801 abstracts were received in March 2010 and were evaluated by the SIOP scientific committee. The accepted abstracts are printed here in order of:

- 174 Oral presentations (O + number), this includes Nurses sessions (N + number), Radiation Oncology Free Paper sessions (RO + number) and all Free Paper sessions (FP + number).
- 26 IPSO Oral presentations (IPSO + number)
- 15 ICCCPPO Oral presentations (ICCCPPO + number)
- 451 Poster presentations (P+ letter discipline + number)
- 71 Publication only (Pub + number)

There are no Symposia lectures, Guest lectures or IPSO Symposia lectures. The IPSO abstracts are all included in the IPSO sessions of the programme.

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- **O001** O004 FP 1 Acute Leukemia 1
- **O005** O006 FP 2 Medulloblastoma
- **O009** O012 FP 3 Late Effects 1
- **O013** O017 FP 4 Ewing’s Sarcoma
- **O018** O023 FP 5 Glioma/Spinal Tumors
- **O024** O029 FP 6 Late Effects 2
- **O030** O035 N 1 Planning Care: Perspectives of Parents, Patients and Professionals
- **O036** O041 FP 7 Osteosarcoma
- **O042** O047 FP 8 New Drugs and Experimental Therapeutics
- **O048** O053 FP 9 Psychosocial 1
- **O054** O059 RO 1 CNS/Ewing’s Sarcoma
- **O060** O065 N 2 International and Multicultural Collaboration in Paediatric Oncology Nursing
- **O066** O071 SIOP SIOP award session
- **O072** O075 N 3 Meeting the Needs of Teenagers and Young People
- **O076** O079 FP 10 Acute Leukemia 2
- **O080** O083 FP 11 CNS Miscellaneous
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- **O088** O091 RO 2 Radiation Miscellaneous
- **O092** O095 N 4 Promoting Safe Care in Cancer Treatments
- **O096** O101 FP 13 Acute Lymphoblastic Leukemia
- **O102** O106 FP 14 Clinical Advances in Neuroblastoma
- **O107** O112 FP 15 Adolescents and Young Adults
- **O113** O118 N 5 Challenges and Collaboration in Care and Aftercare
- **O119** O124 FP 16 Leukemia and Lymphoma
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- **O131** O136 FP 18 Epidemiology
- **O137** O142 FP 19 Clinical Aspects of Renal Tumors
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#### IPSO Oral presentations (IPSO + number)

- **IPSO001** IPSO002 IPSO 1 Renal Tumors
- **IPSO003** IPSO006 IPSO 2 Soft Tissue Tumors
- **IPSO007** IPSO012 IPSO 3 Surgical Techniques & Bone Tumors
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- **IPSO022** IPSO026 IPSO 7 Germinal, Endocrine Tumors and Rare Tumors

#### ICCCPPO Oral presentations (ICCCPPO + number)

- **ICCCPPO001** ICCCPPO015 Parents and Survivors
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43rd CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP) 2011
AUCKLAND, NEW ZEALAND, 28th–30th OCTOBER, 2011
SIOP ABSTRACTS

ORAL ABSTRACTS

O001

COST-EFFECTIVENESS OF CHEMOTHERAPEUTIC TREATMENT OF CHILDHOOD ACUTE LYMPHOBlastic LEUKEMIA: THE INFLUENCE OF NEW MEDICATION AND DIAGNOSTIC TECHNOLOGY

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Purpose: Survival for childhood acute lymphoblastic Leukemia (ALL) has reached 80–90%. Future improvement in treatment success will involve new technologies and medication, adding to limited resources and financial constraints. Therefore a retrospective cost-effectiveness analysis of childhood ALL treatment with chemotherapy only according to the two most recent Dutch Childhood Oncology Group treatment protocols was performed. The most recent protocol ALL10 included more expensive medication (pegasparaginase) as compared to the ALL9 version.

Method: Fifty children from a single center cohort were included. All direct medical costs made during treatment, including those in satellite hospitals, were determined. Costs per life year saved (LYS) were calculated. The incremental cost-effectiveness ratio (ICER) of the latest treatment protocol was determined. LYS were calculated based on national 5-year event free survival.

Results: Mean total costs were €8,821 and €121,000 in ALL9 and ALL10 (p < 0.001), respectively. Hospital admissions (57%) and medication (11–17%) were important drivers of overall costs, and were higher in the ALL10 protocol. Mean LYS were higher for ALL10 (66.6 versus 60.2). Costs per LYS were higher for ALL10 (€1,967) compared to ALL9 (€1,483, p = 0.007) and the ICER for treatment according to the ALL10 protocol was €6,085.

Conclusion: Treatment of childhood ALL with chemotherapy only is well within the accepted range of cost-effectiveness. The use of new technology and more expensive medication in the latest protocol lead to higher costs but also more LYS. In future (ALL) treatment protocols, costs in relation to effects should be taken into account in order to establish more cost-effective disease management without jeopardizing survival and quality of life.

O002

THE VALUE OF MONITORING FOR MRD AT LATE TIMEPOINTS IN PAEDIATRIC ALL TREATMENT

Rosemary Sutton1, Tamara Law1, Nicola C Venn1, Rachael Sh1, Mawar Karsa1, Anita V Bahar1, Anne Mitchell1, Ram Suppiah1, Frank Alvardo1, Heather Tapp1, Michelle Haber1, Murray Norris1, Luciano Dalla Pozza2, Glenn M Marshall3

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Purpose: To confirm the prognostic value of MRD after 12 and 24 months of chemotherapy in ALL patients.

Method: MRD was measured in DNA from remission bone marrow samples by real-time quantitative PCR according to EuroMRD guidelines in a cohort of 400 ANZCHOG Study 8 patients.

Results: MRD negativity and MRD < 1×10-4 at 12 and 24 months post induction were highly prognostic of patient relapse-free survival (Log rank Mantel Cox test P < 0.0001). MRD testing after 12 months of therapy predicted all 8 of the very early bone marrow relapses (defined as occurring before 18 months) and MRD results at 24 months predicted most (7/10) of the early off therapy relapses (24–30 months post diagnosis).

However, MRD testing of bone marrow samples failed to predict isolated extramedullary relapses and missed many late bone marrow relapses (> 30 months post diagnosis and > 6 months after the collection of the last sample tested for MRD). Almost all (95%) of patients who had initially achieved MRD negativity in the bone marrow collected at either 3, 5 months or 12 months post diagnosis.

Conclusion: In contrast to MRD levels during induction which reflect the kinetics of disease clearance, we conclude that the detection of MRD levels (> 1×10-4) at 12 and 24 months represents the molecular detection of relapse which precedes clinical presentation of relapse by up to 6 months. These results in ANZCHOG Study 8, an MRD intervention clinical trial using a BFM protocol, confirm our previous findings on the prognostic value of MRD testing at late time points in both ANZCCSG Study VI (Marshall et al JCO 2003) and ANZCCSG Study VII (Sutton et al BHJ 2009).

O003

ABSOlUTE LYMPHOCYTE COUNTS REFINE MINIMAL RESIDUAL DISEASE-BASED RISK STRATIFICATION IN CHILDHOOD ACUTE LYMPHOBlastic LEUKEMIA

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Purpose: Low absolute lymphocyte counts (ALC) have been found to predict poor outcome in a variety of malignancies including pediatric acute lymphoblastic leukemia (ALL). Risk classification for pediatric ALL now relies heavily on measurement of minimal residual disease (MRD), an expensive test with limited availability in some resource-limited countries. Here we investigate the potential role for using absolute lymphocyte counts to refine risk stratification in settings where minimal residual disease (MRD) is unavailable.

Method: We reviewed 171 cases of pediatric acute lymphoblastic leukemia for ALC during induction, age at diagnosis, cytogenetics, initial white blood cell count (WBC), and MRD status at Day 29 of Induction.

Results: We found ALC at Induction Day 29 to be an independent, clinically significant predictor of relapse-free and overall survival. Patients with Day 29 ALC > 1500 cell/µl had a...
superior 6-year relapse-free survival (80±4% vs. 62±8%, p=0.018) and overall survival (96±2% vs. 74±8%, p=0.001). This retained significance in a multivariate analysis with known prognostic factors including Day 29 MRD and significantly improved MRD-based risk stratification. Importantly, Day 29 ACL alone identified 72% (10/14) of deaths and 52% (16/31) of relapses, compared to Day 29 MRD which identified 58% (7/12) deaths and 41% (11/27) of relapses. Indeed, ACL identified 80% (4/5) of deaths not identified by MRD.

Conclusion: Day 29 ACL, taken from a single complete blood count with differential, constitutes a novel and powerful prognostic factor in pediatric ALL that contributes independent prognostic information. Where MRD is routinely available, ACL can refine MRD-based risk stratification. However, in low income countries where the cost and/or availability of MRD testing makes current MRD-based risk stratification schema irrelevant, Day 29 ACL may contribute significantly to non-MRD risk stratification and allow improved choice of therapy and resource utilization.

**O004**

**ASSESSMENT OF QOL DURING TREATMENT OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: PROSPECTIVE COHORT STUDY OF THE JAPAN ASSOCIATION OF CHILDHOOD LEUKEMIA STUDY GROUP**

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**Purpose:** To compare quality of life (QOL) of the children with acute lymphoblastic Leukemia (ALL) using self-rating questionnaires from their parents’ and 10 years of age or older patients’ viewpoint.

**Method:** We conducted a prospective cohort survey on QOL of the children who were treated with two kinds of JACLS protocols (ALL-97 and ALL-02) from April 1997 to March 2008. Five domains including physical well-being (PWB), emotional well-being (EWB), relationship to medical stuffs (RMS), family well-being (FWB) and parental QOL (PQL) for parents or daily activities (DA) for patients were evaluated each 4 times during treatment.

**Results:** We received 2,152 sheets from the parents and 401 from the patients. Comparison of QOL scores of ALL-97 (n = 898) with those of ALL-02 (n = 1066) by proxy revealed that subtotal scores of PWB, FWB and PQL domain were higher in ALL-97 than in ALL-02. On the other hand the subtotal scores of EWB domain were lower in ALL-97 than in ALL-02. Total scores of standard risk group were always higher in ALL-97 than in ALL-02 during any treatment phases. Multi-linear regression analysis revealed that treatment intensity (risk stratification) and therapy phase were the most significant predictors for total QOL scores than the protocols (ALL-97 or -02) themselves. Comparison of QOL scores of ALL-97 (n = 2151) with those of ALL-02 (n = 167) by patients showed that total scores and subtotal scores of DA, EWB and FWB domain were higher in ALL-02 than in ALL-97. There is good correlation in total scores and subtotal scores of PWB domain but poor correlation in EWB, FWB and RMS domains between the patient-rating and their parent-rating.

**Conclusion:** This study suggested that QOL can be measured by the self-rating and parent-rating questionnaires and that a clinical research on childhood QOL should be conducted multi-dimensionally including the patient’s观点 of possible use.

**O005**

**MOLECULAR SUBTYPES IN MEDULLOBLASTOMA: AN INTERNATIONAL META-ANALYSES FOR TRANSCRIPTOMIC PROFILES, GENETIC ABERRATIONS, CLINICOPATHOLOGICAL FEATURES AND SURVIVAL**

Marc Koel1, Jan Koster2, Marc Remke3, Andrey Korshunov4, Thomas Hieseler5, Hendrik Witt6, Paul A. Northcott7, Sebastian Bender8, Marcel Kool9, Axel Benner10, Marina Ryzhova11, Dominik Sturm12, Hendrik Witt8, Daniel Haag13, Grischa Toedt14, Andre O. von Bueren15, Stefan Rutkowski16, Wolfraam Scheurlen17, Andreas E. Kulitz18, Michael D. Taylor19, Peter Lichter20, Stefan M. Pfister21

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9Hospital for Sick Children, Neurosurgery, Toronto, Canada

**Purpose:** Medulloblastoma is the most common malignant pediatric brain tumor. Remarkable clinical heterogeneity is now comprehensively reflected by recent molecular studies from several groups indicating that medulloblastoma comprises a collection of distinct subtypes. A better understanding of each of these molecular subtypes is urgently warranted to improve treatment strategies and the overall survival of patients and ultimately also the quality of life for those that survive medulloblastoma.

**Method:** We have brought together all the recent molecular studies on medulloblastoma into one database (R2.amc.nl) to perform a meta-analysis on these molecular subtypes in a large series of tumors. Data from six independent series of medulloblastomas (n = 521) were collected and analyzed. All cases were analyzed by expression profiling and most cases were also analyzed for genetic aberrations using SNP or CGH arrays. Other data collected for most cases included histology, gender, age at diagnosis, metastatic stage and survival.

**Results:** Recent profiling studies have shown that medulloblastoma comprises four to six molecular subtypes. The consensus in the field is now that there are four major subtypes of medulloblastoma and each of these major subtypes may be further subdivided into smaller groups based on additional characteristics within these subtypes. Two of the most distinct subtypes are characterized by activated WNT or activated SHH signalling, while the other two subtypes share certain molecular characteristics. The latter show elevated expression of neuronal differentiation and/or photoreceptor genes. Non-WNT/Non-SHH tumors are much more frequent in males than in females and are strongly associated with metastatic disease. A subgroup of these Non-WNT/Non-SHH tumors, showing frequent MYC amplifications, has an extremely poor outcome.

**Conclusion:** The meta-analyses revealed new insights in differences that exist between molecular subtypes. Data of these meta-analyses will be presented and we will give an overview of the core characteristics for each subtype.

**O006**

**FSTL5 ENHANCES PROGNOSTIC SUBCLASSIFICATION OF MEDULLOBLASTOMA**

Marc Remke1, Thomas Hieseler2, Andrey Korshunov3, Paul A. Northcott4, Sebastian Bender5, Marcel Kool6, Axel Benner7, Marina Ryzhova8, Dominik Sturm9, Hendrik Witt10, Daniel Haag11, Grischa Toedt12, Andre O. von Bueren13, Stefan Rutkowski14, Wolfraam Scheurlen15, Andreas E. Kulitz16, Michael D. Taylor17, Peter Lichter18, Stefan M. Pfister19

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17Hospital for Sick Children, Neurosurgery, Toronto, Canada

**Purpose:** Integrated genomic approaches reveal distinct biological variants in medulloblastoma. Comprehensive molecular classification strategies utilize cytogenetic and immunohistochemical biomarkers to improve outcome prediction. Novel complementary markers may ameliorate risk stratification particularly in intermediate or high-risk tumors.

**Method:** Transcriptome and DNA copy-number analyses were carried out and integrated for 64 primary tumors. Bioinformatic tools were applied to investigate marker genes of molecular variants. The prognostic value of differentially expressed transcripts was assessed in the entire screening cohort. Immunohistochemical markers were used to determine molecular subgroups in adult and pediatric medulloblastoma samples. FSTL5

*Pediatr Blood Cancer DOI 10.1002/pbc*
immunopositivity was correlated with molecular and clinical information for 235 non-overlapping medulloblastoma samples on two independent tissue microarrays (TMA).

**Results:** Unsupervised cluster analyses of transcriptome profiles demonstrated four distinct molecular variants: WNT, SHH, Group C, and Group D. Interestingly, Group C medulloblastomas were almost exclusively present in pediatric age groups as determined by immunohistochemistry. Delimited expression patterns of FSTL5 mRNA in each molecular variant were validated by quantitative real-time PCR. High FSTL5 expression levels were observed in Group C and Group D tumors with generally unfavorable outcome, whereas WNT medulloblastomas with excellent prognosis showed marked down-regulation of this marker. Immunopositivity of FSTL5 identified a large proportion of patients (84 of 235 patients; 36%) at high risk for relapse and death in particular in patients with Non-WNT/Non-SHH tumors. Multivariate analysis demonstrated that FSTL5 immunopositivity constituted an independent prognostic marker in pediatric and adult patient cohorts (p < 0.0001). Notably, we could substantially reduce the prediction error of the model by adding this biomarker to comprehensive outcome prediction schemes.

**Conclusion:** Analysis of integrated transcriptional and cytogenetic information unraveled four distinct disease variants. FSTL5 immunoprofile effectively complements existing molecular stratification schemes and substantially enhances prognostic sub-classification of Non-WNT/Non-SHH medulloblastomas. This approach may ultimately define clear prognostic groups to individualize treatment intensities in upcoming clinical trials.

**References:**

1. University Children’s Hospital Würzburg, Ped. Hematology, Oncology, Würzburg, Germany
2. University Children’s Hospital Würzburg, Ped. Hematology, Oncology, Stem Cell Transplantation, Würzburg, Germany
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**Purpose:** Medulloblastoma, a primitive neuro-ectodermal tumour that arises in the posterior fossa, is the most common malignant brain tumour occurring in childhood. Even though 60–70% of children with medulloblastoma will be cured with intensive multimodal therapy, data on the host immunological environment in medulloblastoma patients are rare, notably data on cytokine expression and immune reconstitution in patients with medulloblastoma undergoing high dose chemotherapy and autologous stem cell transplantation (HSCT) are lacking.

**Method:** In this present study, we therefore decided to prospectively assess immune function following 24 consecutive autologous HSCT in 17 children with medulloblastoma treated according to the German-Austrian-Swiss HHT-2000 protocol.

**Results:** Th1 predominance, as assessed by intracellular cytokine staining, was found to be the most important factor for probability of survival. Already before HSCT, survivors showed higher IFNγamma levels in sera as well as higher numbers of IFNγamma positive T-cells. After transplant, this effect was even more pronounced. Patients with higher numbers of IFNγamma and TNFα positive T-cells had a more favourable outcome at all analyzed time points.

**Conclusion:** Taken together, we were able to demonstrate for the first time that high expression of IFNγamma and TNFα in T-cells of medulloblastoma patients in the early post-transplant period correlates with a better prognosis.

**References:**

1. University Children’s Hospital Hospital, Paediatric Haematology/Oncology, Auckland, New Zealand
2. Paediatric Oncology Steering Group and Paediatric Children’s Hospital, Paediatric Haematology/Oncology, Auckland, New Zealand
3. University Children’s Hospital, Paediatric Haematology/Oncology, Auckland, New Zealand
4. Paediatric Oncology Steering Group and Children’s Oncology Centre, Paediatric Haematology/Oncology, Christchurch, New Zealand

**Purpose:** The epidemiological features of paediatric central nervous system (CNS) tumours remain undefined in New Zealand (NZ), where there is a unique Maori and Pacific population makeup. We aim to characterise the incidence and overall survival (OS) of childhood CNS tumours in NZ children, and compare results with historical and international data.

**Method:** We identified children from 0 to 14 years with a primary CNS tumour diagnosis over an 8-year period (2000–2007) using data from the New Zealand Children’s Cancer Registry. Tumours were classified according to the International Classification of Childhood Cancer.

