Sun, F.F., P-0269
Sun, H.Z., PUB-0151
Sun, L., P-0049
Sun, L.r., PUB-0061, PUB-0059, P-0387, PUB-0058
Sun, N., P-0041, PUB-0082
Sun, X., P-0250, O-0123, P-0176, P-0420, P-0053, P-0105, P-0165
Sun, X.F., P-0107, P-0269
Sun, Y., PUB-0059, P-0387, P-0278
Sung, K.W., P-0075, P-0208
Sung, L., P-0481, O-0098, O-0099, O-0107, P-0497, PUB-0080, P-0450
Sung, S., P-0069
Suphakunpinyo, C., PUB-0142
Supiot, S., PUB-0044
Suraci, S., P-0517
Surayuthpreecha, K., P-0499
Suxiang, L., P-0401, P-0400
Suyin, L., P-0105
Suzuki, E., P-0561
Suzuki, K., P-0287
Suzuki, T., P-0328
Svedberg, P., O-0163
Svojgr, K., P-0184, P-0241
Swaidan, M., P-0358
Swansbury, J., O-0013
Sweedan, S., PUB-0185
Syed, R., P-0364
Szafranski, A., P-0300
Szalai, C., P-0004
Szany, E.V., P-0344
Szathmari, A., P-0327
Szczepanski, T., P-0470, P-0469, PUB-0133
Szegedi, I., P-0045
Szolkiewicz, A., PUB-0252
Szumera, M., P-0172

T

T, K., PUB-0127
Tabak, B., O-0069
Tabori, U., O-0067, O-0044, P-0353, P-0325, P-0465
Taborska, K., P-0241
Tacyildiz, N., PUB-0193, P-0159, P-0393, P-0210, P-0139, PUB-0218, PUB-0217
Taga, T., O-0015
Taguchi, T., PUB-0208, O-0178
Taha, H., P-0280, P-0507
Taheri, S., PUB-0007
Tai, M.H., PUB-0022
Taj, M., P-0111
Taj, M., PUB-0211, O-0125
Tajiri, T., O-0060, O-0085, P-0279, O-0112, O-0173, P-0254
Takahashi, H., O-0112
Takayasu, H., P-0220
Takei, Y., P-0540
Takimoto, T., O-0085, P-0279, O-0112
Takita, J., O-0063, O-0018, O-0062, P-0170
Takizawa, D., P-0167
Tal, S., P-0481
Talole, S., P-0125
Taluja, A., O-0204
Tam, P.Y.H., O-0194
Tam, Y., P-0264
Tam, Y.H., PUB-0146, P-0204
Tamburrini, G., PUB-0262
Tamminga, R.Y.J., O-0150
Tan, A.M., P-0060, PUB-0184, P-0261, P-0212
Tan, G.M., O-0174
Tan, H., PUB-0106
Tan, J., O-0090, P-0097
Tan, L., PUB-0010
Tan, L.H., PUB-0030, O-0191
Tan, P., PUB-0224
Tanaka, M., PUB-0209, O-0118
Tanaka, Y., O-0060, PUB-0209, O-0118, P-0279, O-0084, P-0188, P-0230, O-0052
Tandon, N., P-0293
Tang, d., P-0198
Tang, D.X., O-0056
Tang, J., P-0062, P-0049, P-0108, P-0158
Tang, Q., P-0380
Tang, S., P-0130
Tang, W., P-0211
Tang, W.P., P-0552
Tang, X., O-0097
Tang, Y., PUB-0126, P-0422, P-0131, P-0496, P-0062, P-0064
Tani, G., O-0108, PUB-0140
Tanimura, M., P-0449
Tanner, L., O-0156
Tanyeli, A., P-0528, P-0276
Tanyildiz, G., PUB-0193, P-0159, P-0393, P-0210, P-0139, PUB-0218, PUB-0217
Tarasevich, R., PUB-0267, PUB-0226, P-0238
Tarlan, B., P-0315
Tashvighi, M., PUB-0149, P-0373
Tatiana, G., PUB-0074
Taub, J., P-0286
Tawa, A., O-0015
Tawfeq, M., PUB-0112
Tayfun, F., PUB-0261, PUB-0241
Taylor, M., O-0048, P-0351, O-0050, O-0044, O-0129
Tazuke, Y., O-0108, PUB-0140
Te Kronnie, G., O-0051
Te Marvelde, J.G., P-0101
Te Winkel, M., O-0035
Te Winkel, M.L., P-0472
Teckchandani, N., O-0196
Teichmann, D., P-0291
Teixeira, S.A., P-0438
Tekchandani, N., P-0301
Tekgunduz, s., PUB-0214
Tekkesin, F., P-0178, P-0181
Temming, P., O-0040
Terasaka, S., PUB-0122
Terenziani, M., O-0195
Ternes, N., O-0001
Terui, K., O-0013
Terwisscha van Scheltinga, S.E.J., O-0172
Tettamanti, S., O-0106, P-0429, P-0430
Thankamony, P., P-0042
Thavaraj, V., PUB-0239, P-0306
Thebaud, E., O-0027, P-0185, P-0272
Thiesse, P., P-0185, P-0327
Thirugnanasambandam, R.P., P-0513
Thomas, D., O-0025
Thomas, K., P-0488
Thomas, P., O-0083
Thorpe, J., P-0485
Thyagarajan, M., P-0459
Tian, L., P-0394, P-0390
Tian, x., PUB-0135, PUB-0152, PUB-0154
Till, H., O-0186
Timofeeva, N.M., P-0036
Timur, C., P-0047
Tiongco, A., PUB-0043
Tissing, W.J.E., P-0533, O-0147, O-0150
Tissir, R., PUB-0037
Tkachenko, A., PUB-0023
To Thuy, N., PUB-0160
Toh, R., P-0378
Tokimasa, S., P-0531
Tokiwa, K., O-0112
Toledano, H., P-0148
Tomilov, A., P-0043
Tomita, T., P-0344, P-0343
Tomizawa, D., O-0015, O-0013
Tomlinson, D., P-0497
Tomlinson, G., O-0059, P-0455
Tomlinson, G.E., P-0414
Tompol, B., P-0172
Tone, L., P-0354, P-0348, P-0019
Tone, L.G., P-0339, O-0026, P-0340, O-0009, P-0438
Tong, Y., O-0128
Tonini, G.P., O-0086
Topuz, U., P-0515
Toriyama, Y., O-0154
Tornesello, A., PUB-0263
Torres, M., O-0031
Tou, J., PUB-0100
Tragiannidis, A., P-0503
Trajkova Antevska, Z., PUB-0248
Tran, T., O-0098
Trechot, p., PUB-0008
Trehan, A., P-0027, P-0521, P-0532, PUB-0199, PUB-0187, P-0026, P-0501, P-0498
Trevino, L., O-0059