**Results:** A total of 258 children were included for analysis. The mean annual incidence rate of CNS tumours was 3.8/100,000 children/year. Maori comprised 20% of the NZ childhood population but accounted for 40% of all medulloblastoma cases, with an incidence of 1.2/100,000 Maori children/year and relative risk Maori: Non-Maori of 2.7 (95% CI 1.5–5.0, P = 0.001). In medulloblastoma, an anterior OS was observed in Maori (5-year OS 58%) compared to non-Maori (5-year OS 80%). No statistically significant differences in incidence were identified between ethnic groups in any other CNS tumour groups. Five year OS for NZ children with CNS tumours was 73% compared to 49% in a historic cohort.

**Conclusion:** A comprehensive cancer registry has allowed us to confirm the unique and high incidence of medulloblastoma among Maori, a disease previously reported to have no racial disparity. It is not clear whether reduced survival in Maori represent specific biological features of the disease, and/or gaps in access to healthcare, and this requires further investigation.

**References:**

1. St. Jude Children’s Research Hospital, Epidemiology and Cancer Control, Memphis, TN
2. St. Jude Children’s Research Hospital, Epidemiology and Cancer Control, Memphis, TN
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**Purpose:** The purpose of this study was to document the prevalence of balance impairment in survivors of childhood cancer, and evaluate the association between platinum exposure and disordered balance.

**Method:** Adult survivors of childhood cancer with diagnoses that did not include CNS tumours were tested for balance impairment with computerized dynamic posturography. Those with scores <70 (lowest 5th percentile when compared to population normative values) on the sensory orientation test were classified with impaired balance. Those with vestibular sensory analysis ratios <0.58 (also in the lowest 5th percentile) were classified with impaired vestibular processing. Diagnosis and treatment data were abstracted from medical records. Prevalence of impaired balance was compared among survivors who were exposed to platinum (<350 mg/m², >350 mg/m²) to those who were not exposed to platinum in logistic regression models adjusted for age, sex, radiation exposure, and amputation.

**Results:** Among 1416 adult survivors (median age 34, range 19–61 years) 10% years from diagnosis, 49% were male, 12% reported their race as non-white, 34.6% were treated with cranial radiation or radiation that included the ear, and 6.2% were treated with platinum (4.8% had >350 mg/m²) in survivors who were exposed to platinum (<350 mg/m², >350 mg/m²) to those who were not exposed to platinum in logistic regression models adjusted for age, sex, radiation exposure, and amputation. Those with impaired balance. Those with impaired balance were more likely to have disordered balance in 1.8% (95% CI 1.3–1.3) times more likely to have problems with vestibular processing than those not treated with platinum.

**Conclusion:** Disordered balance is a problem for a significant proportion of childhood cancer survivors and is associated with platinum exposure more than 350 mg/m².

**References:**

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3. University Hospital of Aarhus at Skejby, Department of Pediatrics Aarhus, Aarhus N, Denmark

**Purpose:** Adverse long term effects of cancer and cancer therapy during childhood on general and dental health have been reported. This study aimed to examine the association between exposure to chemotherapy for childhood cancer before the age of 8 years, and microdontia and hypodontia of premolars and permanent molars.

**Method:** In The Danish Registry of Childhood Cancer (DBCR) we identified 243 children who met the following inclusion criteria: (1) age less than 8 years at the start of treatment; (2) age at dental examination: 12 to 18 years. Exclusion criteria were: (1) radiotherapy to the head and neck area; (2) the 190 who were eventually included in the study as a control group of 193 children of similar age was also included. Diagnostic material was obtained from the municipal dental clinics, where the children were treated.

**Results:** Microdontia of premolars or permanent molars was found in 88 teeth in 29 (15.3%) of the 190 children, who had been exposed to chemotherapy, while none of the controls had.
microdont premolars or permanent molars (p < 0.001). The younger the child at the time of diagnosis, the more frequent was microdontia. Hypodontia was found of 28 premolars and permanent molars in 14.7% of the exposed children and of 18 premolars and permanent molars in 8.4% of the controls (OR: 1.839; 95% CI: 0.753; 4.492).

Conclusion: The present study confirms the suggestions from previous studies, that chemotherapy, especially in very young children, causes microdontia and hypodontia.

**D011**

**VISUO-MOTOR INTEGRATION AND MOTOR CO-ORDINATION IN SURVIVORS OF CHILDHOOD CANCER**

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Purpose: Visuo-motor integration deficits have consistently been reported in childhood posterior fossa brain tumour patients given the involvement of motor planning regions. More recently, children undergoing treatment for leukaemia have also demonstrated poor gross motor skills, with the suggestion that fine motor development is affected following treatment. While the use of Vincristine can result in peripheral neuropathy, the relationship between the type of motor co-ordination difficulties attributable to this pathology, and the visuo-motor integration deficits displayed on assessment, are unknown. In particular, studies have failed to distinguish between higher-order motor skills such as visuo-motor integration and lower-order motor skills such as fine-motor co-ordination. This study aimed to assess the visuo-motor integration skills of childhood cancer survivors treated with CNS-directed therapies and compare this to motor co-ordination abilities to determine the rate and type of deficits experienced by this population.

Method: One hundred and one survivors of childhood cancer (mean age = 11.12 years; SD = 3.7) and 61 age-appropriate controls (mean age = 10.13 years; SD = 3.5) were assessed using the Beery-Buktenica Test of Visuo-Motor Integration. Ninety-eight of the patients and all the controls also completed the supplemental Motor Co-ordination task.

Results: Survivors displayed significantly poorer visuo-motor integration skills than controls. In the control groups performed equally well on motor co-ordination. Co-varying for Vincristine did not alter the findings, and no significant difference was found between survivors of a brain tumour or blood cancer.

Conclusion: The presence of visuo-motor integration difficulties in the absence of motor co-ordination deficits for survivors of childhood cancer suggests that higher-level integration systems are affected by cancer treatments. Interestingly, a large group of survivors appear to be at risk than previously thought, with children undergoing treatment for blood cancers also displaying difficulties in this area. While the deficits are not severe, they have the potential to impact on academic performance, and, therefore, require monitoring and intervention.

**D012**

**LEAP-IT - A PASSPORT TO HEALTH: AN INTEGRATED LATE EFFECTS ASSESSMENT PROGRAMME AND ELECTRONIC HEALTH PASSPORT FOR LONG TERM FOLLOWUP OF CHILD CANCER SURVIVORS IN NEW ZEALAND**

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Purpose: To develop a single national health record of cancer treatment and late effects for survivors of childhood cancer suggesting that higher-level integration cits for survivors of childhood cancer suggests that higher-level integration systems are affected by cancer treatments. Interestingly, a large group of survivors appear to be at risk than previously thought, with children undergoing treatment for blood cancers also displaying difficulties in this area. While the deficits are not severe, they have the potential to impact on academic performance, and, therefore, require monitoring and intervention.

Method: To address the needs of clinical teams, and young adult patients, we developed an electronic personalized health passport for use in our clinics and as a patient held record of future health care and providing a personalized health care passport for the patient and family.

Results: While the use of Vincristine can result in peripheral neuropathy, the relationship between the type of motor co-ordination difficulties attributable to this pathology, and the visuo-motor integration deficits displayed on assessment, are unknown. In particular, studies have failed to distinguish between higher-order motor skills such as visuo-motor integration and lower-order motor skills such as fine-motor co-ordination. This study aimed to assess the visuo-motor integration skills of childhood cancer survivors treated with CNS-directed therapies and compare this to motor co-ordination abilities to determine the rate and type of deficits experienced by this population.

Conclusion: The presence of visuo-motor integration difficulties in the absence of motor co-ordination deficits for survivors of childhood cancer suggests that higher-level integration systems are affected by cancer treatments. Interestingly, a large group of survivors appear to be at risk than previously thought, with children undergoing treatment for blood cancers also displaying difficulties in this area. While the deficits are not severe, they have the potential to impact on academic performance, and, therefore, require monitoring and intervention.
**Baseline Serum Albumin - An Independent Prognostic Factor in Non-Metastatic Ewing Sarcoma Family of Tumors: A Prospective Study of 343 Patients from India**

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**Purpose:** To analyze the impact of prognostic variables on survival of 343 patients of non-metastatic Ewing Sarcoma Family of Tumors (ESFT).

**Method:** 343 patients were enrolled and analyzed on an IRB (Institutional review board) approved clinical trial of a uniform multigent chemotherapy regime (EFT-2001) in patients of ESFT at Tata Memorial Hospital, India from January 2002–December 2009.

**Results:** Of the 343 patients enrolled, 220(64%) were males 123(36%) females. 171(50%) were aged < 15 yrs. Baseline LDH was elevated (> 500) in 86(22.5%) patients. Albumin was low (< 4 gr/dl) in 82(33.2%) and 30(23.9%) of the 210 patients in whom necrosis post induction was available, 100% necrosis was recorded in 94(44%). At a median follow-up of 28 months, the EFS of the whole group (n = 343) is 62% and OS is 71%. On univariate analysis, the EFS was significantly better for young age < 15 yrs (88% vs 53%, p = 0.006), male gender (61% vs 56%, p = 0.05), patients with albumin > 4 gr/dl (68% vs 43%, p = 0.002), and in patients with 100% necrosis (64% vs 55%, p = 0.029). High LDH was not found to be a significant prognostic marker in our analysis (56/37% vs 52%, p = 0.45). On multivariate analysis, using cox proportional hazards analysis (n = 206), normal S Albumin was the strongest prognostic factor with HR = 0.485(95% CI: 0.262-0.90) followed by 100% necrosis post induction with HR = 0.539(95% CI: 0.284-1.023). Age and sex were not found to be significant prognostic factors on multivariate analysis.

**Conclusion:** S Albumin is a strong and independent prognostic factor in patients of non-metastatic ESFT. Low serum albumin, a highly sensitive indicator of malnutrition, may impact drug delivery and chemotherapy tolerance, since most drugs are albumin bound. Therapeutic decision making should include consideration for this correctable prognostic marker, especially in developing countries. The pharmacokinetic and pharmacodynamic interaction of albumin, chemotherapeutic agents and cancer biology should be investigated further.

**How to Measure Long-Term Outcome of Ewing Sarcoma Treatment**

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**Purpose:** The main focus of tumor treatment is to cure the disease. This challenging struggle has resulted in survival rates of up to 75% in localized Ewing sarcomas. Rising survival rates has led to increasing interest in long-term consequences of intensive multimodal bone tumor treatment. The ongoing cohort study ‘Functional and Clinical Long-Term Outcome of Ewing Sarcoma Treatment’ is aimed at analysing functional outcome and quality-of-life in long-term survivors of Ewing sarcoma with subjective and objective measurement tools.

**Method:** Survivors of Ewing sarcoma diagnosed from 1980–2009 are recruited from phase III trials of the German Society of Pediatric Hematology and Oncology (GPOH). A first cohort of 118 former patients (47.5% female) with the longest follow-up was analyzed. Median follow-up was 22.3 years (range 12.8-28.9). Median age was 37 years (range 20.1-63.2). Outcome measures were a multi-tool questionnaire, i.e., including the Short Form Health Survey (SF-36), the Toronto Extremity Salvage Score (TESS), and a two-week step activity measurement with an accelerometer (SAM) as an objective indicator of daily-life activity.

**Results:** The SF-36 standardized Physical Component Summary (PCS) score was 47.3 (SD = 9.7), and the standardized Mental Component Summary (MCS) score was 50.1 (SD = 10.2). SF-36 norm-based z-values ranging from –0.53 (physical functioning) and –0.11 (general health) to 0.05 (social functioning) and 0.11 (role physical). The TESS score (0–100) ranged from 88.2 (SD = 12.1) for lower extremity tumors to 90.2 (SD = 7.2) for upper extremity tumors. Patients just reached the level of being active with an average number of 1052 steps/day versus (median = 987; SD = 397) and a low intensity with only 10.8 minutes/day exceeding 100 steps/day.

**Conclusion:** Results indicate that former patients in this sub-cohort returned to a normal and active lifestyle with only minor limitations. Further investigations have to identify discriminating factors for the individual degree of recovery after intensive treatment of the disease.

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INTEGRATIVE GENOMICS APPROACH PROVIDES INSIGHT INTO MOLECULAR CHARACTERISTICS OF PEDIATRIC GLIOBLASTOMA

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Purpose: In contrast to their adult counterparts, pediatric glioblastomas are rare tumors. Although glioblastomas in children and adults share similar histological features, they may differ in terms of tumor biology, molecular genetics, and patient survival. Since knowledge of the molecular aberrations in pediatric glioblastomas is sparse, we aimed to elucidate disease-defining molecular lesions by determining alteration profiles at genomic, epigenetic and transcriptional levels.

Methods: Genomics-wide tumor profiles of 55 children were generated by array-CGH, DNA methylation, and transcriptome analyses, and complemented by sequencing analysis of the TP53, IDH1 and IDH2 genes. DNA copy-number aberrations, transcriptomic and epigenetic changes, and sequencing data were integrated and correlated with clinical follow-up information. A validation cohort of 139 uniformly treated pediatric glioblastoma patients is currently being investigated by immunohistochemistry and FISH.

Results: Childhood glioblastomas displayed balanced genomic profiles in 15% of cases. Specific recurrent alterations affected chromosomes 1q, 7, 10p, 16q, 19q and 20. While MYC/ MYCN amplifications constituted the most common high-level amplification (10/52), PDGFRα and EGFR loci were amplified at lower frequencies compared to adults (5/52 and 6/52, respectively). Beyond well-known alterations, such as homozygous CDKN2A deletion (8/51), CDK4B (8/51), and MDM2/4 (3/52) amplifications, low-frequency events targeted well-recognized oncogenes (MET, CCND2, PTEN, and PIK3CA), and novel loci such as NTRK1 and IGFR1. Expression of aberrant genes was found to be consistently altered. Tumors harbored loss-of-function mutations of the TP53 gene in 50% of cases. However, IDH1 mutations were only detected in four adult patients (7%).

Conclusion: Reporting on one of the largest cohorts of pediatric glioblastoma investigated for molecular alterations to date, this study comprehensively delineates frequent genetic and epigenetic features of these rare tumors. The identification of commonly altered signalling pathways will help to characterize molecular biomarkers for improved prognostic assessment and risk-adapted treatment stratification, and may facilitate the development of novel therapeutic strategies.

PEDIATRIC BRAIN TUMORS

THE IMPACT OF EXTENT OF RESECTION ON THE RESULTS OF COPMILEX MANAGEMENT OF MALIGNANT GLIOMAS IN CHILDREN

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Purpose: To determine whether survival is influenced by the extent of resection in newly diagnosed patients with malignant gliomas who were treated with surgery followed by irradiation and chemotherapy.

Methods: We studied retrospectively patient’s data in 3 institutions. Between 1996 and 2010 were treated 85 children with anaplastic astrocytoma (43 y) and glioblastoma multiforme (42 pts). All patients underwent surgical resection (75 pts) or biopsy (10 pts) of the tumor.

Results: In our study there was a statistica significant difference in overall survival (OS) survival between patients with anaplastic astrocytoma (5 - year OS 91, 8 vs. 96, 8 ± 10, 16 P = 0.008) who underwent total and subtotal/partial resection. The 5-year event-free survival (EFS) rates were 74, 1 ± 3, 0% and 36, 8 ± 10, 15%, respectively (P = 0.033). There wasn’t difference in overall and event free survival based on extent of resection in the group of patients with glioblastoma.

Conclusion: Total surgical resection of newly diagnosed anaplastic astrocytoma in children confers a statistically survival advantage when followed by local field irradiation and chemotherapy.

STEREOTACTIC BRACHYTHERAPY WITH 125-IODINE SEEDS (SBT) FOR THE TREATMENT OF INOPERABLE LOW GRADE GLIOMAS IN CHILDREN

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Purpose: Resection is widely considered as the gold standard for the treatment of Low Grade Gliomas (LGG) WHO Grade I and II in childhood. However, approximately half of these patients are inoperable due to tumour localisation in highly eloquent brain areas. Scarce reports have suggested stereotactic brachytherapy (SBT) with implantation of 125Iodine seeds as a safe and effective local treatment alternative. This single-centre study reports the long-term outcome after SBT in one of the largest reported series.

Methods: All paediatric patients treated in our institution with SBT (125Iodine seeds, permanent implantation, surface dose 50-65 Gy) for LGG WHO Grade I & II with a follow-up > 6 months were included. Clinical and radiological outcome, time to progression and overall survival were retrospectively evaluated. Prognostic factors (age, gender, Karnofsky Performance Status (KPS), tumor volume, histology) for survival and disease progression were investigated.

Results: Between 1992 and 2009, 147 patients underwent SBT. There was no procedure related mortality. The 30-day morbidity was transient and low (5.4%). The median follow-up was 67 months. The survival rates at 5 and 10 years were 93%, and 82%, respectively. No difference between WHO grade I and II was found. 21/147 patients (14, 3%) presented with tumor relapse; 11 died from malignant tumor transformation after multimodal treatment. The remaining 126 patients achieved complete response in 27.8%, partial response in 34.9% and stable disease 33.3%. Neurological status improved in 57.8% or remained stable in 23.0%. The variables age, gender, KPS and histology had no significant impact on the endpoints of the study. Only tumor volume >15 ml was significantly associated with a higher rate of tumor recurrence (p < 0.05).

Conclusion: We demonstrate that SBT represents a safe, minimal invasive and highly effective local treatment option for patients with inoperable LGG WHO grade I & II.

PSEUDOPROGRESSION IN PEDIATRIC BRAIN TUMORS

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Purpose: Pseudoprogression is well described in adults with high grade brain tumors, but it has not been well documented in children. We therefore sought to determine if pseudoprogression occurs in children and whether it is associated with particular tumor types and therapeutic modalities.

Methods: Between 2000-2009, we identified 181 consecutive children <21 years of age at our center who were treated for brain tumors and had at least 3 MRI scans within a year of completing therapy. Pseudoprogression was defined as MRI abnormalities characterized by increase in size, enhancement, or edema within 12 months following therapy, and stabilization or improvement on subsequent imaging.

Results: One hundred and forty one patients with brain tumors were evaluable. Fifty-six (40%) had imaging abnormalities initially suggestive of disease progression; of these, 34 (24%) had true disease progression. The remaining 22 (16%) had pseudoprogression based on either stability (n = 10), decrease in enhancement, edema, or size (n = 10), or disappearance (n = 2) of these abnormalities. Pseudoprogression occurred in patients with low grade (n = 20) and high grade lesions (n = 2). The median time to pseudoprogression was 2.4 months (range, 0.7–8.3 months). The median time to stability, decrease, or disappearance of pseudoprogression was 4 months (range 1.4–7.7 months). Five patients were clinically...
symptomatic from pseudoprogression and were treated with steroids (n = 5), cyst drainage (n = 1), and/or surgery (n = 2).

Conclusion: Pseudoprogression occurs in children treated for brain tumors with similar frequency to adults. It can occur after any therapeutic approach, and in patients with low as well as high grade tumors.

O022

RISK FACTORS IN PEDIATRIC SPINAL HIGH GRADE GLIOMA

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Purpose: Glioma located in the spine might differ biologically from those located in the cerebrum. We aimed to analyze risk factors.

Method: Between 1991 and 2010 the HIT-GBM group collected data from pediatric high grade glioma. The following eligibility criteria were applied: Astrocytic histology, WHO Grade III or IV, age at diagnosis < 18 years, and spinal cord tumor location.

Results: Spinal high grade glioma had been documented in 28 patients (mean age 11.1 years, 14 male). The tumor sizes were measured in numbers of verteabrae and varied greatly (range: 1 to 19, median: 4). The histology was classified as WHO grade III in 15 and grade IV in 13 tumors. Four very large tumors were grade III. Surgery was classified as complete resection (n = 6), subtotal resection (n = 6), partial resection (n = 12) or biopsy only (n = 3). Two patients received chemotherapy, 22 chemo plus radiation. With the mean follow up time of 3.0 years, 14 patients were still alive with a median overall survival of 2.5 years (SE: ± 1.6). The positive prognostic indicators for OS were: age younger than 5 years (p = 0.047), WHO grade III (p = 0.056), and Gross total resection was of (Log Rank test p = 0.013).

Conclusion: The survival of spinal high grade glioma is better than expected Gross total resection is of benefit. Larger data sets and meta-analysis are necessary to identify patient sub-groups.

O023

SPINAL TUMORS IN CHILDREN: 50 YEARS OF EXPERIENCE AT MDANDERSON CANCER CENTER

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Purpose: Spinal tumors are rare in children, and little is known about their epidemiology.

Method: A retrospective chart review, approved by the institutional review board, was conducted to describe the epidemiology of spinal cord tumors in patients under the age of 21 years treated at MD Anderson Cancer Center from January 1958 to September 2008. Eligibility criteria included histopathological and radiological confirmation.

Results: Among 1840 central nervous tumors, only 86 (4.7%) were located in the spine. The median age was 10.7 years, 43 were male. Tumor locations were reported in spinal cord and membrane (n = 26, 30.23%), in spinal cord only (n = 50, 58.13%), caudaequina (n = 9, 10.46%), and spinal meninges only (n = 1). The most frequent histological diagnoses were ependymal tumors 22.1%, followed by low grade astrocytoma (19.8%), other low grade tumors (17.4%), high grade glioma (16.3%), PNET (7%), other high grade tumors (9.3%), and unknown (8.1%). Complete outcome data were reported in 53 patients: The median overall survival was 14.6 years. Surgery was performed in (87%, surgery and radiation in (42.6%), radiation and chemotherapy in (5.5%), only radiation and only chemotherapy in (3.7%) and 13% had no treatment. Complete resection of the tumor was possible in 38.3%. The overall survival rate after complete resection, and partial resection was 83.3%, and 72.4%, respectively. Histology had the largest impact on survival. Long term survival differed by location: cervical – 14.3%, thoracical - 16.7%, lumbar - 23.1%, cervical-thoracical 20%, thoraco-lumbar-60%, and lumbosacral – 100%.

Conclusion: Histology has the largest impact on survival. Survival was lower in cervical tumors.

O024

SECONDARY COLORECTAL CARCINOMA IN SURVIVORS OF CHILDHOOD CANCER

Pediatr Blood Cancer DOI 10.1002/pbc

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Purpose: Colorectal carcinoma is described as a subsequent malignant neoplasm though little is known about risk factors for its development. We aimed to quantify the long-term risk of secondary colorectal carcinomas (s-CRC) and identify treatment-associated risk factors.

Method: In this nested case-control study, 19 cases of adenocarcinoma of the colon or rectum were identified from 4,839 survivors treated at St. Jude Children’s Research Hospital (SJCRH). Controls were selected among 13,064 SJCRH oncology patients. Control group 1 (n = 148) was matched for age at diagnosis of primary malignancy and follow-up interval. Control group 2 (n = 72) was matched on primary diagnosis in addition to group 1 criteria.

Conclusion: Exposure to alkylators and radiation are independently associated with s-CRC. The risk is associated with dose and volume of radiation. Follow-up surveillance for s-CRC should be initiated at a young age among survivors receiving high risk exposures.

O025

LONGITUDINAL CHANGES IN HEALTH STATUS OF THE CHILDHOOD CANCER SURVIVOR COHORT

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Purpose: To evaluate health status as a function of age among childhood cancer survivors and compare the trajectory of change in health status of survivors to that of siblings.

Method: Adult survivors of childhood cancer and siblings in the Childhood Cancer Survivor Study completed health surveys in 1995, 2003 and 2007. Participants were classified as having poor outcomes in general and health, mental health, functional status, or daily activities, if they indicated moderate to extreme impairment in any domain. Generalized estimating equations were used to compute marginal models comparing survivors to siblings for each outcome as a function of age, and to identify host and treatment related factors associated with age related worsening health status.

Results: Among 9711 survivors, 53.3% were male and 87.1% Caucasian. Among 3206 siblings, 47.4% were male and 88.3% Caucasian. In models adjusted for race, age and sex, survivors were more likely to report poor general health (13.2% vs. 5.9%, p < 0.001), poor mental health (17.6% vs. 10.8%, p < 0.001), functional impairments (16.8% vs. 4.0%, p < 0.001) and daily activity limitations (13.9% vs. 6.3%, p < 0.001). Age was a significant predictor of poor health status. There was a survivor by age interaction (as the percentage of survivors with more than 3 poor health status outcomes increased by 5.4% from youngest to oldest age group compared to a 1.5% increase among siblings (p < 0.001). In adjusted models limited to survivors only, exposure to alkylating agents, cranial or chest radiation, surgery involving the brain or bladder, and lower extremity amputation were associated with poor general health, functional impairments and activity limitations.

Conclusion: Childhood cancer survivors have an inferior health status compared to a sibling control group. Health status declines more rapidly with age among survivors than among siblings, and is related to treatment exposure.
10

O026

DO SURVIVORS OF CHILDHOOD CANCER HAVE AN INCREASED RISK OF DIABETES MELLITUS? A REPORT FROM THE ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS) STUDY

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Purpose: Using the unique resources in the Nordic countries to conduct epidemiological research, we investigated whether survivors of childhood cancer had an increased risk of diabetes mellitus compared with the general population in a large population-based setting.

Method: From the Danish and Swedish cancer registries, we identified 21,244 patients who were diagnosed with cancer at age <20 years from 1943 in Denmark and 1958 in Sweden to 2010. A population comparison group of 123,925 individuals was randomly selected from the central population registries in the two countries, matched on sex, age and county of residence. Study subjects diagnosed with diabetes mellitus were identified in the national hospital registries in Denmark and Sweden which includes all discharge diagnoses from hospitals since 1977 in Denmark and 1987 in Sweden. Cox proportional hazards models were used to estimate the relative risk of diabetes in childhood cancer survivors in comparison with population comparisons.

Results: Childhood cancer survivors had a 60% significantly increased risk of diabetes compared with population comparison subjects (hazard ratio, HR = 1.64, 95% CI 1.46–1.83; median follow-up time: 20.6 years). The younger the patient was at cancer diagnosis, the higher the risk of developing diabetes. Preliminary results indicated that the relative risk of diabetes was highest in the first years after cancer diagnosis and diminished with time since diagnosis, i.e., the HR was 2.15 (95% CI 1.62–2.85) 1–5 years after diagnosis, 1.60 (CI, 1.31–1.94) after 5–15 years, 1.63 (CI, 1.40–1.91) after 15–30 years, and 1.10 (CI 0.69–1.74) after 30 years, respectively. Further details will be given.

Conclusion: An elevated risk of developing diabetes adds significantly to the burden of late complications seen in survivors of childhood cancer. This knowledge is important both for the planning of future treatment protocols minimizing late complications and for optimal patient counseling and follow-up care.

O027

USE OF INHIBIN B AND FOLLICLE STIMULATING HORMONE (FSH) AS MARKERS OF AZOOSPERMIA: A REPORT FROM THE 7TH LESTIMATE HOOD CORET (SILIFE)

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Purpose: To determine the sensitivity, specificity, true positive and false positive values for inhibin B and FSH as markers of azoospermia.

Method: Semen analyses, serum inhibin B and FSH were obtained on 280 participants in SILIFE who were treated with alkylating agents, direct gonadal or hypothalamic/pituitary irradiation, had not undergone bilateral orchiectomy and were not receiving androgen supplementation. Inhibin B was categorized as undetectable (< 30 ng/ml) or detectable (≥ 30 ng/ml). FSH was categorized as normal (≤ 9.2 mIU/ml) or increased (> 9.2 mIU/ml).

Results: 95 had azoospermia, 80 had oligospermia and 105 had a normal sperm count. 166 had an inhibin B level < 30 ng/ml. The correlation between inhibin B level and sperm concentration among the 85 participants with an inhibin B level > 30 ng/ml was 0.411 (p < 0.0001). The sensitivity of inhibin B for detecting azoospermia was 98.8%. The specificity was 50.3%. The true positive rate was 50.0%. The false positive rate was 50.0%. The sensitivity of FSH for detecting azoospermia was 80.0%. The specificity was 62.3%. The true positive rate was 52.4%. The false positive rate was 48.0%.

Conclusion: The serum level of inhibin B is correlated with sperm concentration. Although inhibin B is a sensitive marker, it is not a specific marker for azoospermia. FSH is less sensitive than inhibin B for identification of individuals with azoospermia. Neither is useful for screening for azoospermia due to the high false positive rates.

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A COMPUTERIZED SYMPTOM ASSESSMENT TOOL: PERSPECTIVES OF CHILDREN AND THEIR PARENTS

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AEDUCATION GIVEN TO PARENTS OF CHILDREN NEWLY DIAGNOSED WITH ACUTE LYMPHOBLASTIC LEUKAEMIA: THE PARENT’S PERSPECTIVE

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Purpose: Over the last thirty years, diagnosis and treatment of childhood cancers has developed significantly due to medical research and advancements in technology. Increasingly parents are taking on the role of providing ‘nursing’ care for their children including managing emergency situations as well as everyday treatment needs.

Method: This study evaluated parent’s perceptions of the current education practices used within children’s haematology and oncology, particularly focusing on parents of children with Acute Lymphoblastic Leukaemia (ALL). In this Grounded Theory study, twelve parents were interviewed using a semi-structured format. Parents were recruited from one tertiary paediatric haematology and oncology setting in New Zealand. Analysis of data was carried out using a model of constant comparative analysis.

Results: Although parents expressed a variety of views in this study, overall they were generally satisfied with the education they received. They identified that the overwhelming nature of having a child diagnosed with cancer affected their experience of the education process. They also identified areas where education could be improved, including using less medical jargon in written information, allowing more time with health professionals and providing an up-to-date and reliable list of Internet websites.

Conclusion: Given the importance of parent education in this setting, this study has the potential to have a significant impact upon clinical practice. The data gathered will aid health professionals in better understanding the family perspective enabling them to provide appropriate and informative education to families. Findings can also be applied to other Children’s Haematology and Oncology units and other paediatric areas both locally and on an international scale.

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parents of these children experience significant stress and are frequently overwhelmed as they provide both physical and emotional care at home. Current methods of support include home care, written information, clinic visits and ongoing phone communication with clinicians. Traditional support groups are not often utilized since parents are reluctant to leave their children and may need to travel great distances to attend meetings. The purpose of this investigation is to evaluate the effectiveness of parent telephone support groups (TSG) to address the educational and emotional needs of parents following their children’s hospital discharge. During the development phase of the TSG, 24 parents were asked to join one of three eight-week sessions. Based on the overwhelming positive response by both parents and the health care team, a research study is currently in progress to formally evaluate the effectiveness of the TSG.

Method: Each session is co-facilitated by the transplant clinical nurse specialist and social worker with occasional guest presentations. A maximum of eight parents participate in the weekly TSG over a two-month period. The weekly one-hour session is audio-recorded and analyzed for content and themes. Parents are asked to journal about care giving issues and complete a post TSG evaluation.

Results: A wide range of topics are discussed, such as: isolation, medication administration/ adherence, nutrition, interpreting tests/labs, adjusting to life at home, self-care and caregiver challenges. Recurrent topics related to care giving have focused on ongoing fear (relapse, complications), isolation, overwhelming stress, fatigue and sleep deprivation.

Conclusion: It is critical to address the ongoing educational and emotional needs of parental caregivers during this difficult period post transplant. The results of this study may lead to improved care of the child with cancer and better parental support.

O035

CANCER PREVENTION EDUCATION FOR THE HEALTHY CHILD

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Purpose: In the field of cancer research and treatment, it is rare to know exactly what causes a particular cancer and how to treat it. It is also a rare and novel approach for pediatric oncology programs to offer healthy child screening and education related to cancer prevention. Committed to educating and treating the child with cancer, our team is also addressing a particular cancer and how to treat it. It is also a rare and novel approach for pediatric caregivers during this difficult period post transplant. The results of this study may lead to improved care of the child with cancer and better parental support.

Method: More than 5 million children alive today in the United States will die prematurely from smoking-related illnesses. Nearly every adult who smokes took their first puff at or before the age of 18 years, unless children make the decision not to smoke, they are at risk of dying from smoking-related disease (National Center for Tobacco-Free Kids, 2010). Research shows a link between sunburns in children and an increase risk of skin cancer and the known cause in 99% of cervical cancer cases is Human Papilloma Virus and that with protection and early detection, prevention is possible (American Cancer Society, 2010).

Results: Establishing a program that includes prevention learning modules involved an assessment of literacy, learning styles, knowledge base and cultural concerns of the middle school student. Design includes a comprehensive, evidenced-based curriculum, with validated tools to measure effectiveness of prevention programs.

Conclusion: Collaboration with Harvard School of Public Health to study the impact this program has on behavior, prevention and outcomes is in progress.

O036

FEASIBILITY AND DOSE DISCOVERY ANALYSIS OF ZOLEDRONIC ACID WITH CONCURRENT CHEMOTHERAPY IN THE TREATMENT OF NEWLY DIAGNOSED METASTATIC OSTEOSARCOMA: A REPORT FROM THE CHILDREN’S ONCOLOGY GROUP

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Purpose: Patients with metastatic osteosarcoma (OS) have a poor outcome with conventional therapies. Zoledronic acid (ZA) is a third-generation bisphosphonate that reduces skeletal-related events in many adult cancers and has encouraging preclinical data suggesting a possible benefit in OS. The purpose of this clinical trial was to assess the MTD and feasibility of ZA when combined with conventional chemotherapy in patients with metastatic OS.

Method: Patients with a histologic diagnosis of OS were eligible if they were <40 years of age, had metastatic disease, and met standard organ function requirements. Patients received a backbone of conventional chemotherapy that included cisplatin, doxorubicin, methotrexate, ifosfamide and etoposide. ZA dose was given concurrent with all non-methotrexate chemotherapy courses (total 8 doses over 36 weeks). There were 3 dose levels of ZA: 1.2 mg/m² (max 2 mg), 2.3 mg/m² (max 4 mg) and 3.5 mg/m² (max 6 mg). The MTD was determined during induction (Week 1–12). Six patients were treated at each dose level with an additional 6 patients treated at the MTD to help assess post-induction feasibility (Week 13–36).

Results: Twenty-four patients (median age 13.5 years (range, 7–22); 16 females) were treated. One of the 6 patients treated at 1.2 mg/m² had DLT, 1 of 6 patients at 2.3 mg/m² had DLT and 3 of 6 patients at 3.5 mg/m² had DLT. DLTS attributed to ZA included hypophosphatemia (n=3), hypokalemia, hyponatremia, mucositis, limb pain and limb edema (3 patients with multiple DLTS). There were no unexpected grade 4 non-hematologic toxicities or reports of osteonecrosis of the jaw. The MTD was defined as 2.3 mg/m². Feasibility data from the expansion cohort of 6 patients is pending.

Conclusion: ZA can be combined safely with conventional chemotherapy for patients with metastatic osteosarcoma. The MTD of ZA when combined with a conventional osteosarcoma chemotherapy regimen is 2.3 mg/m² (max 4 mg).

O037

HIGH-GRADE OSTEOSARCOMA OF THE MOBILE SPINE

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Purpose: This analysis explored the clinical features of high-grade osteosarcomas of the mobile spine (without sacrum) and the outcome after multimodal therapy.

Method: The Cooperative Osteosarcoma Study Group database was searched for eligible patients. Since 1977, twenty patients had a confirmed diagnosis of primary high-grade osteosarcoma of the mobile spine and their patient-, tumor- and treatment-related variables and outcome were reviewed in this retrospective analysis.

Results: Median age was 29 years (range 5–58), nine were male, eleven female. All patients presented pain as a symptom, nine also a motoric and a sensibility dysfunction. Tumor involved cervical (1), cervico-thoracic (1), thoracic (9) and lumbar (9) spine. Osteoblastic (10) and telangiectatic (4) osteosarcoma were the most frequent subtypes. Three patients had metastatic disease at diagnosis. Every patient received surgery and chemotherapy thirteen were also irradiated. Eight patients failed to achieve a macroscopically complete surgical remission (5 local, 1 primary metastasis, 2 both), 6 died, 2 are alive, both with radiotherapy. Local macroscopic resection was achieved in thirteen individuals (one with residual primary metastases). Three of 12 patients whose tumors were completely resected recurred (2 local, 1 bone metastases), and died. Median follow-up of the 11 survivors was 7.2 years (range 1.8–22.3). Five-year overall and event-free survival rates were 56% and 39%. Local and systemic complete remission, nonmetastatic disease and age younger than 40 years predicted for better overall and event-free survival (log rank p < 0.05).

Conclusion: Osteosarcomas of the mobile spine are rare. With complete resection and chemotherapy (and potentially radiotherapy), prognosis may be comparable to that of osteosarcomas of the extremities.

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O038

BORTEZOMIB ACTIVATES UNFOLDED PROTEIN RESPONSE AND KILLS OSTEOSARCOMA CELL LINES SYNERGISTICALLY WITH CISPLATIN

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Purpose: Bortezomib is a potent and specific inhibitor of the 26S proteasome that induces skeletal-related events in many adult cancers and has encouraging preclinical data suggesting a possible benefit in OS. The purpose of this clinical trial was to assess the MTD and feasibility of ZA when combined with conventional chemotherapy in patients with metastatic OS.