Trippett, T., O-0068
Trippett, T.M., O-0105
Triwatanawong, J., PUB-0048
Trka, J., O-0051, O-0014, P-0001
Trofimov, I., P-0316
Trubnikova, G.V., PUB-0213
Truong, J., P-0355
Truong, T., P-0426
Trzonkowski, P., P-0179
Tsaur, G., P-0039, P-0043, O-0109, P-0038, P-0259
Tsaur, G.A., P-0036
Tseng, C., PUB-0085
Tsuboi, K., P-0167, PUB-0148, PUB-0071
Tsuchida, M., P-0050
Tsuchiya, K., P-0254, O-0137
Tsui, S.B., PUB-0146
Tsvirenko, S., O-0109
Tsyrlina, E.V., PUB-0242
Tu, L., P-0053
Tucci Jr, S., O-0026, O-0009
Tugcu, D., PUB-0190, PUB-0175, PUB-0065
Tumer, T.B., P-0005
Tuncer, M., P-0068
Tuncer, S., P-0311
Tuponogov, S., O-0109, P-0259
Turanyi, E., P-0338
Turazzi, N., P-0429
Turk, K., P-0415
Turkkan, E., P-0047
Turpin, B., P-0447, P-0439, P-0247, P-0248
Tuysuz, G., PUB-0096, PUB-0095, PUB-0019
Tytgat, G., P-0283, O-0003, P-0249
Tzanoudaki, M., PUB-0159
Tzen, K.Y., O-0110