Method: Patients with a histologic diagnosis of OS were eligible if they were <40 years of age, had metastatic disease, and met standard organ function requirements. Patients received a backbone of conventional chemotherapy that included cisplatin, doxorubicin, methotrexate, ifosfamide and etoposide. ZA dose was given concurrent with all non-methotrexate chemotherapy courses (total 8 doses over 36 weeks). There were 3 dose levels of ZA: 1.2 mg/m² (max 2 mg), 2.3 mg/m² (max 4 mg) and 3.5 mg/m² (max 6 mg). The MTD was determined during induction (Week 1–12). Six patients were treated at each dose level with an additional 6 patients treated at the MTD to help assess post-induction feasibility (Week 13–36).

Results: Twenty-four patients (median age 13.5 years (range, 7–22); 16 females) were treated. One of the 6 patients treated at 1.2 mg/m² had DLT, 1 of 6 patients at 2.3 mg/m² had DLT and 3 of 6 patients at 3.5 mg/m² had DLT. DLTS attributed to ZA included hypophosphatemia (n=3), hypokalemia, hyponatremia, mucositis, limb pain and limb edema (3 patients with multiple DLTS). There were no unexpected grade 4 non-hematologic toxicities or reports of osteonecrosis of the jaw. The MTD was defined as 2.3 mg/m². Feasibility data from the expansion cohort of 6 patients is pending.

Conclusion: ZA can be combined safely with conventional chemotherapy for patients with metastatic osteosarcoma. The MTD of ZA when combined with a conventional osteosarcoma chemotherapy regimen is 2.3 mg/m² (max 4 mg).

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unfolded protein response (UPR). While it has been used in several adult cancers, the data on osteosarcoma are sparse.

**Method:** We examined bortezomib-induced cell death and its underlying mechanism in four osteosarcoma cell lines.

**Results:** We found that bortezomib inhibits growth in all 4 osteosarcoma cell lines examined at a very low concentration. Interestingly, cisplatin-resistant U2OS cells were more sensitive than the other three cell lines. Suggesting that bortezomib could be a potent agent against refractory osteosarcoma. On the other hand, normal human epidermal keratinocytes were very resistant to bortezomib. Furthermore, combining cisplatin with a very low concentration of bortezomib significantly increased the cytotoxicity compared to either single agent alone. In parallel with the cell growth inhibition, immunoanalysis revealed an increase in the cleaved (active) form of PARP and FACS analysis demonstrated positive annexin V surface staining following bortezomib treatment, indicating that bortezomib-induced osteosarcoma cell growth arrest is the result of apoptosis. Furthermore, significantly increased protein expression of the UPR-related proteins ATF-4, GADD34 and BIP were observed following bortezomib treatment prior to the cell death, supporting our previous finding that bortezomib can exacerbate the adaptive arm of the UPR and induce apoptosis. On the other hand, striking protection against bortezomib/Vindeliciduced death was observed in murine fibroblasts derived from animals that were null for Ad-4, Chop, and Ire-1N, supporting the notion that increased ER stress is necessary for bortezomib-induced cytotoxicity. Finally, immunoblot analysis with phospho-specific antibodies demonstrated that the JNK, p38 and ERK signaling pathways were activated in osteosarcoma cells following treatment with bortezomib.

**Conclusion:** Considered together, these results suggest that bortezomib could be a valuable agent in the treatment of osteosarcoma.

**O039**

**METHOTREXATE-RELATED NEUROTOXICITY IN THE TREATMENT OF OSTEOSARCOMA: LONG TERM OUTCOME**

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**Purpose:** To investigate long term outcome of patients experiencing methotrexate (MTX) leukoencephalopathy during the treatment of osteosarcoma.

**Method:** We studied clinical and radiological characteristics of patients treated for osteosarcoma, at the Pediatric and Adolescent Oncology Department of Institute Gustave Roussy between 1986–2010, and who developed MTX induced-leukoencephalopathy characterised by typical clinical and radiological features (periventricular high signal intensity on FLAIR and T2 weighted MRI sequences).

**Results:** A leukoencephalopathy was diagnosed in 16 out of 274 patients (5.8%) treated during this period. All patients presented headache which was the unique symptom in 7 patients (43.7%). The severity of neurological symptoms was variable, combining confusion and cognitive symptoms. Initial acute symptoms disappeared in all patients, allowing good scholar and socio-professional insertion. The neurocognitive evaluation performed in 8 patients, several months or years after the initial acute symptoms, did not show significant abnormalities. Persistent abnormal MRI images were present in 5 out of 6 evaluated patients, more than 18 months after the acute initial symptoms.

**Conclusion:** MTX-related leukoencephalopathy is a rare complication with usually favourable clinical outcome but without radiological normalisation. Headaches are constant and might be considered as a warning symptom. Different treatment according to the hypotheses on the physiopathological characteristics might be considered to prevent this toxicity.

**O040**

**EPIGENETIC REGULATION OF STEMINNESS AND MALIGNANCY IN EWING TUMORS**

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**Purpose:** Although microRNAs (miRNAs) were shown to be involved in cancer progression of many tumor entities, very little is known about their participation in Ewing Tumor (ET) pathogenesis. ET are characterized by oncogenic ews/enl translocations with EWS-FLI1 being the most prominent aberrant transcription factor. We previously observed the histone deacetylase inhibitors Ezh1, Drosophila, Homolog 2 (EZH2) to be regulated by EWS-FLI1 and highly increased in ET.

**Results:** We demonstrate that EZH2 mediates silencing of miRNA expression via histone modification as well as DNA methylation and that these miRNAs are reactivated upon EZH2 knock down or treatment with histone deacetylase and DNMT inhibitors. In addition, we show that the well known oncogenic miRNA-221 is highly expressed in ET and processed in the presence of Argonaut (AGO) 2. Moreover, knock down of AGO1 and 2, which are key players in miRNA processing and non-coding RNA-induced gene regulation, influenced the expression of stem cell and differentiation genes. While AGO2 suppressed ET cells exhibited less contact-independent and invasive growth in vitro as well as reduced metastatic potential and delayed local tumor growth in immunodeﬁcient mice, AGO1 knock down resulted in opposite phenotypic changes and was associated with increased expression of the stem cell markers NGFR, ABCG2 and PROM1. Taken together, we demonstrate the pivotal role of EZH2 in ET pathogenesis and critical involvement of Argonaute proteins and non-coding RNAs for maintaining the highly malignant and reversible stemness phenotype.

**Conclusion:** These results open the avenue for new therapeutic modalities, i.e. the implementation of epigenetic drugs or miRNA therapeutics, speciﬁcally targeting oncogenic miRNAs or proteins, such as miRNA-221 or EZH2.

**O041**

**TRIAL FOR OPTIMAL SURVEILLANCE IN SARCOMA**

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**Purpose:** Modern multidisciplinary therapy has improved patient survival; hence follow-up surveillance strategies are becoming increasingly important with significant clinical and fiscal implications. However, the ideal postoperative protocol vis a vis frequency and appropriate screening modalities for bone and soft tissue sarcomas (BSTS) remains ill-defined. A prospective randomized controlled trial to evaluate the impact on overall survival of an intensive follow-up protocol (as practiced today) against a more cost effective follow-up protocol in patients operated for extremity BSTS was conducted at our institute.

**Method:** Five hundred patients non metastatic at presentation who were operated for primary or recurrent extremity sarcomas (both limb salvage and amputations) were recruited between Jan 2006 and June 2010. They were stratified as (i) Bone or soft tissue sarcomas (ii) High or low grade tumors and (iii) Size (< 8 cm for bone and < 10 cm for STS). They were randomised into 4 groups (1) - Intensive 3 monthly follow-up (2) - Intensive 6 monthly follow-up (3) - Cost Effective 3 monthly follow-up (4) - Cost Effective 6 monthly follow-up. The primary end point was overall survival and secondary endpoint was disease free survival (local or distant relapse).

**Results:** Early results indicate that increased frequency of surveillance does not seem to significantly impact on either earlier recognition of relapse or overall survival. (DFS p = 0.676, OS p = 0.557). Though increased intensity of surveillance may identify earlier recognition of relapse in bone sarcomas it does not significantly impact on overall survival. (DFS p = 0.012, OS p = 0.555).

**Conclusion:** Thus in recurrent sarcomas, it is likely that in the majority of cases the outcome and efficacy of salvage treatment is determined more by inherent tumor biology rather than the treatment itself.

**O042**

**TOLERABILITY AND PHARMACOKINETIC PROFILE OF SUNITINIB GIVEN AS A POWDER FORMULATION TO CHILDREN WITH REFRACTORY SOLID TUMORS: A CHILDREN’S ONCOLOGY GROUP STUDY**

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**Purpose:** Sunitinib is an oral tyrosine kinase inhibitor of VEGF, PDGF, c-KIT, and flt-3 receptors. A pediatric phase 1 study of sunitinib capsules identified the maximum tolerated dose as 15 mg/m²/day. This study was conducted to evaluate sunitinib given as a powder formulation to children with refractory solid tumors.
14 SIOP ABSTRACTS

**Method:** Sunifatinib 15 mg/m² was administered orally daily for 4 weeks on/2 weeks off to patients 4–21 years old with refractory solid tumors. Sunifatinib capsules were opened and the powder sprinkled onto apple sauce or yogurt. Plasma levels of sunifatinib were obtained to estimate pharmacokinetic parameters, with comparisons made to previous pediatric trials using capsules.

**Results:** 12 patients (6 patients < 12 years old; 10 with primary brain tumors) were treated with a median of 1 cycle of therapy. The most common first-cycle toxicities were leukopenia (n = 6), fatigue (n = 5), neutropenia (n = 4), and hypertension (n = 4). Three patients had dose-limiting toxicities (DLTs) in cycle 1 (dizziness/back pain, hand-foot syndrome, and intratumoral hemorrhage/hypoxia). Two patients had DLTs in subsequent cycles (proteinuria and alkaline phosphatase). A median peak plasma sunifatinib concentration (Cmax) of 21 (range 6–36) ng/mL was reached at a median of 4 (Tmax; range 4–8) hours after the first dose, compared to median Cmax of 17 (range 10–61) ng/mL and Tmax of 7 (range 2–48) hours for the capsules. The median exposure (AUC) was 585 (range 196–1059) hour·ng/mL, compared to 492 (range 347–1111) hour·ng/mL for capsules. The median half-life was 23 (range 13–36) hours, compared to 38 (range 24–62) hours for capsules. The median trough concentration measured before Day 14 dosing was 33 (range 12–58) ng/mL, compared to 30 (range 12–62) ng/mL for capsules.

**Conclusion:** The pharmacokinetic profile of sunifatinib appears similar between powder and capsule formulations. The powder formulation allows patients unable to swallow capsules to receive sunifatinib.

**Study background:** Sunifatinib (S41513) is a selective receptor tyrosine kinase inhibitor (TKI) of the platelet-derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor (VEGFR), epidermal growth factor receptor (EGFR) and insulin-like growth factor receptor (IGFR) family. Sunifatinib is a multi-targeting TKI that has demonstrated antitumor activity in a variety of solid tumors. Further industrial development of a liquid formulation of CPM and evaluation in a multicentric study are needed to confirm our data.
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**O047**

**TARGETING OF THE ACUTE MYELOID LEUKEMIA STEM CELLS THROUGH IMMUNOTHERAPY: DEVELOPMENT OF A NOVEL CHIMERIC RECEPTOR SPECIFIC FOR THE CD123 ANTIGEN**

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**Purpose:** Despite the progresses in the treatment of acute myeloid leukemia (AML), a significant number of patients are still refractory to standard cures. It has been hypothesized that one of the mechanisms underlying this phenomenon might be the failure of current therapies to target AML leukemic stem cells (LSCs). Therefore it is crucial to develop treatments selectively directed against LSCs. Immunotherapy with T-cells genetically modified to express chimeric receptors (CARs) represent a valid option. A suitable antigen to be targeted is the IL-3 receptor α chain (CD123), which is selectively expressed at higher levels on LSCs compared to normal hematopoietic progenitors (HSPCs) and whose overexpression is associated with poor prognosis and resistance to apoptosis.

**Method:** We developed two different CD123-specific CARs: one is a scFv-based CAR derived from the anti-CD123 TEG monoclonal antibody and one exploits the CD123-ligand IL-3 as binding subunit. These domains were subcloned in frame with the CH2-CH3-domain (CD123), which is selectively expressed at higher levels on LSCs compared to normal hematopoietic progenitors (HSPCs) and whose overexpression is associated with poor prognosis and resistance to apoptosis. Cytokine Induced Killer (CIK) cells, ex-vivo expanded T cells with potent antitumoral activity, were then transduced with these vectors and the functionality of the CARs has been evaluated by quantifying the transduced cells to lyse different leukemic targets (4-hours 51Chromium-release and 6-days co-cultures assays on stromal mesenchymal cells).

**Results:** Both the scFvCD123 and IL-3 CARs could be stably expressed on CIK cells (80% ± 10%), without altering their native phenotype. Expression of these CARs rendered these cells able to potently kill (up to 70% at 4 hours) CD123 expressing targets (THP-1 and TF-1 and artificially expressing CD123-CEM cell line), whereas sparing a CD123-negative cell line (CEM), as also confirmed in long-term killing experiments.

**Conclusion:** Our preliminary results indicate that CD123-specific CARs strongly enhance anti-leukemic CIK functions. Further studies are needed to assess the capacity of these CAR to discriminate among LSCs and HSCs both in vitro and in vivo.

**O048**

**RISKY HEALTH BEHAVIOR IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER AND THEIR SIBLINGS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY**

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**Purpose:** To complete a multi-site randomized clinical trial (RCT) comparing the efficacy of Problem Solving Skills Training (PSST) to Non-Directive Support (NDS) for mothers of children recently diagnosed with cancer. NDS provides mothers with a viable therapeutic experience that would be structurally similar to PSST in terms of the number, length, setting of sessions, and therapist support, but without the active skills building training of PSST.

**Method:** Mothers from were recruited for participation 2–16 weeks after their child was diagnosed with any form of cancer at any of four pediatric cancer centers in the United States. PSST: consisted of six to eight 1-hour individual sessions conducted according to a comprehensive protocol. PSST was presented as a general coping skill applicable to a range of challenging circumstances. NDS: included active listening, reflection of feelings, clarification, and “being there” for the subject. The focus was on the present moment and on expressing and experiencing feelings. Measures: Demographics; Social Problem Solving Skills Inventory-Revised; Beck Depression Inventory; Profile of Mood States Scale; Impact of Event Scale-Revised; and Credibility and Expectancy.

**Results:** Demographic data, and credibility and expectation for improvement were similar. Assessments occurred at baseline (T1), immediately post intervention (T2), and 3 months after T2 (T3) (Figure 1 and Table 1). NDS is clearly beneficial in the moment, but PSST provides the added benefit of continued skill development and feeling significantly less distressed as long as 3 months later (T3).

**Conclusion:** Both PSST and NDS alleviate distress in mothers of children recently diagnosed with cancer; however, the skills learned in PSST allow continued improvement after direct contact ends. We are investigating an online version of Bright IDEAS that requires little or no in-person support, making the intervention available to mothers and other caregivers wherever/whenever the Internet is available.

**O049**

**PSST VERSUS NDS FOR MOTHERS OF CHILDREN WITH CANCER: FINDINGS FROM A MULTI-SITE RANDOMIZED CLINICAL TRIAL**

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**Purpose:** In pediatric patients with refractory/refractory Leukemia, 20 mg/m2/day is the MTD for CLO in timed sequential combination with CY. Increased DNA damage with the use of this combination suggests a mechanism for the sequential timing of these two chemotherapeutic agents.

**Results:** No dose limiting toxicities (DLT) occurred at DL1. Two patients at DL2 had DLT characterized in one case by hypotension with cardio-respiratory failure and the other hepato-rennal failure. Two of thirteen (15%) patients had a partial remission and 7/13 (54%) patients showed disease progression. The use of this combination suggests a mechanism for the sequential timing of these two chemotherapeutic agents.

**Conclusion:** Our preliminary results indicate that CD123-speciﬁc CARs strongly enhance anti-leukemic CIK functions. Further studies are needed to assess the capacity of these CAR to discriminate among LSCs and HSCs both in vitro and in vivo.

**O050**

**‘BEING MINDFUL’: DOES IT HELP ADOLESCENTS AND YOUNG ADULTS WHO HAVE FINISHED CANCER TREATMENT?**

Pandora Patterson, Fiona McDonald

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**Purpose:** Finishing cancer treatment can be a very distressing and uncertain time for adolescents and young adults (AYAs), even more so than at diagnosis and during treatment.
This is the time when young people reflect on the past, what has been, and the future, what is to come. Recent research in the area of mindfulness points to the benefits of being in the present moment. Mindfulness can be a protective factor in the experience of cancer. The purpose of this study therefore was to examine whether having a higher level of mindfulness functioning was associated with better adaptive outcomes for AYAs who have finished treatment.

Method: AYAs aged between 12 and 24 years (N = 53; 38 females; M = 17.8 years) who had finished their cancer treatment completed a self-report questionnaire containing a measure of psychological distress (Kessler 10), the Child and Adolescent Mindfulness Measure (CAMM), and questions assessing ease of communication with others about the cancer experience, coping with school or work, and uncertainty.

Results: Significant differences were found between AYAs with low and high mindfulness scores across all measures. People with high levels of mindfulness had significantly lower levels of psychological stress and less uncertainty. They also found it significantly easier to communicate with others about their cancer experience, and easier to cope with school and/or work.

Conclusion: The current study provides evidence that the characteristics of present-moment awareness and non-judgemental, non-avoidant responses to thoughts and feelings are associated with better adaptive outcomes for young people who have finished cancer treatment. Given the previously established need for ongoing supportive care for this population and the results of the present study, it would be worthwhile to consider developing mindfulness-based interventions.

THE IMPACT OF PAEDIATRIC CANCER ON THE SIBLINGS IN THE FAMILY AND THE RESULTS OF A THERAPEUTIC PEER SUPPORT PROGRAM FOR THIS POPULATION

Ranita Sidhu1, Anne Passmore2, David Baker3

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2Curtin University of Technology, Occupational Therapy, Perth, Australia
3Princess Margaret Hospital- Oncology [now retired], Oncology, Perth, Australia

Purpose: Siblings of children with cancer have higher levels of psychological stress and adaptional difficulties compared to siblings of healthy children and children with other chronic illness. This is the first study to report on the mental health of Australian siblings of children with cancer and examines the effects of a therapeutic peer support camp- Camp Onwards, as an intervention.

Method: A protocol for a peer support camp designed to enhance mastery, decrease anxiety, and improve sibling understanding of the impact of the cancer diagnosis and treatment was developed. Siblings of children with cancer (n = 26) aged 8–13 years were assessed using standardised measures at pre and post camp and again at -8 weeks follow-up. Data were collected using three self-report tools: the Behaviour Assessment for Children (BASC) (Reynolds & Kamphaus, 1992), Self-Perception Profile for Children (SPP-C) (Harter, 1985), Sibling Perception Questionnaire (SPQ) (Carpenter & Sahler, 1991).

Results: Change over time was measured using t tests. At pre-test, 40% of the sample demonstrated increased levels of emotional distress when compared to the normal population. At post-test, siblings who attended Camp Onwards demonstrated improved mental health outcomes that were sustained at follow-up. Specifically siblings demonstrated lower levels of distress as demonstrated by decreased anxiety (p = 0.01), and positive changes in the overall self-report of personality on the BASC (p = 0.00). Improved social competence was noted by improvements in the interpersonal domain of the SPQ (p = 0.01) and also greater social acceptance scores (p = 0.01) on the SPP-C. Improved knowledge about the impact of cancer and its treatment was evidenced by significant reductions in the fear of disease domain on the SPQ (p = 0.01).

Conclusion: These results demonstrate the effectiveness of Camp Onwards - a therapeutic peer support camp as an intervention strategy for siblings of children with cancer. An overview of the program in a longitudinal context will also be described.
patients underwent hyperfractionated dose escalation to a median dose of 70.2 Gy. The median follow-up of all patients was 1.4 years (range of 0.1–46 years). The median follow-up of survivors was 18.8 years (range 4.7–46 years). A grading system was devised stratifying patients as low (n = 10), intermediate (n = 16), or high (n = 16) risk based on patient age, duration of symptoms, and imaging characteristics. Results: The 5 year overall survival (OS) for all patients was 38% and has not significantly improved over the past 40 years. Hyperfractionated dose escalation did not confer a survival advantage (5 year OS 38% vs. 35%, respectively (p = 0.49). The low and intermediate risk patients demonstrated an 80% and 44% 5 year OS, respectively. The high risk patients were among patients with classic unfavorable features. Based on our long term data in patients had a tissue diagnosis.

The 5 year overall survival (OS) for all patients was 38% and has not significantly improved over the past 40 years. Hyperfractionated dose escalation did not confer a survival advantage (5 year OS 38% vs. 35%, respectively (p = 0.49). The low and intermediate risk patients demonstrated an 80% and 44% 5 year OS, respectively. The high risk patients were among patients with classic unfavorable features. Based on our long term data in patients had a tissue diagnosis.

**Results:**

- **Objective:**
  - **Purpose:** The purpose of this study is to assess the role of adjuvant RT in pediatric MPE.
  - **Method:** Sixteen patients with MPE seen at Johns Hopkins Hospital between November 1984 and December 2010 were retrospectively reviewed. Fifteen of these patients were evaluable with a mean age of 16.5 years (range 12–21). Descriptive statistics were used for analysis.

**Results:**

Patients received surgery as the initial treatment modality. Five patients received surgery alone and 10 received RT given as either adjuvant or salvage therapy. The median dose of radiation was 50.4 Gy (range 48.6–54). After a median follow up of 7.2 years (range 0.3–26.2), all patients were alive with stable disease. 50% receiving surgery alone were progression-free at 5 years compared to 66.7% of patients receiving RT. Patients treated with surgery alone had a median progression-free survival (PFS) of 2.4 years compared to 6.2 years for patients treated with adjuvant RT. Specifically, patients treated with GTR had a median PFS of 2.6 years compared to a median PFS of 5.0 years in patients treated with GTR and RT. Of the patients receiving surgery alone, 43% developed local recurrence. In contrast, no patient who received adjuvant RT failed locally. No late toxicity was reported at last follow-up and neurologic symptoms either improved or remained stable following surgery and/or radiation. Conclusion: The results of this study demonstrate that adjuvant RT can improve local control and PFS as compared to GTR alone. Adjuvant RT should be considered following surgical resection in pediatric patients with MPE.

**Conclusion:**

- **Purpose:** Myxopapillary ependymoma (MPE) is a rare tumor in children with the majority of publications and treatment recommendations based on adults. The primary treatment is gross total resection (GTR) with no clearly defined role for adjuvant radiation therapy (RT).
- **Method:** Prospective neurocognitive testing of the HC and CC suggests a relationship between structural volume following CSRT and neurocognitive performance. Better understanding of RT effects on neuropsychological development in children has future implications for tailoring RT fields in an effort to reduce late effects.

**Method:**

- **Purpose:** To evaluate local control and functional outcome of localized spinal Ewing sarcoma (EWT) above sacrum.
  - **Method:** We propose a dose escalation study declined in two scenarios: (1) a tumor located within a single vertebral body and (2) a locally advanced disease involving the vertebral foramen and paraspinal soft tissues. Five dose-levels are proposed: 44.8 Gy, 54.4 Gy, 59.2 Gy, 65.6 Gy and 70.4 Gy (1.6 Gy/session, 8 Gy/week). The 3D-conformal technique is compared with Static Intensity Modulated Radiotherapy (IMRT), helical tomotherapy, Volumetric Modulated Arc Therapy (VMAT), Stereotactic Body Radiotherapy (SBRT) and protontherapy (passive scattering). Two constraints had to be respected in order to skip to the next level: the PTV coverage must exceed 95% and the D2% on the spinal cord shall not exceed a given constraint set at 50 Gy in case (1) and 44 Gy in case (2) due to initial neurological suff erance.

**Results:**

- **Objective:** Although radiosensitive, spinal locations of Ewing tumors (EWT) are challenging for the radiologist due to the anatomic and physiologic complexity of the spinal region. A better local control is described in retrospective studies. However in a recent study we performed, some favorable anatomic compartments - that may represent more than 20% - were associated with a better outcome. Here we postulate that the dose may be escalated using the most recent radiobiological techniques in these cases.

**Method:** We propose a dose escalation study declined in two scenarios: (1) a tumor located within a single vertebral body and (2) a locally advanced disease involving the vertebral foramen and paraspinal soft tissues. Five dose-levels are proposed: 44.8 Gy, 54.4 Gy, 59.2 Gy, 65.6 Gy and 70.4 Gy (1.6 Gy/session, 8 Gy/week). The 3D-conformal technique is compared with Static Intensity Modulated Radiotherapy (IMRT), helical tomotherapy, Volumetric Modulated Arc Therapy (VMAT), Stereotactic Body Radiotherapy (SBRT) and protontherapy (passive scattering). Two constraints had to be respected in order to skip to the next level: the PTV coverage must exceed 95% and the D2% on the spinal cord shall not exceed a given constraint set at 50 Gy in case (1) and 44 Gy in case (2) due to initial neurological suff erance.

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recurrences had occurred with a median time of 26 (1–50) and 23 (12–38) months, respectively. The 5-LC rate was 75% (95% CI: 64–85). Involved vertebral compartment was the only prognostic factor (5y-LC rate 100% vs 67% for favorable and unfavorable compartment, p < 0.02). Prognosis was unrelated to age, tumor volume and local treatment modalities. Among the 5-year survivors (n = 43), we observed spinal curvature deformation (33%) growth retardation (28%), spinal reduction mobility (36%), spinal pain (25%) and neurological sequelae (33%) at 6 months. Surgery was associated with increased pain frequency as compared to definitive RT (30% vs 13%). Definitive RT was associated with a poor activity level (mean score 2.5/4), spinal hypo-motility (63%), and neurallogic sequelae (50%).

Conclusion: Localized spinal EWT represent a local challenge due to the proximity of the spinal cord or cauda equina.

O059

DEFINITIVE RADIATION THERAPY FOR PELVIC EWING SARCOMA: EARLY OUTCOMES

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Purpose: To evaluate the clinical outcome of patients with Ewing sarcoma (ES) of the pelvic bones treated using definitive radiation therapy.

Method: From February 2001 to December 2009, 22 patients (median age 15.5 years, range 5 to 40) with non metastatic ES who received definitive external beam radiation therapy (EBRT) as part of loco-regional treatment were included. There were 14 males and 7 females. All patients received neo-adjuvant chemotherapy (NACT) for 9 weeks using the indigenous EFT 2001 protocol and then evaluated for local therapy. Patients with inoperable disease after completion of neo-adjuvant chemotherapy were considered for definitive radiation therapy. Radiation therapy was delivered using 3-Dimensional Conformal Radiation Therapy (3D-CRT) or Intensity Modulated Radiation Therapy (IMRT). The radiation dose ranged from 45 Gy to 70.2 Gy @ 1.8 Gy per fraction (Median: 55.8 Gy @ 1.8 Gy per fraction).

Results: The 5-yLC rate was 75% (95% CI: 64–85). None of the patients had neurological sequelae (33%). Surgery was associated with increased pain frequency as compared to definitive RT (30% vs 13%). Definitive RT was associated with a poor activity level (mean score 2.5/4), spinal hypo-motility (63%), and neurallogic sequelae (50%).

Conclusion: Localized spinal EWT represent a local challenge due to the proximity of the spinal cord or cauda equina.

O060

SUSTAINABLE PEDIATRIC ONCOLOGY NURSING EDUCATION IN LOW-INCOME COUNTRIES

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Rita Cart4, Pedro de Alarcon5, Ching-Hon Pui6, Raúl Ribeiro7, Scott Howard8

1St. Jude Children’s Research Hospital, International Outreach, Memphis, TN
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Purpose: The widespread absence of pediatric oncology education for nurses in low-income countries contributes to the disparity in outcomes for children with cancer in high- versus low-income countries. In 2006, the International Outreach Program at St. Jude Children’s Research Hospital began to establish full-time nurse educator positions within partner-site pediatric oncology units. Because this model had not been tested and a feasible and sustainable method of providing nursing education was needed, we evaluated its effectiveness at the National Pediatric Oncology Unit in Guatemala.

Method: From 2007 to 2009, we measured 1) the rate of completion of a pediatric oncology nursing education course by newly hired nurses, 2) the rate of central- venous line care competency, 3) the rate of chemotherapy competency, 4) the provision of continuing education, and 5) the cost relative to 3 traditional nursing education models.

Results: All 25 nurses hired during the study period completed the pediatric oncology education course (mean test score, 86% ± 7%). Of the 49 nurses who were employed on the unit during the study period, 22 (45%) achieved competency in central- venous line care (mean score, 78% ± 15%) and 39 (80%) achieved competency in chemotherapy administration (mean score, 87% ± 9.7%). The 49 nurses completed a mean of 26 ± 8.3 hours of continuing education per year. The annual direct cost of the educator ($244/nurse) was markedly less than that of other educational methods: a short series of lectures ($4,415/nurse), an expanded series of lectures ($5,190/nurse), and a residential training program ($6,554/nurse), and it provided the essential advantage of continuing education.

Conclusion: A full-time pediatric oncology nurse educator is an effective, affordable, and sustainable means of providing specialty-trained nurses for pediatric cancer care in low-income countries.

O061

PEDIATRIC ONCOLOGY TWINNING: A NURSING PERSPECTIVE IN AFRICA

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5California State University Long Beach, School of Nursing, Long Beach, CA

Purpose: To assist pediatric oncology nurses through collaborative problem solving/education/support in a new twinning program in Ethiopia. There are 85 million inhabitants; the vast majority live in rural areas on < $2/day. There is only one public hospital in the country (in the capital, Addis Ababa) offering cancer treatment.

Method: Determined nursing needs for 40 children on two general pediatric wards (0–12 years old) as identified in a pre-visit questionnaire completed by the two head nurses. Results informed visiting nurses and allowed for a custom-designed curriculum for didactic teaching, as requested. During the site visit (6 days), five nurses from the US worked to increase skills and knowledge about cancer, chemotherapy, and management of side effects. A class was attended by 20 local nurses and 8 nurses from outlying cities. A focus group identified nursing strengths, challenges and recommendations for future collaboration and support.

Results: Assessment of nursing care and suggestions for improvement, as well as cooperative problem solving was performed over three days on the local unit. The nurses attended two days of a Georgetown University/INCTR and Mathewos Wondo-Ye Ethiopian Cancer Society sponsored conference with physicians and pharmacists.

Conclusion: Results from the focus group and direct observation on the unit directed recommendations and strategies for long-term collaboration. Urgent nursing and child/parent needs were identified for action including safety issues for chemotherapy preparation and administration, nutrition, and infectious disease challenges. Pre-visit data collection was crucial to allow visiting nurses to create context-specific teaching materials. Time on the units over several days allowed for trust so visiting nurses would be viewed as supporters and not critics of nurses working in severely constrained circumstances. Historically, nursing inclusion in any twinning program has been shown to be essential for success; but it is challenging due to language, on-going communication needs (lack of internet access) and local cultural hierarchies.

O062

PEDIATRIC ONCOLOGY NURSING CURRICULUM FOR DEVELOPING COUNTRIES

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Purpose: Through previous meetings of SIOP, the medical and nursing community in Africa raised the need for ongoing education programs and expressed their need and desire for assistance in developing a pediatric oncology nursing curriculum. Working in collaboration with an interdisciplinary team consisting of staff from Chris Hani - Baragwanath Hospital (CHBH), Johannesburg General Hospital (JGH) and British Columbia’s Children’s Hospital (BCCH), the goal was to collaboratively develop a pediatric oncology nursing curriculum for nurses in these two hospitals with the long term goal of adapting the education framework for other centres in Africa.

Method: An initial site visit by the BCCH clinical nurse educator and the pediatric oncologist was planned to conduct an assessment of the learning needs and infrastructure resources on the oncology units at CHBH and JGH. Meetings with staff at JGH and CHBH were conducted to explore learning needs and determine how to best use the established pediatric oncology nursing curriculum at BCCH and adapt it to the cultural and resource context at JGH and CHBH. Learning modules will be created, tested, and evaluated as to the efficacy, practicality and sustainability for the learning needs of the nursing staff. Follow up site visits will allow further evaluation and the ability to assess how education has changed the care provided by the nursing staff at JGH and CHBH.
0O63
DEVELOPING A NURSING EDUCATION PROGRAM IN PEDIATRIC ONCOLOGY IN A LOW INCOME COUNTRY: THE ROLE OF TWINNING
Paula Aristizabal1, Alicia Sanchez2, George Velez3, Raul Ribeiro3, William Roberts4, Sara Day5

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Purpose: In 2008, St. Jude Children’s Research Hospital and Rady Children’s Hospital-San Diego initiated a Twinning Program (TP) at the Hospital General-Tijuana (HGT), Mexico to improve pediatric cancer care. The quality of nursing care for pediatric oncology (PO) patients at HGT was assessed using standards from six Joint Commission International domains. Quality standards were found lacking in all domains; however, the most critical was the Staff Qualifications and Education domain.

Method: To meet the identified education needs and, as a first step in improving the quality of nursing care, a full time nurse educator (NE) position was developed and filled by an experienced nurse from HGT. The NE’s responsibility was to implement an education program for newly hired nurses including continuing education classes. A total of 13 courses were provided every 6 weeks. The core content included chemotherapy administration and safety, central venous line care, infection control, transfusions and care of the cancer patient. To assess the knowledge retention, written pre and post-tests with an average of 20 questions were provided during each course.

Results: After 18 months, the NE with the TP Medical Director’s support, provided the staff (n = 16) at HGT with over 600 hours of PO education, including courses and individual skills training. The overall mean knowledge level score changed significantly from 23% (range: 19–28) in the pre-tests to 79% (range: 67–90) after each course. The NE completed a monthly report describing the educational content, number of education activities and evaluation test scores.

Conclusion: The NE was able to implement a locally sustainable PO education program by providing comprehensive education to the nurses and improving the staff’s knowledge level scores by 56%. Ongoing initiatives include continuing education and measuring the long-term retention. Nursing education is critical to quality nursing care and an important component of a successful TP.

0O64
PROVIDING CARE TO NAVAJO CHILDREN AND FAMILIES RECEIVING HEMATOPOIETIC STEM CELL TRANSPLANTS
Linda Abramovitz
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Purpose: There are 300,000 to 350,000 indigenous peoples (<6% of the world population) representing 5000 distinct peoples in over 72 countries throughout the world. The Native American (USA), Maori (New Zealand), Aboriginal (Australia) and Ashankina (Peru) are examples of indigenous peoples. There are unique challenges to provide health care to these populations.

The United States is a multicultural society consisting of peoples from many different traditions and diverse cultural backgrounds. Due to a high incidence of severe combined immunodeficiency disease (SCID) in the Navajo population, our program cares for many of these infants who receive hematopoietic stem cell transplants (HSCT). The purpose of this presentation is to explore the issues facing the health care team as they provide care to Navajo children/families facing HSCT.

Method: Examples of clinical situations and case studies from my practice over the last 20 years will be used to illustrate the delivery of care within the framework of Navajo beliefs. Similarities and differences will be explored between indigenous cultures and the philosophy of Western Medicine. Issues related to cultural sensitivity and establishing trust will be addressed.

Results: Deeply held traditional beliefs impact the way an individual responds to “Western” care and treatments. Taboos and superstitions impact the manner in which information is relayed during informed consent. For example, many Navajo patients believe that the discussion of negative information is a dangerous violation of traditional Navajo values and can lead to illness and negative consequences. A child’s care may involve ceremonies, healers and decision making by elders in the community.

Conclusion: Miscommunication occurs when patients and providers do not understand each other’s cultural practices. It is imperative that the health care team be educated to provide the best care possible. Despite the challenges, caring for Navajo children who undergo HSCT is both a rewarding and an enriching experience.
20 SIOP ABSTRACTS

useful for detecting necrosis than conventional MRI sequences. Differentiation of marrow edema vs. actual marrow involvement and adjacent soft tissue edema and actual involvement can be better predicted by DWI MRI. DWI can be used for pre-treatment tumor detection, characterization including predicting tumor response to therapy, monitoring tumor response during therapy and follow-up study after treatment to detect possible tumor recurrence. However, further investigation in a large series is necessary.

Conclusion: BARD1 and LMO1 function as oncogenes in NB susceptibility and progression to high-risk disease. The translational application of GWAS in pediatric cancer will come from the unbiased discovery of novel genes and pathways essential to sustaining the high-risk phenotype, and thus providing opportunities for therapeutic target development.

O067

A SURVEY OF DESTINATION IN CHILDREN TREATED FOR Burkitt LYMPHOMA IN RURAL CAMEROON

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Purpose: The aim of the study was to determine the magnitude of potential risk factors that may affect outcome of children treated for Burkitt lymphoma in the Baptist Convention Hospitals. Specific objectives included the access to financial means, housing, and food.

Method: A questionnaire, named the Scale of Destination, was used to determine the following: number of dependent children in the family; receiving mutual insurance/family friends or other financial support; owning or renting a home; food security; and income. The scale had a final score from 0 to 8. A score of 0–2 was obtained for a family with adequate resources; score 3–5 indicated limited resources; and scores of 6–8 indicated destitution.