U
Uchida, H., P-0237
Ueda, K., P-0541
Ueda, Y., O-0060, PUB-0136
Uehara, S., O-0112, P-0441, PUB-0070
Uemura, M., O-0178
Ueno, T., PUB-0070
Uesugi, T., P-0220
Uffman, J., O-0190
Ugras, N.S., P-0122
Ugur Dincaslan, H., P-0139
Ullrich, N., P-0350, P-0352
Uludag, D., P-0202
Uluoglu, O., P-0178
Ulusoy, G., P-0005
Umeda, S., O-0108, PUB-0140
Umnova, S., O-0043
Umutoglu, T., P-0515
Unal Cabi, E., P-0393, P-0210
Unal, E., P-0239, PUB-0256, PUB-0255, PUB-0254, PUB-0193, P-0159, P-0139, PUB-0218, PUB-0217
Unal, S., P-0068, P-0098
Uner, A., P-0122
Unuvar, A., PUB-0178, P-0055, P-0033, PUB-0033
Upadhyay, S., P-0032
Uppal, p., PUB-0247
Urban, C., P-0342
Urbanik, A., P-0172
Urbieta, M., PUB-0210, PUB-0197
Urita, Y., P-0220
Úriz, J.J., P-0018
Urla, I.C., O-0181, O-0176
Ushakova, T., PUB-0161, P-0316
Usui, H., P-0230
Usui, N., PUB-0070
Usychkina, A., PUB-0092, P-0260
Uysalol, E., P-0033
Uyttebroeck, A., P-0103

V
V K, S., PUB-0168
Vaidya, S., P-0244
Vaitkeviciene, G., O-0013
Valera, E., P-0354, P-0348
Valera, E.T., P-0340
Valis, K., P-0001
Valsecchi, M., O-0051
Valteau Couanet, D., O-0167
Valteau-Couanet, D., O-0001, O-0096, O-0111, O-0117, O-0091, P-0330, O-0113, P-0166
Valverde, P., O-0021
van Baren, R., O-0172
Van Broeck, N., O-0143
Van Damme, D., PUB-0145
van de Loosdrecht, A.A., P-0101
Van de Velde, V., P-0574, O-0143, O-0158
van de Ven, C., P-0428, O-0120
van de Ven, P., O-0020
van de Wetering, M., P-0493
van de Wetering, M.D., P-0500
Van den Berg, H., O-0094
van den Heuvel-Eibrink, M., P-0495, O-0102, O-0035, P-0464, P-0461, P-0115, O-0013
van den Heuvel-Eibrink, M.M., P-0088, P-0101, P-0472, O-0080, O-0014, O-0079, O-0156, O-0016
van der Burg, M., P-0101
van der Geest, I., P-0495, O-0102
van der Lely, A.J., P-0464, P-0461
van der Pal, H., P-0249
van der Sluis, I., O-0035
Van der Veer, A., O-0051, P-0427, P-0021
van der Velden, V., O-0013
Van der Velden, V.H., P-0427
van der Velden, V.H.J., P-0088, P-0101
van Dongen, J.J.M., P-0088, P-0101
van Dorp, W., P-0461, P-0115
van Eck-Smit, B., O-0003
Van Eyssen, A., PUB-0200
van Galen, J.F., O-0014
van Laar, M., O-0005
van Lier, R., P-0493
Van Neck, A., O-0158
van Noesel, M., O-0132, P-0283, O-0003, P-0249
van Noesel, M.M., O-0172
van Tinteren, H., O-0080, O-0079
van Vuurden, D.G., P-0347
van Waas, M., P-0472
van Wijk, M.P., P-0347
Vandenbussche, J., P-0266
Vandesopele, J., P-0266
Varan, A., P-0239, P-0240, P-0118, P-0114, PUB-0056, P-0216, PUB-0054, P-0126, P-0213, PUB-0016, PUB-0055
Varfolomeeva, S., PUB-0092, P-0260, P-0038
Varlet, P., PUB-0084, P-0330
Varma, D.R., PUB-0249
Varo Rodriguez, A., P-0309, P-0318
Varo, A., PUB-0073
Varrasso, G., P-0517
Varvoutsi, M., PUB-0230
Vassal, G., PUB-0084
Vasta, I., PUB-0263, PUB-0262
Veal, G., P-0281
Veerakul, G., PUB-0034
Veerman, A., O-0035
Vega-Vega, L., P-0151, P-0142
Velasco-Hidalgo, L., P-0023, P-0174
Veldhuijzen van Zanten, S.E., P-0347
Vemuganti, G., O-0028
Ven, V., P-0397
Venkatraman, P., P-0513
Vergin, C., P-0047
Verité, C., O-0027
Verkarre, V., P-0274
Verlooy, J., O-0158
Verma, I.C., PUB-0194, P-0057
Verma, S., P-0519, PUB-0196
Vermeulen, J., PUB-0183
Vermund, S.H., O-0114
Verschuur, A., P-0185
Verzhbitskaya, T., P-0043
Veselska, R., P-0446
Viani, K., O-0148, P-0494
Vianna de Carvalho, R., P-0294
Vicha, A., P-0241
Vicuña, C., PUB-0269, PUB-0265
Viehmann, A., O-0040
Vieth, V., P-0436
Vigicancer, O.b.o., O-0054
Vigneron, C., P-0326
Villafruela Alvarez, C., PUB-0144
Villanueva, E., PUB-0269, PUB-0265
Villegas, M., PUB-0224
Vince, G., P-0336
Vindrola, C., O-0146
Vinks, A.A., P-0417
Virgone, C., O-0195
Vishnubhatla, S., O-0189
Visser, J., P-0461
Visudibhan, A., PUB-0035
Vlahopoulos, S., P-0368, PUB-0159
Vogel, E., P-0546
Volkova, K., PUB-0032
Volochnik, A., P-0039
von Büren, A.O., O-0047
von Essen, L., O-0022, O-0159
von Hoff, K., O-0047
von Hoff, K.v.H., O-0127
von Schweinitz, D., P-0253, O-0052
von Stackelberg, A., O-0105
Vora, T., O-0133, P-0281, P-0252
Vorstermans, l., O-0179
Vossen, M., P-0493
Vossough, P., PUB-0149, P-0373
Vreeman, R., O-0020, P-0397
Vue, N., O-0131
Vujanic, G., O-0079, PUB-0049
Vujanic, G.M., O-0080
Vural, S., P-0240
Vyatkin, I., P-0259