Results: There were 105 questionnaires completed by the research nurse after obtaining informed consent from the parents. More than half the families scored between 6–8, indicating destitution in 58% of families. More than a third of the families (39%) had limited resources, while only 3% had adequate access to food, money and housing. Of great concern is that 35% of families who experienced difficulties to obtain food. The majority of the families had more than one child (94%), while the average income was 55 US dollars per month (80%). The one-year survival rate was 59% in this study population treated for Burkitt lymphoma.

Conclusion: Poverty is a major problem in rural Cameroon. Treatment programs for children with cancer need to include partnerships with charity organizations that can assist in the provision of additional financial and other support to address destitution in these families. This will minimise risks of abandonment and other individual risks for the index patient.

O068

GERMLINE VARIATIONS ARE ASSOCIATED WITH SUSCEPTIBILITY TO HIGH-RISK NEUROBLASTOMA AND IDENTIFY PATHWAYS WITH GAIN OF FUNCTION


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Purpose: A genome-wide association study (GWAS) has identified common genetic variants that predispose to neuroblastoma (NB, Maris NEJM 2008; Capasso Nat Gen 2009; Diskin Nature 2009; Wang Nature 2011; Nygum PLOS Gen 2011), but the functional and regulatory gene expression data from 112 NB tumors. The effects of risk-allele genotype on gene expression, splice variations, proliferation, and apoptosis were characterized in NB cell lines, tumors and the developing nervous system. Tumor and matched normal DNAs were deep sequenced to discovered rare variants.

Results: Germline risk alleles at BARD1 were associated with differential overexpression of a specific BARD1 isoform that transformed NIH-3T3 cells and protected against apoptosis. BARD1 isoform-specific RNA knockdown inhibited NB proliferation in a risk-allele specific manner. LMO1 overexpression in NB tumors was associated with the LMO1 risk-allele genotype, chromosome 11p segmental duplication, and was inversely associated with MYCN amplification. Next generation sequence analyses of 81 tumor exomes and 20 full genomes identified multiple unique germline haplotypes or variations predicted to have a larger effect on tumor susceptibility. Somatically acquired mutations were not discovered.

Conclusion: BARD1 and LMO1 function as oncogenes in NB susceptibility and progression to high-risk disease. The translational application of GWAS in pediatric cancer will come from the unbiased discovery of novel genes and pathways essential to sustaining the high-risk phenotype, and thus providing opportunities for therapeutic target development.

O069

DOWN SYNDROME ALL IS CHARACTERIZED BY A HIGH FREQUENCY OF IKZF1 DELETIONS AND ABRERRATIONS OF CRLF2

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Purpose: Children with Down syndrome (DS) have an increased risk of developing acute lymphoblastic Leukemia (ALL). There is a lower frequency of well-known genetic aberrations in DS ALL than in non-DS ALL. We therefore aimed to determine which genetic abnormalities are involved in the pathogenesis of DS ALL, and studied the frequency and the prognostic value of aberrations in B-cell development genes including PAX5, VPREB1, E2A, EBF1 and IKZF1, and aberrations in Jak and CRLF2 pathways.

Method: To identify molecular aberrations, we performed 105-K exome capture and targeted re-sequencing of 17 genes. Comparative genomic hybridization (CGH) analysis of 34 DS ALL patients and validated this with Multiplex Ligation-dependent Probe Amplification (MLPA). MLPA Genomic DNA was PCR-amplified for mutation analysis of Jak2 and for IKZF1 isoform 6. Fluorescent in-situ hybridization (FISH) was performed to identify AML2 re-arrangement.

Results: In total, 50% of DS ALL patients had 1 or more deletions in B-cell development genes. Three B-cell development genes were affected: PAX5 (12%), VPREB1 (18%), and CRLF2 (35%). Jak2 was mutated in 15% of the patients and CRLF2 in 62%. Outcome was significantly worse in patients with IKZF1 deletions than in wildtype IKZF1 patients (6 year EFS 45% vs. 16% < 0.001). IKZF1 aberrations were more frequent in DS ALL patients than in all patients with ALL in recent pediatric studies, (16% vs. 95% p = 0.014). IKZF1 Isoform 6 and WBC > 20x109/L independently predicted prognosis, whereas CRLF2 and Jak2 did not.

Conclusion: In total, 35% of DS ALL patients have IKZF1 aberrations and patients with IKZF1 Isoform 6 have a high risk for relapse. When confirmed in other series IKZF1 abnormalities may be used for further risk-group stratification of DS ALL patients. Therefore, we recommend routine screening for IKZF1 abnormalities, especially isoform 6, in all patients with DS ALL, which can effectively be done by using MLPA.

O070

DOSE DENSE CISPLATIN IMPROVES SURVIVAL IN CHILDREN PRESENTING WITH METASTATIC HEPATOBLASTOMA: LESSONS FROM SIOP 1 TO 4

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Purpose: To review the treatment and outcome of patients with metastatic, predominantly pulmonary, hepatoblastoma treated on 4 consecutive SIOPEL trials. Method: Methods: In SIOPEL 1990–1994 treatment was 21-day cycles of PLADO, cisplatin80 mg/m2+doxorubicin60 mg/m2; x4 pre and x2 post surgery. In SIOPEL 2 1995–1998 and SIOPEL 3 1998–2004 treatment became 14-day superfLADO, cisplatin80 mg/m2.

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alternating with carboplatin 500 mg/m² + doxorubicin 60 mg/m² x 7 pre and x 3 post-surgery in SIOPEL4. 2005–2009 treatment was 3 cycles of pre-operative chemotherapy (cisplatin 70 mg/m² x 1, 8.15; doxorubicin 30 mg/m² x 1, 8.9), surgery and post-operative chemotherapy (carboplatin AUC6.6 mg/ml.min day 1, 22.43, doxorubicin 25 mg/m² x 1, day 1, 22.23, 43.44). Patients whose tumour remained unrespectable received additional chemotherapy (carboplatin AUC10.6 mg/ml.min day 1, 22.12; doxorubicin 25 mg/m² x 1, 2, 23, 22-23.24) before surgery was attempted. Lung disease: one node larger than 10 mm or several nodules with at least one larger than 5 mm. Both cisplatin cumulative dose and preoperative doses were increased from SIOPEL1 cumulative -480 mg/m² preoperative 240 mg/m² through SIOPEL4 cumulative all preoperative 570 mg/m².

Results: In SIOPEL1 304 metastatic patients were identified; 5-yr EFS and OS were 28% and 57%. Persistent lung disease was the main reason for PLADO failure; 4/4 patients where metastasectomy was performed became long term survivors. In SIOPEL2 25/125 patients were metastatic; 3-yr EFS and OS were 40% and 44%; 38 patients who had surgery following chemotherapy for residual metastases survived. In SIOPEL3 60/151 were metastatic, 52.2% achieved metastatic complete remission with chemotherapy alone; 3-yr EFS and OS were 56% and 62%. In SIOPEL4 the 3-yr EFS and OS for the 39 metastatic patients were 76 and 79% respectively.

Conclusion: Conclusion: From 1990 to 2009 continuous improvement in 3-yr EFS and OS of patients with metastatic hepatoblastoma has been documented in SIOPEL studies. This seems mainly related to more intense use of platinum derived drugs. The results from the SIOPEL 4 intensive approach are the best ever reported in metastatic hepatoblastoma studies.

**O072**

**THE DEVELOPMENT OF AN ADOLESCENT/YOUNG ADULT CANCER SERVICE**

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Purpose: Care of adolescents/young adults diagnosed with cancer is complex and therefore requires specialised care. The New Zealand Cancer Control Strategy (2003) recognised that the current model of health care delivery was not addressing the needs of this population adequately and as a result negative outcome measures were evident for this age group.

Method: In April 2007 funding was allocated to look specifically at the needs of adolescents and young adults with cancer being cared for under Starship Children’s Hospital and Auckland City Hospital. The objective of the allocated funding was to improve the care for AYA’s with cancer, increase entry onto age appropriate clinical trials. Improve the psychosocial care delivered to the patient and their family and whanau and to adopt a youth development approach to care.

This paper will examine how Starship/Auckland Hospital went about adopting a youth development approach to care within their services while also improving psychosocial care delivered to their patients and their families.

Results: This presentation will detail how a youth development approach has improved the care and service for adolescents and young adults including a change of physical environment, introduction of youth appropriate resources, formation and support of a MDT approach and a systematic approach to assessment, treatment and follow-up of young people. A number of non traditional youth  focused programmes addressing the psychosocial needs of the adolescent young adult have also been established and implemented.

Conclusion: In the four years since the programme has been introduced there is now a clear pathway of care for the young person diagnosed with cancer. Success of the programme is also evident by the young people’s engagement and participation in the service.

**O073**

**EVALUATING SPECIALIST TEENAGE AND YOUNG ADULT CANCER SERVICES: FIRST ADDRESS THE ‘4 PS’**

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Purpose: Traditional cancer services fail to meet the unique needs of teenagers and young adults (TYAs). Policy in England recognises these needs and age-appropriate services are being implemented. However, the evidence to underpin this is limited. Our overriding aim was to evaluate the benefits of specialist TYA cancer services. Such a proposal required a substantial phase of exploratory and feasibility work. These focused on the ‘4 Ps’: Personal experience; Place of care; Professional competence; and Policy.

Method: This mixed methods study was based on the Medical Research Council’s framework for developing and evaluating complex interventions. Studies were conducted in two centres in England; collaborating with a TYA patient group trained in research methods; TYA (n = 20); health professionals (n = 25); and policy commissioners (n = 4). Eleven sub-studies employed a range of methods including: systematic reviews of the literature; semi-structured interviews and peer interviews; documentary analysis; non-participant observation; participatory workshops; and analysis of National Health Service informatics. Results: Data from these sub-studies have informed the design and conduct of Phase 2: identification of the pathway of referral that will allow all TYA to be recruited within 3-months of cancer diagnosis; description of the key characteristics of a specialist TYA cancer unit; and the core competencies of professionals working in the field have informed an international Delphi survey. Eight key themes emerged from interviews with TYA, together with results from the systematic review, these provide the core domains and preliminary questions for a descriptive survey and confirmed an approach to recruitment, retention and data collection that we are confident TYA will engage with.

Conclusion: This paper will briefly describe the relevance and results from the ‘4 Ps’, with an emphasis on how the results have informed the main study that seeks to evaluate the value of specialist TYA cancer care.

**O074**

**THE VOICES OF THE YOUNG ADULT CANCER PATIENTS**

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Purpose: In the world today there is a focus on cancer care among teenagers and young adults (TYAs). There are several studies describing the situation for TYAs with cancer in different parts of the world. The purpose of this study is to analyse the current situation for TYAs (18–29) with cancer, treated at adult cancer units, in Sweden, by listening to their opinions. The overall aim of this project is to improve the cancer care for this age group.

Method: The chosen method for this study is focus group interviews with former cancer patients. The inclusion criteria for participants were that they had finished cancer treatment and that no more than 3 years had passed since the end of treatment. Participants were recruited from two university hospitals in Sweden. In every focus group there were a number of 4–6 participants. The interviews were recorded, transcribed into text and analyzed through content analysis.

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**SIOP ABSTRACTS**

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Results: The results of the focus group interviews are currently under analyzing process and will be concluded during the summer 2011. The preliminary results show that young adults need to be cared for by experts in every moment of the health care to feel secure.

Conclusion: The result will assist the health care professionals in their aim to improve the organization of the cancer care for the teenagers and young adults with cancer during their treatment.

0075

UNDERSTANDING PARENTS AND ADOLESCENTS’ PERCEPTION OF A RESEARCH CLINICAL TRIAL AND THE INFORMED CONSENT/ASSENT PROCESS IN THE PAEDIATRIC ONCOLOGY SETTING

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Purpose: Around 80% of children receive cancer treatment through a clinical trial. Understanding informed consent underpins the integrity of good clinical practice in clinical trials however the stress of a life threatening diagnosis challenges the absorption of information. The aims of this study were to establish families understanding of this process and identify what information was important to them.

Method: Children and adolescents aged 8–16 years, enrolled on a clinical trial, were given questionnaires one month after diagnosis. Parents were asked to complete all questions for children less than 12 years old, while older adolescents completed their own. Consent was received from all participants.

Results: Responses were received from 50 parents and 27 adolescents. Diagnosis of participants included leukaemia’s (50%), lymphoma (10%) and solid tumours (40%). The majority of parents (94%) agreed that they understood the diagnosis and information regarding the purpose of the clinical trial. Parents relied primarily on their Oncology consultant although also sought information from nursing staff (72%), psychosocial staff (62%), the internet (58%) and printed resources (50%). Parents discussed the diagnosis with their children although only 60% felt that their child understood what the treatment meant. Adolescents also agreed (96%) that they understood the diagnosis, but the clinical trial treatment and consent/assent process was poorly understood with 52% being unsure if this discussion had occurred and only 29% indicating that they understood what this meant. 60% preferred that their parents make the decisions but more information was wanted on the impact of the treatment and the subsequent ability to return to their normal life.

Conclusion: Parents indicated a good understanding of the informed consent process. Adolescents wanted to be involved in discussions regarding treatment and the clinical trial process, but had a limited understanding and many preferred their parents to make decisions for them.

0076

A MULTI-CENTER STUDY OF TREATMENT PROTOCOL FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN CHINA: CCLG 2008 STUDY.

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Purpose: To establish a multicenter collaborative study on treatment of childhood ALL in China. Uniform diagnostic and stratification criteria were adopted with treatment intensity adjusted. Toxicity profiles of maintenance treatment were studied by a randomized study. 

Method: All patients eligible to inclusion criteria were recruited. A 7-day prednisone and Day 15 BM response were included as initial response criteria. Four drugs induction (daunomycin, vincristine, doxorubicin, asparaginase) was followed by an early intensification, with standard risk adopted an abbreviated BFM protocol Ib (CAM) for 2 weeks, and the others adopted two CAM. Four doses of methotrexate were given as 2 gm or 5 gm to the patients with lower and higher risk respectively. Methotrexate was administered once or twice for standard risk (SR) and intermediate risk (IR). High risk (HR) patients received more intensive consolidation blocks. Maintenance treatment was daily 6-mercaptopurine and weekly methotrexate (MP/MTX), 4 weekly pulse of vincristine and dexamethasone (VCR/DEXA). Patients were randomized to either continuous MP/MTX, or one week rest of 6MP/MTX during the monthly pulse of VCR/DEXA. 

Results: 18 hospitals from 8 cities participated in the study. From 02/2008 to 10/2010, total of 8040 patients were enrolled. The distribution of SR, IR and HR patients were 42.3%, 36.9% and 20.8% respectively. 

Conclusion: The induction death rate and death in CR was low. Relapse rates were not excessive despite treatment reduction. Long term follow up is required to observe the efficacy and toxicity profile.

0077

EARLY MORTALITY IN CHILDHOOD LEUKEMIA’S: DATA FROM THE ARGENTINEAN PEDIATRIC ONCOLOGY REGISTRY ROHA - NATIONAL CANCER INSTITUTE

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Purpose: In addition to aggressive tumor biology, early deaths (ED) in childhood Leukemia may reflect inadequacies in initial supportive care. Leukemia cancer treatments in Argentina are in general well standardized. We report the standardized incidence rate (SIR) and analyzed regional and institutional factors associated with ED in children with Leukemia.

Method: Children with Leukemia who were <15 years old at diagnosis, registered in ROHA between 2000–2008 and for whom information was complete were included. Using multivariate logistic regression analysis we modelled factors associated with ED (within 1 month of diagnosis). 

Results: The SIR for 2000-2008 was 47.5 cases-per-million (n = 4205. Lymphoblastic: 3332, Myeloblastic: 821, Other: 52). There were 243 ED (6.3%) out of 3831 eligible cases of Leukemia. After adjusting by age and gender, and comparing children born in the central region, and diagnosed at high volume patient centers (>60 new pts/yr), children who had an ED were more likely to be from the northeast or northwest regions (OR 1.8 and 1.9; 95%CI 1.2–2.7 and 1.3–2.7 respectively), and diagnosed at medium volume patient centers (21–60 new pts/yr) (OR 1.3; 95%CI 1.0–1.8) compared to those who survived beyond the first month. A 6% yearly reduction in the risk in ED (95%CI 1%–10%) was observed from 2000 to 2008.

Conclusion: While the Leukemia SIR is comparable to that from high income countries ED is higher, although a slightly decreasing trend was observed during the study period. Beyond child’s age and gender, region and diagnosing institution volume are important sources of variation in Leukemia-related ED and indicate disparities probably related to socioeconomic factors as well as training and support capacities. A more accurate understanding and training in supportive care is needed to improve survival in Leukemia.

0078

MTIFR C677T AND A1298C POLYMORPHISMS ARE NOT USEFUL AS TOXICITY PREDICTORS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose: Methotrexate (MTX) is a key component in the treatment of childhood Acute lymphoblastic Leukemia (ALL). Methylene tetrahydrofolate reductase (MTFR) is a central enzyme in the folate acid metabolism, interrupted by methotrexate. The polymorphisms C677T and A1298C are non synonymous aminoacid changes that have been associated with the decreased activity of MTFR. Previous works have associated MTFR 1298C and 677T alleles with MTX toxicity with contradictory results. This lack of replication could be blamed on different factors such as MTX dose given. The aim of the present study was to determine if there was a correlation between MTFR C677T and A1298C polymorphisms and toxicity during therapy with high doses of methotrexate (consolidation) versus low doses (maintenance) in paediatric Spanish ALL patients.

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Method: DNA was extracted from blood samples of 115 pediatric ALL patients treated with the LA/SHOP protocol by standard phenol-chloroform method. We analyzed MTHFR C677T and A1298C polymorphisms by PCR-RFLP, designed and optimized in our laboratory. We analysed the association between the polymorphisms and toxicity using the Fisher exact test (p value < 0.05).

Results: Despite what was expected by the functional effect of both polymorphisms, we found no association with toxicity in children with B-ALL treated with the LA/SHOP protocol. In most studies in pediatric ALL by other authors, they did not find either association with toxicity. The previously observed associations can be explained if we consider that they studied small or heterogeneous samples.

Conclusion: Despite the fact that the functional differences in enzyme activity due to MTHFR C677T and A1298C polymorphisms are not useful to predict toxicity in childhood acute lymphoblastic Leukemia.

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O079

THE GERMLINE GENOMIC VARIANTS IN THE RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN KOREA

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Purpose: Recent western studies have showed the implication of the germline genomic variations in IKZF1 gene at 7p12.12, ARID5B gene at 10q21.2 and CEBPE gene at 1q11.2 on the risk of childhood acute lymphoblastic Leukemia (ALL). The aim of this study is to show the impact of these genetic variants in childhood ALL in Korea.

Method: To examine the association between genetic variations (IKZF1 rs4132601, ARID5B rs7089424, and CEBPE rs2239633) and the risk of childhood ALL, we here analyzed 228 children with ALL and 508 healthy individuals in Korea.

Results: In ARID5B rs7089424, TG and GG genotypes were significantly associated with a risk for ALL (odds ratio [OR], 1.63; 95% confidential interval [CI], 1.07–2.48; P = 0.02 for TG genotype, OR, 2.69; 95% CI, 1.42–5.07; P = 0.002 for GG genotype). The allele incidence of ARID5B rs7089424 was also significantly associated with a risk for ALL (OR, 1.66; 95% CI, 1.24–2.22; P = 0.0068). CEBPE rs2239633 TT genotype showed a significant association with a decreased risk for ALL (OR, 0.54; 95% CI, 0.33–0.89; P = 0.02 for TT genotype). The allele incidence of CEBPE rs2239633 was also associated with a decreased risk for ALL (OR, 0.77; 95% CI, 0.61–0.97; P = 0.02). There was no significant association between IKZF1 rs4132601 polymorphism and a risk for ALL in this study.

Conclusion: These results suggest that genomic variations of ARID5B and CEBPE may play an important role in the risk for childhood ALL in Korea, compared with findings from western countries showing a significant relation between IKZF1 and childhood ALL. Several factors should be considered to explain a discrepancy between our results and the previous studies, which include different genotype frequencies in polymorphisms and varied susceptibility to ALL in different ethnic groups. Further studies incorporating larger number of cases and analyzing other SNPs or other Asian countries are warranted in childhood ALL.

O080

EXPRESSION STATUS OF WD REPEAT DOMAIN 16 (WDR16) PREDICTS PATIENT OUTCOME IN INTRACRANIAL EPENDYMOMA

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Purpose: Ependymoma is a heterogeneous neoplasm of the central nervous system, including tumors with relatively favorable prognosis but also tumors which cannot be treated successfully and therefore remain incurable. Because risk-stratification remains a major clinical challenge, the development of a novel stratification system that enables the prediction of disease risk based on molecular variables is desperately needed. The aim of our study was the identification of a new prognostic biomarker, whose expression status helps to predict clinical outcome in intracranial ependymoma.

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SIOP ABSTRACTS 23

INITIAL HYPOTHALAMIC INVOLVEMENT IS THE MAJOR RISK FACTOR FOR IMPAIRED QUALITY OF LIFE IN CHILDHOOD CRANIOPHARYNGIOMA REGARDLESS OF CHOSEN TREATMENT STRATEGIES - RESULTS OF KRAINO PHYRNGIOMEO 2000

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Purpose: In the SIOP ABSTRACTS 23
recommendations are based on recognizing craniopharyngioma as a chronic disease that initial hypothalamic involvement has an a priori effect on the clinical course, our potential to exacerbate hypothalamic obesity and impaired QoL. Because our results show

Conclusion:

Strategies leading to posterior hypothalamic lesions are not recommended due in independent risk factor for severe obesity (p = 0.033; +2.1BMISD, p = 0.011), negatively impacting QoL in patients with posterior hypothalamic lesions. Surgical strategies varied between the 50 centres (3 large, 24 middle-sized, 23 small centres). Patients treated in small centres in patients with posterior hypothalamic lesions. Surgical strategies varied between the 50 centres (3 large, 24 middle-sized, 23 small centres). Patients treated in small centres presented with a higher rate of hypothalamic involvement compared to middle- and large-sized centres. Treatment in large centres was less radical, the rates of complete resection and hypothalamic surgical lesions lower than those of middle-small-sized centres. However, a multivariable analysis showed that pre-operative hypothalamic involvement was the only independent risk factor for severe obesity (p = 0.002).

Conclusion: Strategies leading to posterior hypothalamic lesions are not recommended due potential to exacerbate hypothalamic obesity and impaired QoL. Because our results show that initial hypothalamic involvement has an a priori effect on the clinical course, our recommendations are based on recognizing craniopharyngioma as a chronic disease requiring experienced multidisciplinary teams in order to provide the best lifetime QoL for the patient.

**O083**

THE UPPER LIMIT OF THE METHOTREXATE (MTX) CSF LEVELS ACHIEVABLE IN CHILDREN WITH BRAIN TUMOURS TREATED WITH HIGH DOSE INTRAVENTRICAL MTX

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Purpose: To examine the correlation between CSF levels of MTX achieved with IV MTX in children with brain tumours.

Method: Matched 24 hour serum and CSF MTX levels were studied after 112 treatments in 38 children with brain tumours.

Results: A trend towards an increase in the 24-hour serum level following increasing doses of MTX was seen but not between the MTX dose and the 24 hour CSF MTX level. There was no correlation between 24 hour serum and CSF levels in both irradiated and non- irradiated patients. All children after radiotherapy had higher MTX levels not related to the dose of MTX used. In patients with no active disease, the CSF levels were not affected by the MTX dose. When disease was present there was no effect of dose but the levels were higher. In patients without disease the 24 hour CSF MTX levels were higher in irradiated children. A slight increase in the 24 hour CSF MTX level was seen only in the non irradiated children with increased doses of MTX. A 24 hour CSF MTX level of at least 1 molar was always achieved after more than 5 g/m2 MTX in previously irradiated children and after 12 g/m2 or more in non irradiated children.

Conclusion: CSF MTX levels plateau and thus the limit value of higher doses of MTX. It is recommended to give 12 g/m2 MTX to children who have not received prior radiotherapy and 6 g/m2 to those who have received radiotherapy, with appropriate folic acid rescue.

**O084**

IDENTIFICATION OF NEW CANDIDATE LOCI IN PROGRESSION OF HEPATOBLASTOMA USING GWAS ANALYSIS

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Purpose: Activation of ß-catenin is a hallmark of hepatoblastoma (HB) and appears to play a crucial role in its pathogenesis. However, while aberrant nuclear accumulation of the ß-catenin is a common event in HB, mutations or deletions in CTNNB1 (the ß-catenin gene) do not always account for the high frequency of protein expression. In this study we have investigated alternative activation of ß-catenin by HGF/C-Met signaling in a large cohort of 98 HB patients enrolled in the SIOPHEL-3 clinical trial.

Method: We performed immunohistochemistry, using antibodies to total ß-catenin and tyrosine654-phosphorylated ß-catenin, which is a good surrogate marker of HGF/C-Met activation. CTNNB1 mutation analysis was also carried out on all samples by direct sequencing.

Results: Sequencing revealed mutations in 15% of our cohort. Aberrant ß-catenin expression was seen in the cytoplasm and/or nucleus of 87% of tumour samples. Our results also revealed a large subset of HB, 83%, with cytoplasmic expression of tyrosine654- phosphorylated ß-catenin and 30% showing additional nuclear accumulation. Statistical analysis showed an association between nuclear expression of c-Met-activated ß-catenin and wild type CTNNB1 (P-value = 0.015). Analysis of total ß-catenin and Y654-ß-catenin in response to HGF activation in the hepatoma cell lines Huh-6 and Huh-7, mirrors that observed in our HB tumour cohort.

Conclusion: Our analysis identifies a significant subset of hepatoblastoma patients for whom targeting of the c-Met pathway with TRK inhibitors may be a treatment option.

**O085**

HGF/C-MET RELATED ACTIVATION OF ß-E-CATENIN IN HEPATOBLASTOMA

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Purpose: Hepatoblastoma (HBL), the most common pediatric liver cancer, may originate from hepatic stem/progenitor cells and demonstrates both low and high grade malignancies such as pure fetal type and undifferentiated small cell types. However, no useful molecular markers except for telomerase activation have been identified. In this study, genome-wide aberrations and expression using microarray were combined to evaluate the mechanism of tumour progression.

Method: Out of 299 HBL cases registered in IPBLT, 96 tumor samples were analyzed by Affymetrix SNP and expression arrays. These microarray data were analyzed by several software’s (CNAG, GTCBrowser, GeneSpring, and Partek). In PRETEXT classification, 9 were I, 29 were II, 34 were III and 22 were IV tumors. Distant metastasis was detected in 16 cases.

Results: The data of SNP array revealed that chromosomal aberrations were observed in 89 cases (93%). Gains in chromosomes 1q, 2q, 7q, 8, 11, 17q, 19, 20, and 22 and losses in chromosomes 4q and 15q, 17q were frequently identified. Insulin-like growth factor II (IGF2), TSSC5 and ORC1L2 genes were included in 11p, while IGFBP1 were involved in 17q gain region. In advanced tumors with metastasis, several types of deletions including 4q, 16p, 17p and 20 were identified. In these loci, TMRPSS11E, TP53, TP53T3G3, and TP53T5G5 were located. Most importantly, gene expression levels of IGF2 TSSC5 and ORC1L2 genes and their target genes were elevated, while TP3 and TP53 target genes were decreased in advanced HBLs. This difference in the gene aberration patterns might influence the clinical features of HBLs.

Conclusion: SNP and expression microarray analysis revealed the main activated pathway in hepatoblastoma. The aberrations of gene dosage might regulate the expression of genes and correlate to tumorigenesis and progression of HBLs. Further analysis of genome aberration provided important candidates of indicators for risk assessment and of therapeutic targets for HBLs.

**O086**

PRETREATMENT PROGNOSTIC FACTORS IN CHILDREN WITH HEPATOBLASTOMAS - A REPORT FROM THE JAPANESE STUDY GROUP FOR PEDIATRIC LIVER TUMOR (JPLT)

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Purpose: Pretreatment staging is a determinant of outcome in hepatoblastoma. The most common pediatric liver cancer, may originate from hepatic stem/progenitor cells and the pathogenic relevance of initial hypothalamic involvement versus treatment-related hypothalamic lesions is a matter of controversy. Body mass index (BMI) and QoL at diagnosis and 36 months after diagnosis were analyzed based on reference assessment of tumour localization and post-surgical hypothalamic lesions using a standardized grading system (no, anterior, posterior involvement/lesion). Treatment was analyzed regarding strategy of 50 participating neurosurgical centres and the centre size. Based on patient load during the 6-year recruitment period, centres were categorized as small (1-5 patients/6 yrs), middle (2-5 patients/6 yrs) or large-sized centres (> 5 patients/6 yrs).

Results: BMISDS at diagnosis was similar in patients with/without hypothalamic involvement. Surgical lesions of anterior/posterior hypothalamic areas were associated with increases in BMISDS during 36 months post-diagnosis compared to patients without or only anterior lesion (+1.8BMISD, p = 0.033; +2.1BMISD, p = 0.011), negatively impacting QoL in patients with posterior hypothalamic lesions. Surgical strategies varied between the 50 centres (3 large, 24 middle-sized, 23 small centres). Patients treated in small centres presented with a higher rate of hypothalamic involvement compared to middle- and large-sized centres. Treatment in large centres was less radical, the rates of complete resection and hypothalamic surgical lesions lower than those of middle-small-sized centres. However, a multivariable analysis showed that pre-operative hypothalamic involvement was the only independent risk factor for severe obesity (p = 0.002).

Conclusion: Strategies leading to posterior hypothalamic lesions are not recommended due potential to exacerbate hypothalamic obesity and impaired QoL. Because our results show that initial hypothalamic involvement has an a priori effect on the clinical course, our recommendations are based on recognizing craniopharyngioma as a chronic disease requiring experienced multidisciplinary teams in order to provide the best lifetime QoL for the patient.
O087

PROPRANOLOL IN HEMANGIOMAS: GROWING EXPERIENCE IN 31 CASES IN A SINGLE INSTITUTE

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Purpose: Numerous reports has been published regarding the efficacy and safety of propranolol in infantile hemangiomas since introduction of this drug in this indication. The aim of this study was to analyse efficacy and safety of propranolol in a larger population after preliminary experience in our institute.

Method: All consecutive patients with hemangiomas in proliferative phase with an indication for treatment were included into this analysis. Basal complete blood count, serum biochemistry, echocardiography were obtained in all patients. Starting dose ranged from 2 – 3 mg/kg/day and included cases were treated with a minimum of 6 weeks. Steroid was added to propranolol in selected cases. Treatment response was recorded both by early and late response criteria. Retrospective records of vital signs during initial treatment and recorded adverse events were examined.

Results: Between September 2009 and January 2011, 31 cases with hemangiomas were retrospectively examined. There were 23 girls. Median age was 6.43 months. The gestational age of was under 37 weeks in 35.5%. Birth weight range was between 830 – 4000 gr. Indications for treatment were rapid growth, ulceration, infection, cosmetic issues, bleeding, breathing, feeding and ocular problems and compartment syndrome. Mean treatment duration was 6.1 months (1.8 – 14.6 months). Steroid was started concurrently with propranolol in 5 cases, and later added to treatment in 2. Treatment response was observed as early as 24 hours, and 48.4% of cases within 15 days. Adverse events resulting in interruption or cessation of treatment were Bradicardia in 1, bronchiolitis in 2, hypoglycemic seizure in 1 patient. Dramatic results were obtained in fascial, respiratory tract and liver hemangiomas.

Conclusion: Growing experience in hemangiomas revealed satisfactory results in majority of cases especially alarming ones. Special attention must be paid for substantial adverse events and education of the family for recognition of them is necessary.

O088

THE UTILITY OF AN AUSTRALASIAN REGISTRY OF CHILDREN TREATED BY RADIATION

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Purpose: To assess the utility of a population based Registry for children undergoing radiation treatment (RT).

Method: From January 1997, a prospective Registry has recorded each episode of RT given to a child < 16 years old in Australia and New Zealand (ANZ). We interrogated the Registry to determine the number of children treated by RT at the various institutions over time, as well as their age at diagnosis, tumour diagnosis, treatment intent and enrolment on a clinical trial.

Results: There were 1734 children enrolled in the 14 years to 31 December 2010, and 1968 episodes of RT. Five Australian institutions enrolled the majority of patients (1505/1734, 87%). Two large centres in ANZ have enrolled patients irregularly due to lack of resources. The most prevalent diagnoses were acute lymphoblastic leukemia (354/1734, 20%), medulloblastoma (167/1734, 9.6%), neuroblastoma (147/1734, 8.5%) and rhabdomyosarcoma (126/1734, 7.3%). The majority of children were > 5 years of age at RT (1421/1734, 72%), although around one in 10 were less than three (214/1734). 343 RT courses were given with palliative intent. Just under half of children were enrolled on a clinical trial (776/1734, 45%).

Conclusion: While identifying numbers of children who receive RT in ANZ, their demographics and basic RT information, the Registry provides only a description of patterns of RT care for children. This is useful for planning RT resources, including training and education in paediatric RT in ANZ. Registry enrolment must be comprehensive, and linked to outcomes including relapse patterns, survival and late effects to achieve the Registry’s greatest potential. Suitable aspects for evaluation are the efficacy of palliative RT in children, and patterns of failure in neuroblastoma and rhabdomyosarcoma according to RT parameters in a population of possibly heterogeneously managed children.

Acknowledgement: On behalf of the Paediatric Special Interest Group of the Royal ANZ College of Radiologists.

O089

OVEREXPRESSION OF THE HYPOXIA-RELATED GENES HIF1A, HIF2A, C9A, CA12, SLC2A1 AND VEGF IS ASSOCIATED WITH RADIOREISTANCE IN HUMAN CANKERS IN VITRO AND IN VIVO STUDIES.

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Purpose: The aim of the present study was to evaluate the effect of radiation in cell lines expressing high (U-343) and low (REH) levels of the hypoxia-related genes CA9, CA12, VEGF, SLC2A1, HIF1A and HIF2A. Additionally we analyzed the mRNA expression levels of these genes in diagnosis samples of radioresistant (glioblastoma) and radiosensitive (acute lymphoblastic Leukemia and medulloblastomas) human cancers.

Method: We used ionizing radiation in a single dose for 2 Gy and 6 Gy fractions in 2 cell lines (U-343 - glioblastoma) and (REH - acute lymphoblastic Leukemia). DNA damage was analyzed by comet assay and apoptosis by fluorescence technique. mRNA expression levels of the hypoxia-related genes were analyzed by real-time quantitative-PCR in the cell lines and in 35 microdissected samples of primary glioblastomas (children/adults), 15 childhood medulloblastomas and 15 childhood ALL samples and the expression levels were compared by the Mann-Whitney test.

Results: All REH cells were apoptotic/necrotic and more than 85% of U-343 cells were viable on day 7 to both radiation doses. We observed an increase of the DNA damage scores by the comet assay since 48 hours to REH cells. No score increase was observed to U343 cells. The gene expression levels were higher in samples of glioblastoma when compared to medulloblastomas to genes CA9 (p<0.0001), CA12 (p<0.0001), VEGF (p<0.0001), HIF2A (p<0.0002) and SLC2A1 (p: 0.01). The expression levels were higher also in glioblastoma when compared to Leukemia to genes CA9 (p<0.0001), CA12 (p<0.0006), VEGF (p<0.0001), HIF2A (p<0.0001) and HIF1A (p: 0.01). A higher expression level of the VEGF (p<0.0001), HIF2A (p: 0.01) and CA9 (p: 0.04) genes was observed in medulloblastoma when compared to Leukemia samples.

Conclusion: Our results suggest that the hypoxia-related genes analyzed could be related to radioresistance and are potential treatment targets in human cancers.

O090

PEDIATRIC MUCOEPIDERMOID CARCINOMAS OF THE SALIVARY GLANDS: IMPLICATIONS ON RADIATION

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Purpose: To evaluate the need of adjuvant radiation in pediatric mucoepidermoid carcinomas of the salivary glands.

Method: Between 1986 and 2016, all the histologically confirmed pediatric mucoepidermoid carcinomas of the salivary glands were analyzed at the Department of Pediatric Hematology and Oncology of the CHRU Montpellier. The decision to perform an adjuvant radiation therapy was based on the evaluation of the risk factors of local failure and/or regional metastases.

Results: A total of 14 patients were included in the study. The median age at diagnosis was 13 years (range: 2 – 18). The median follow-up was 5 years (range: 0.5 – 16). Nine patients were referred for relapse, and 5 for prophylaxis. The median tumor size was 7 cm (range: 3 – 17). Two patients had local recurrence, and 1 had regional metastasis. The median RT dose was 50 Gy (range: 44 – 54). The 3-year overall survival was 100% (95% CI: 80% – 100%). No acute or late complications were observed.

Conclusion: Our results suggest that adjuvant radiation therapy is not necessary in pediatric mucoepidermoid carcinomas of the salivary glands, except in selected cases with high risk factors. Further studies are needed to confirm these findings.
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SIOP ABSTRACTS

1. Factors against risks of growth defect & cancer.
   Conclusion: Most tumors are low grade and good prognosis. RT can be recommended for high-grade and/or T3-4 & discussed in other adult cases. We investigated the role of RT in children.