W
Wagner, A., P-0464
Wai, S., P-0524, P-0489
Wakefield, C., PUB-0188, P-0538
Wakefield, C.E., O-0162, P-0471
Wakisaka, M., PUB-0105
Wallace, W., P-0378
Wallace, W.H., P-0475
Wallingford, S., O-0007
Wan, S., PUB-0181
Wan, Z., P-0109, P-0010
Wang, B., P-0002, P-0284, P-0089, P-0262, P-0081
Wang, C., P-0456
Wang, D., P-0444
Wang, G., P-0286
Wang, H., P-0226, P-0297, PUB-0157, P-0082, P-0073, P-0108, P-0082, PUB-0147, O-0192, PUB-0091, P-0262
Wang, H.f., P-0127
Wang, H.M., PUB-0053
Wang, J., P-0250, O-0123, PUB-0100, P-0176, P-0107, O-0119, P-0158, P-0165, P-0269
Wang, J.M., P-0076, P-0381
Wang, L., P-0232, PUB-0046, PUB-0045, O-0124
Wang, L.z., PUB-0059, P-0387, PUB-0058
Wang, N., P-0094, P-0049, P-0278, P-0022
Wang, R., PUB-0079
Wang, S., O-0008, P-0403, PUB-0158, PUB-0091, PUB-0024
Wang, T., P-0046
Wang, W., P-0268
Wang, Y., PUB-0087, P-0557, P-0557
Wang, Y.L., P-0551
Wang, Z., P-0200, PUB-0158, PUB-0145, PUB-0126, P-0422, P-0286
Waragai, T., P-0067
Wari, M.N.U., O-0189
Warmann, S.W., O-0181, O-0176
Warmuth Metz, M., P-0345
Warmuth-Metz, M., O-0047
Watanabe, K., O-0200, O-0060, P-0058, O-0052
Watanabe, S., P-0037
Watanabe, Y., P-0328
Watkins, D., O-0025, O-0025
Watson, J., P-0497
Wattwil, H., O-0205
Wawrzenczyk, A., O-0121
Wechsler Reya, R., O-0049
Weclawek- Tompol, J., P-0172
Wedi, O., P-0186
Wee Sævig, B., P-0565

Weeks, M., P-0197
Wegner, O., O-0121
Wehner, P.S., P-0468, PUB-0015
Wei, C., P-0459
Wei, D., O-0004
Wei, J., P-0024, P-0130, PUB-0104, PUB-0102, PUB-0067, PUB-0045
Weidman, D., P-0351
Weiner, M., P-0529
Weiss, B., P-0447, P-0439, P-0247, P-0248, O-0004
Weiss, B.D., P-0417
Weiss, W., O-0089, O-0071
Weitzman, S., P-0426
Weizman, A., P-0277
Weltman, E., P-0304
Wen, S., PUB-0088
Wen, X., P-0072, PUB-0081, P-0383
Weng, W., PUB-0021
Wenli, Z., P-0401, P-0400
Westermann, F., O-0087
Westmoreland, T., O-0190
Weyl Ben Arush, M., PUB-0258, P-0545
Wharin, P., P-0558
Whelan, J., O-0094, O-0117
Whetton, T., P-0335
White, J.E., O-0114
Whitlock, J., O-0105, O-0103
Wiangnon, S., PUB-0142
Wiegering, V., P-0379
Wieland, R., O-0040
Wijnen, m., O-0179
Wijnen, M.H.W.A., O-0172
Wijnen, R.M.H., O-0172
Wilde, j., O-0179
Wilejto, M., P-0450
Willems, E., P-0574
Willemse, M.E., P-0427
Williams, D., P-0103
Williams, L., O-0073, P-0534
Wilson, B., O-0067
Winick, N., O-0032, O-0103
Winick, N.J., O-0034
Winkler, B., P-0379
Winstanley, M., O-0013
Witt, H., O-0129
Witt, O., P-0342
Witte, D., P-0447
Witte, K.E., P-0063
Wolden, S.L., O-0042
Wolff, J., P-0355, P-0345
Wölfl, M., P-0379, P-0336
Wong Salazar-Abshire, M., O-0151
Wong, H., P-0264
Wong, H.Y., PUB-0146
Wong, K., PUB-0251
Wong, K.F., O-0013
Wong, Y.S., PUB-0146, P-0204, O-0194
Wongchanchailert, M., O-0152, P-0402
Woo, S.Y., P-0389
Wood, B., O-0034
Woode, J., O-0161
Woodgate, R., O-0146
Worawut, C., P-0144
Wos, H., PUB-0176, PUB-0174
Woszczyk, M., P-0172
Wozniak, W., P-0300, O-0168
Wozniak-Rowley, A., P-0526
Wright, J.M., P-0417
Wrobel, G., O-0121
Wu, C., P-0456
Wu, D., P-0094, P-0198
Wu, D.H., O-0056
Wu, J., P-0002, P-0089, P-0081
Wu, J.R., P-0010
Wu, L., PUB-0088
Wu, M., P-0008, P-0046, P-0086
WU, Q., P-0312
Wu, X., O-0129, P-0053
Wu, Y., P-0226, P-0009, P-0130, PUB-0104, PUB-0154
Wu, y.p., PUB-0135, PUB-0152
Wyrebek, R., PUB-0252

X

Xavier Scott, J., P-0512, PUB-0168
Xi, L., PUB-0102, PUB-0067
Xi, Z.j., PUB-0018
Xian, Y., P-0072, PUB-0081, P-0056, PUB-0036, P-0383
Xiang, L., P-0278, O-0010
Xiao, J., P-0072, PUB-0081, P-0056, PUB-0036, P-0383
Xiao, P., P-0094, P-0022
Xiao, X., P-0251, P-0267, P-0456
Xiaojun, Y., PUB-0078
Xiaoli, H., P-0180
Xiaoqin, F., P-0404
Xie, H., PUB-0018
Xie, X.Y., PUB-0030
Xiong, H., P-0078
Xiong, Q., PUB-0100
Xiong, X., PUB-0067, PUB-0047, PUB-0046, PUB-0045
Xirong, L., P-0180
Xu, B.J., PUB-0030, O-0191
Xu, G., P-0082
Xu, h., P-0383
Xu, H.J., PUB-0059
Xu, M., P-0435
Xu, S., O-0056, P-0198
Xu, W., P-0496, P-0064
Xu, X., P-0496
Xu, Y., P-0435
Xu, Z., P-0108
Xue, H., PUB-0047, P-0108, P-0158, P-0049
Xuedong, W., P-0404

Y

Yadav, A., P-0281
Yadav, D., O-0196
Yadav, D.K., P-0301
Yadav, S., P-0413, PUB-0243, P-0519, PUB-0196, PUB-0195
Yadav, S.P., PUB-0257, PUB-0194, P-0057, P-0221, P-0077, P-0029, PUB-0050, P-0384
Yagasaki, H., P-0263
Yagmurlu, A., P-0210
Yagyu, S., P-0254
Yahel, A., P-0554
Yalcin, B., P-0118, P-0114, PUB-0056, P-0216, PUB-0054, P-0126, P-0213, PUB-0055
Yamamoto, T., PUB-0148
Yamani, Y., PUB-0111
Yamashita, A., P-0219, PUB-0130, PUB-0129
Yamashita, T., PUB-0153
Yan, C., P-0105
Yan, J., P-0009
Yan-long, D., P-0104
Yanagisawa, T., P-0328
Yang, C., PUB-0085, PUB-0024
Yang, J., PUB-0058
Yang, l., PUB-0137
Yang, m., PUB-0154, P-0100, PUB-0137
Yang, Q., P-0025
Yang, S., P-0496, P-0064
Yang, W., PUB-0155
Yang, X., P-0109
Yang, Y.L., O-0110
Yanik, G., O-0004
Yaniv, I., P-0510, P-0277, P-0467, P-0148
Yankelevich, M., PUB-0145
Yanofsky, R., O-0098
Yao, W., P-0251
Yao, X., O-0068
Yasmeen, N., PUB-0063
Yasmin, F., P-0031, PUB-0101, P-0388, PUB-0060, P-0085, PUB-0042
Yasui, N., P-0237, P-0462
Yau, J., P-0478
Yau, P., P-0473
Yavuz, G., PUB-0193, P-0159, P-0393, P-0210, P-0139, PUB-0218, PUB-0217
Yaxiang, H., P-0087
Yazici, P., PUB-0219
Ye, L., P-0401, P-0400
Ye, Q., P-0226, P-0108, P-0158
Ye, Q.d., P-0381
Ye, T., P-0053
Yeh, M.L., P-0568
Yekeler, E., PUB-0175
Yeoh, A., P-0060, P-0477
Yesil, s., PUB-0214
Yesilipek, A., PUB-0261
Yetgin, S., P-0068
Yi, S., PUB-0062
Yi, W., P-0401, P-0400
Yihuan, C., P-0401, P-0400
Yildiz, I., PUB-0095
Yildiz, Y., P-0159, P-0139
Yilmaz, E., PUB-0255, PUB-0254
Yilmaz, O., P-0440
Yilmaz, S., P-0054
Yin, C., P-0428, O-0120
Yin, M.z., P-0381
Yip, F., PUB-0237
Yiping, H., P-0087
Yokoi, A., PUB-0153
Yoneda, A., O-0108, O-0112, PUB-0140
Yonekawa, S., P-0287
Yong Cheng, Y., P-0017
Yong-hong, Z., P-0104
Yoo, E.S., P-0389, P-0245
Yoo, J.Y., P-0140
Yoo, K.H., P-0075, P-0208
Yoon, J.H., P-0155
Yoshida, H., P-0441, O-0137
Yoshida, K., O-0063, O-0018, O-0062, P-0170
Yoshida, M., O-0118, PUB-0153
Yoshihara, H., P-0287, P-0037
Yoshimi, A., P-0088
Yoshimura, K., O-0052
You, y., PUB-0154
You, y.l., PUB-0135, PUB-0152
Youkhta, T.V., P-0527, PUB-0234
Yount, S., O-0101
Youssef, A., P-0416, P-0362
Yu, B., P-0442
Yu, C., P-0478
Yu, F., O-0131
YU, G., P-0312
Yu, J., P-0046, P-0072, PUB-0081, P-0056, PUB-0036, P-0383
Yu, J.g., O-0191
YU, J.L., P-0229
Yu, l., PUB-0091
Yu, Y., P-0557, PUB-0137
Yu, Y.S., P-0314
Yuan, L.X., P-0010
Yuan, X., P-0226, P-0049
Yucel, T., P-0213
Yudhasompob, N., P-0402
Yudina, N., P-0341, O-0043
Yuelin, H., P-0404
Yuen, A.N.Y., P-0542
Yuen, H., P-0070, P-0235, P-0329, PUB-0107, P-0116, P-0106, PUB-0029, P-0323, P-0487
Yuen, H.L., P-0060, P-0141, P-0508, P-0372, P-0371, P-0542, P-0074
Yuhki, K., O-0178
Yujin, L., P-0448
Yunes, J., P-0354, P-0348, P-0019
Yunes, J.A., O-0026, O-0009
Yung Wen, P., O-0069
Yunus, R., P-0426
Yunus, S., P-0502

Z

Zaairi, F., PUB-0169
Zacharoulis, S., O-0127
Zaharov, T., P-0468
Zaidman, I., P-0510
Zajecki, W., P-0470
Zakova, M., P-0035
Zaky, I., P-0416, P-0362
Zalacain-Diez, M., P-0133, O-0092
Zalewska- Szewczyk, B., P-0172
Zaliova, M., O-0051
Zanetti, I., P-0163
Zangooei, R., PUB-0149, P-0373
Zapata-Tarres, M., P-0313

Zaychikov, A., P-0259
Zborovskaya, A., PUB-0232
Zecca, M., PUB-0263, P-0088, P-0101
Zekri, W., P-0280
Zelada, O., O-0031, P-0048
Zelcer, S., O-0067, O-0098, PUB-0080
Zeng, p., P-0100
Zeng, q., P-0262
Zeng, X., P-0009
Zerah, M., PUB-0113
Zhai, X., P-0108
Zhang, b., PUB-0154
ZHANG, D., P-0312, P-0485, P-0262
Zhang, F., O-0123, P-0176, P-0107, P-0269, P-0165
Zhang, H., P-0009
Zhang, J., O-0071, PUB-0158, P-0158, PUB-0024
Zhang, J.R., P-0443
Zhang, K., P-0226
Zhang, L., P-0002, P-0437, P-0093, P-0089, P-0081
Zhang, P., P-0073
Zhang, R., P-0046, O-0090
Zhang, R.f., PUB-0018
Zhang, W., PUB-0072
Zhang, X., PUB-0106
Zhang, Y., P-0072, O-0124, P-0232, P-0065
Zhang, Z., P-0006
ZHAO, J., P-0312, P-0082
Zhao, N., P-0496
Zhao, P., P-0443
Zhao, Q., P-0284
Zhao, W., PUB-0001, P-0065, P-0022
Zhao, X., P-0009, PUB-0072
Zhao, Y.x., P-0127
Zhao, Z., P-0278, PUB-0024, PUB-0024
Zheludkova, O., P-0369, PUB-0032
Zhen, P., PUB-0010
Zhen, Z., P-0250, O-0123, P-0176, P-0420, P-0105, P-0165
Zhen, Z.J., P-0107, P-0269
Zheng, H., P-0025, P-0009, PUB-0072
Zheng, L., PUB-0139, P-0099
Zheng, S., P-0251, P-0211
Zheng, Y., P-0456
Zhenghua, J., P-0087
Zhenghua, L., P-0080
Zhengjun, X., P-0391
Zhibao, L., P-0391
Zhiy, P., P-0404
Zhong, H., P-0267
Zhong, X., P-0232, O-0124
Zhou, C., P-0109, P-0262
Zhou, D., PUB-0027
Zhou, L., P-0072, P-0056, PUB-0036
Zhou, M., PUB-0120, P-0108, P-0381, P-0158
Zhou, X., P-0086, P-0097
Zhu, H., PUB-0158
Zhu, J., P-0250, O-0123, P-0176, P-0420, P-0107, P-0269, P-0165
Zhu, K., P-0083
Zhu, X., P-0046, O-0192, P-0096
Zhu, x.j., PUB-0135, PUB-0152
Zhu, Y., P-0079, P-0109, P-0268, P-0014
Zhu, Y.P., P-0010
Zhuang, Y., P-0015, P-0444
Zhukova, N., P-0465
Zhukovskaya, E., PUB-0032
Ziff, O., O-0008
Ziko, O.A.O., P-0319
Zilber, R., P-0536
Zimmermann, M., O-0014, O-0013
Zirngibl, F., P-0024
Zitterbart, K., P-0446
Zolk, O., P-0474
Zöllner, S., P-0201
Zollo, M., P-0266
Zong, Z., P-0401, P-0400
Zou, h., PUB-0135, PUB-0152, PUB-0154
Zou, L., P-0073, O-0090, P-0097
Zou, r., PUB-0154
Zou, X., P-0226
Zubarovskaya, L.S., PUB-0234
Zubieta, M., P-0546
Zubizarreta, P., P-0227, PUB-0207, P-0168, P-0030, P-0061, P-0090
Zuckermann, M., O-0070
Zugmaier, G., O-0105
Zulfikar, B., P-0515, PUB-0180, P-0202
Zuo, y., P-0081
Zupanec, S., P-0497
Zwaan, C.M., P-0088, P-0101, O-0014, O-0105, O-0016, O-0013

Q1: Please check Abstracts missing from P-0443 to P-0447.