2. Method: This survey was conducted in 34 departments between 1980 & 2010.
   Results: Among 38 patients (median age 14; 51% male), 36% & 25% had a history of cancer & RT, respectively. Tumors involved the parotid, submandibular & minor salivary gland in 82%, 10% & 8%, respectively. Tumors were of high, intermediate & low grade in 14%, 19% & 67%, respectively. Stages were 83% & 17% for T1-2 & T3-4 respectively with median size of 2.5 cm. 11% were node-positive, none were metastatic. All but one underwent surgery, 79% with clear margins, 13% with nerve sacrifice. Neck dissection was performed in 52%, RT (23%) in 17%, 1% & 75% of grade 1, 2 & 3 tumors, respectively: 22%, 14%, 50%, 67% of T1, 2, 3 & 4 tumors, respectively & in 22% following prior irradiation vs 25%. The overall, local, regional & metastatic relapse rates were 19%, 16%, 3% & 3%, respectively. Most patients (94%) were alive with mean follow-up of 71 months. 3% died of MEC. Adverse prognosis factors included perineural invasion, vascular emboli & bone involvement in 19%, 13% & 3%, respectively. Local relapse occurred in 17% of patients undergoing RT & 24% without (NS). Given similar local control rates within T3-4 and high grade MEC, RT probably added a benefit in this subset.
   Conclusion: Most tumors are low grade and good prognosis. RT can be recommended for high grade MEC but should be weighted in low/intermediate grades with poor prognosis factors against risks of growth defect & cancer.

0091

RADIOLOGICAL DIAGNOSIS OF INTRAPARAVERTEBRAL NEUROGENIC TUMORS IN CHILDREN

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Purpose: To research characteristic features of intraparavertebral neurogenic tumors in children.

Method: An analysis of 69 (100%) children aged from 3 months to 15 years with intraparavertebral neurogenic tumors. This group consisted of benign neurogenic tumors (ganglioneuroma) 10(14.4%) and malignant neurogenic tumors 59 (85.6%) of them are neuroblastoma (75.4%) and ganglioneuroblastoma (10.2%). All children (100%) carried out X-ray chest cavity, ultrasound mediastinum 25(36.2%) and soft tissue back 34(49.3%), abdominal ultrasound the and retroperitoneal space 26(37.7%), CT of the chest 20(28.9%), angiographic abdominal CT 12(17.4%), spine MRI 17(24.6%).

Results: Neurogenic tumors in children revealed cervical 2(2.9%), thoracic 39(56.5%), lumbar 26(37.7%), sacral 2(2.9%) level of the spine. All neurogenic tumors were located in the paravertebral areas, adjacent to the vertebrae, had intra- and paravertebral components, interconnected through the intervertebral foramens. Neurogenic tumors had oval shape 47(68.1%), bone pressure atrophy 35(50.7%) and besides 10 cases of them was ganglioneuroma; neurogenic tumors increased distance between the transverse processes of vertebrae 37(53.6%), had calcinates 35(50.7%).

Conclusion: Intraparavertebral neurogenic tumors in children have the characteristic features: they revealed at any level of the spinal column in the paravertebral areas, often at the thoracic level. Neurogenic tumors in children have the right oval shape form with calcinates, cause pressure atrophy of vertebrae, increased distance between the transverse processes of vertebrae.

0092

DEVELOPMENT OF CYTOTOXIC COMPETENCY STANDARDS

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Purpose: Cytotoxic agents are considered hazardous to healthcare workers and so exposure must be minimised. Occupational exposure may occur during preparation, administration or disposal of these agents. Specifically the accidental release of these agents can occur when expelling air from syringes/needles, spiking, priming or changing IV lines. Contact with cytotoxic agents can also occur when handling leaking tubing or connection sites, spills or handling waste from a patient who has received chemotherapy. All staff involved in handling cytotoxic agents should undergo specific education and training, to protect themselves, colleagues, patients and families. The patients and family also require support and education.

Method: A literature review was undertaken on safe handling standards/policies and a clinical audit was carried out ensuring correct safety precautions were being followed when handling cytotoxic agents and waste. The need for a set of competencies for administration was identified and these were developed using an evidence informed approach.

Results: We have developed 3 competencies in relation to Cytotoxic Handling: Cytotoxic Competent RN (CCRN) Stage 1, CCRN Stage 2, and CCRN Stage 3. The competencies cover administration, education of patients/family, handling of waste, spills and extravasation.

Conclusion: A practice gap was identified through auditing procedures and a literature review. Due to the nature of and complexity of cytotoxic drugs and waste handling, competency standards were developed. Competencies are currently being implemented on the ward. Competency evaluation will be presented at the conference.

0093

STANDARDS FOR ADMINISTRATION OF CYTOTOXIC/BIOOTHERAPY AGENTS

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Purpose: A growing number of cytotoxic and biotherapy agents have been and continue to be introduced for use in paediatric oncology. These agents have very specific requirements for each individual therapy. There was an increased demand for nursing guidelines on safe administration and patient care. It was also recognised that administering these agents require knowledge of the specific care, including education of the patient and/or patient’s family, receiving the cytotoxic or biotherapy agent. In response, Standard Operating Procedures (SOP’s) were developed and evaluated.

Method: This Quality Improvement activity included the development of standards and their evaluation. Standards of drug administration and care were developed using recommendations from pharmaceutical guidelines which were evidenced based. Nursing, pharmacy and medical opinion was sought to develop the patient management and education regimes for each SOP. A pre and post test was undertaken for two of the SOP’s to evaluate nurse’s knowledge. The post knowledge tests also allowed nurses to comment on the SOP. Comments have been grouped into themes for reporting.

Results: The evaluation demonstrated that SOP’s have been useful reference guides that assist nursing and medical staff in administering cytotoxic and biotherapy agents. There was a statistically significant increase in the mean scores of post tests for the two SOP’s evaluated. The results demonstrated that SOP’s improved knowledge and understanding of the care required for patients receiving the specific therapy.

Conclusion: Standard Operating Procedures have become embedded in our practice for the administration and care of patients receiving cytotoxic and biotherapy agents. The standards recognise that specialist skills and knowledge around the safe administration and ongoing care that is required when delivering these agents. SOP’s are not just another drug administration manual, more a reference guide for skilled clinicians around the care and management of paediatric patients receiving cytotoxic and biotherapy agents.

0094

THE SAFETY AND RISK OF ADMINISTERING IV VINCristINE BY BOLUS IN AN INSTITUTION DELIVERING INTRATHECAL THERAPY

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Purpose: 20 years ago in Western Australia an inadvertent administration of Intrathecal Vincristine occurred resulting in the worst outcome - death of a patient. Many practice and process changes were made at the time. This has become a national and international safety issue with recommendations being widely published. In response, several Australian and New Zealand Institutions moved from IV bolus to mini-bag infusions of Vincristine for the Paediatric patient. Western Australia was unique in their process changes of Vincristine administration. Consensus to change to mini bag infusion has not been reached. It is therefore pertinent to evaluate the safety and cost of both administration methods, utilising an evidence based approach for the safe administration of Vincristine in an institution who also administers Intrathecal therapy.

Method: A multi-faceted information and audit approach was used. This included direct cost comparison between the two techniques, nursing time/patient contact time for the procedure, total number of administration of IV Vincristine in a 12 month period, scientific risk assessment and incident data.

Results: Data on procedural time showed: Intravenous bolus mean time is 12.89 minutes (n = 38), Intravenous Infusion mean time is 40.94 minutes (n = 75). Total administrations averaged over 2 years = 11565y. This equated to 32 426 more hospital contact hours for the infusion technique. The cost comparison showed a fourfold increase in consumable costs for mini bag delivery.

Conclusion: Cost can never be the only consideration following a sentinel outcome. As scientific risk assessment is currently underway, we are asking, can the existing changes be considered an alternative to mini-bag administration ensuring the same, better risk ratio for our patients?
OFF-LABEL AND UNLICENSED USE IN A PEDIATRIC HEMATO-ONCOLOGY UNIT

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Purpose: A significant number of drugs used in pediatric hematologic oncology have not been specifically developed or assessed for use in this population. This is of major concern as pharmacological data cannot be extrapolated from adults to children as such. As a consequence, the drugs are either not licensed for use in this population (unlicensed) or are prescribed outside the terms of their product license (off-label). Although many reports describe the extent of off-label and unlicensed use in pediatrics and neonatology, only few publications highlight the importance of the problem in pediatric hematologic oncology.

Method: A prospective, observational cohort-study (11 non-consecutive weeks) in hospitalized patients (Ghent University Hospital, Belgium). Prescriptions were analyzed and classified according to the classification of Turner.

Results: A total of 83 patients, representing 1918 prescriptions, were analyzed. Of these, 243 (∼12.7%) were classified as unlicensed. Pharmaceutical preparations and import of medication were responsible for 86.4%, respectively 13.6%. Pharmacological groups most frequently involved according to the classification of Turner were antibiotics (36%), corticosteroids (10.8%) and antibiotics (12.2%). Off-label use was observed in 917 out of 1675 (54.7%) licensed prescriptions. Remarkably, 41.9% was classified as off-label in terms of dose, followed by age (23.2%), administration frequency (12.8%), indication (11.5%) or alternative route of administration (10.7%). Pharmacological groups most frequently prescribed off-label were cytotoxics (57.7% out of all cytotoxics), followed by antibiotics (71.4%) and corticosteroids (70%).

Conclusion: The data obtained in this study (representing a large population) are comparable with those from literature data. The study confirms the urgent need for public discussion of off-label and unlicensed drug use issues to develop appropriate policies, also because of liability and reimbursement problems. Cooperation between the pharmaceutical companies, regulatory authorities and health-care professionals is essential and required to ensure a safe, effective and high quality drug therapy in pediatric hematologic oncology.


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Purpose: HDM has been used for forty years in the Nordic countries in the treatment of childhood ALL. From NOPHO ALL-92 to ALL-2008 there have been a change from 5 g/m2 in low-risk ALL to 6 g/m2. High risk given as a 24 hours infusion followed by folinic acid rescue at hour 36 and then onwards at 6 hours intervals until the plasma MTX concentration is < 0.2 μM to only 5 g/m2 with rescue at 42 h. To explore HD-MTX pharmacokinetic, elimination time, nephrotoxicity and toxicity - MTX concentrations, LV doses, creatinine, dates and times were collected from the patients in Denmark, Finland, Norway and Sweden.

Method: Data on all children with ALL in the Nordic countries are registered in the NOPHO database, from which basic demographic and prognostic information and follow-up are obtained. Of the 2735 patients during the observation period 1992–2008 treated by NOPHO ALL-92/2000 detailed data on treatment were collected from 1862 patient. Practically all HDM treatments from ALL-2000 in Denmark and Sweden were collected. The relationship between time to relapse and different exposure variables (serum methotrexate 23, 36 and 42 h after start of administration, MTX-elimination time and folinic acid doses (FA)) were analyzed.

Results: There was a pronounced intravariability for both FA dose and Mtx23. Results suggest that high FA doses during HDM increase the risk for relapse in children treated for ALL. The negative influence of high FA doses on relapse was obtained despite the fact that they correlated with high MTX levels at 23, 36 and 42 h and longer elimination time which, anything else alike, are expected to give a better prognosis. Oversolving of FA appears to overcome the presumed beneficial effects of high MTX concentrations.

Conclusion: The choice of MTX and FA doses may be regarded as an intricate balance between effect and counter-effect.

THE USE OF GLUCARPIDASE (CARBOXYPEPTIDASE G2 - VORAXAZE®) IN HIGH-DOSE METHOTREXATE TREATMENTS IN NOPHO ALL-2008

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Purpose: HDM-induced nephrotoxicity is a medical emergency. Renal methotrexate excretion is delayed resulting in prolonged exposure to high methotrexate concentrations. The duration of exposure is the primary determinant of the drug’s toxic effects. Early recognition and prompt efforts to lower methotrexate concentrations are critical to preventing severe systemic toxicity. HDM-induced renal dysfunction is signaled by an increasing serum creatinine concentration during or shortly after the methotrexate infusion. In NOPHO ALL-2008 it was decided to use Glucarpidase that rapidly lowers the serum methotrexate concentration by providing an alternative route of elimination, to prevent the toxic effects of HDM.

Method: In ALL-2008 it was recommended to give Glucarpidase if the 24 hour levels of MTX was > 250, 36 hour levels > 20 or 42 hours levels > 10 μM together with a reduced kidney function. Glucarpidase should optimal take place within 48 hours.

Results: Until now Glucarpidase has been used 17 times (app 3% of patients), 14 times according to the ALL-2008 protocol. Median age 9 (range 3–18) at time point 44.5 (32–61) at a dose of 50 unit/kg (31–57). Elimination time to cMx ≤0.20 μM was 231 hours (54–336). Max creatinine 167 μM (86–303). Urine output was maintained despite a rapid decline in glomerular filtration. None of the patients suffered from other MTX-toxicity. A clinical problem is that most commercial methotrexate assays will underestimate the impact of Glucarpidase on serum methotrexate concentrations because of the interference by the inactive by-product, DAMPA, leading to folinic acid over-rescue during the minimal 2 days DAMPA circulates in the bloodstream. Failure to recognize the interference could lead to even further unnecessary Glucarpidase and potentially harmful interventions.

Conclusion: Glucarpidase rapidly and efficiently lowers the serum methotrexate concentration by providing an alternative route of elimination and, when administered as soon as possible after the recognition of nephrotoxicity, can effectively prevent methotrexate toxicity.

References:

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Purpose: Event-free survival (EFS) for patients with late (CR1 > 18 mo) isolated CNS relapse of ALL has improved with intensive systemic chemotherapy and delayed CNS radiation. However, bone marrow (BM) relapse and radiation related morbidity remain major causes of treatment failure and long-term sequelae, respectively. The purpose of this study was to prevent BM relapse using intensive systemic chemotherapy and to decrease long-term neuropsychological sequelae by reducing cranial radiation (CRT) to 12 Gy. BM minimal residual disease (MRD) was determined at study entry.

Method: One hundred-eighteen patients with first isolated CNS relapse of ALL were enrolled. Pre-radiation chemotherapy included systemic agents with effective CNS penetration. Induction (dexamethasone, VCR, daunomycin and triple intra-arterial chemotherapy- ITT), was followed by consolidation (high-dose ARAC [3 g/m2]/PEG-asparaginase), intensification phases (CTX/VP-16, high-dose MTX [5 g/m2]/6-MP, high-dose ARAC [3 g/m2]/PEG-asparaginase) and reinduction. Concomitant ITT was given as CNS directed therapy. CRT (12 Gy) was scheduled to be given at 12 months. Maintenance therapy included dexamethasone pulses every 10 weeks followed by weekly MTX/6-MP alternating with CTX/VP-16.

Results: At study entry, 1579 patients (19%) had detectable BM MRD using flow-cytometry. Fifty two percent of patients experienced significant delays (>14 mo) in receiving CRT on schedule. There was a high incidence of myelosuppression but few other severe toxicities. Overall 3-year EFS was 58 ± 7% (n=118). NCI standard-risk and NCI high-risk patients had a 3-year EFS of 62 ± 8% (n=75) and 48 ± 15% (n=41), respectively. Treatment failure resulted mainly from late 7-26/62 mo and in 16/26.

Conclusion: Intensified systemic chemotherapy with reduced dose (12 Gy) CRT was inferior to a similar regimen plus 18 Gy of CRT (POG-9412 4-year EFS 77 ± 6%) for children with late isolated CNS relapse. The reduction in efficacy may reflect the lower dose of CRT or the

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delay in its delivery. New approaches are needed to prevent relapse while allowing further CRT dose reductions.

Q099
ABSENCE OF GLOBAL HYPMETHYLATION IN PROMOTER HYPERMETHYLATED MLL-REARRANGED INFANT ACUTE LYMPHOBLASTIC LEUKEMIA
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Purpose: MLL-rearranged acute lymphoblastic Leukemia (ALL) in infants represents one of the most aggressive types of childhood Leukemia as reflected by high incidence of early relapses. The majority of MLL-rearranged infant ALL cases display severe promoter CpG island hypermethylation. The general and dogmatic believe in current epigenetics dictates that gene promoter hypermethylation is accompanied by DNA hypomethylation in non-promoter regions of the genome.

Method: In this respect we examined global methylation densities in MLL-rearranged infant ALL using high-resolution bisulfite pyrosequencing on the repetitive elements LINE-1, Alu, and SAT-1 as surrogate markers for global methylation.

Results: Interestingly, we found that MLL-rearranged infant ALL is not characterized by global hypomethylation, despite its characteristic gene promoter CpG methylation patterns. Instead, compared to normal bone marrow samples, we observed a modest but consistent trend towards increased levels of global methylation. We recently showed that exposure of MLL-rearranged ALL cells to DNA methyl transferase (DNMT) inhibitors (like zebularine and decitabine) leads to demethylation of hypermethylated gene promoters and reactivation of transcription. Moreover, compared with other ALL subtypes, MLL-rearranged ALL cells appeared to be highly sensitive to these drugs, effectively eliminating the vast majority of leukemic cells in vitro. Therefore we asked whether the observed repetitive element methylation in MLL-rearranged ALL is also affected by demethylating compounds. To study this, repetitive element methylation was assessed in two t(4;11)-positive B-ALL cell line models exposed to the demethylating agents zebularine and decitabine. We found that all repetitive elements were effectively demethylated to comparable methylation densities as observed in healthy bone marrow samples.

Conclusion: Thus, MLL-rearranged infant ALL cells are characterized by an overall methylated genomic state and both promoter and non-promoter methylation respond to demethylating agents. We postulate that the lack of global hypomethylation in these cells is of additional therapeutic value providing supplementary targets to disturb epigenetic deregulation.

Q010
HDAC INHIBITORS SILENCE HYPMETHYLATED PROTO-ONCOGENES AND EFFECTIVELY INDUCE LEUKEMIC CELL DEATH IN T(4;11)-POSITIVE INFANT ALL
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Purpose: MLL-rearranged infant acute lymphoblastic Leukemia (ALL) represents an aggressive type of childhood Leukemia and the development of more effective treatment strategies remains a major challenge. Recently we demonstrated that MLL-rearranged infant ALL is characterized by distinct genome-wide DNA methylation patterns. This study showed that the majority of these patients display high levels of promoter methylation leading to silenced transcription. However, besides vast amounts of hypermethylated gene promoters, we also found numerous genes to be hypomethylated and highly expressed, including that the majority of these patients display high levels of promoter methylation leading to aggressive type of childhood Leukemia and the development of more effective treatment.

Method: On this basis, we also found numerous genes to be hypomethylated and highly expressed, including that the majority of these patients display high levels of promoter methylation leading to aggressive type of childhood Leukemia and the development of more effective treatment.

Conclusion: Given the presented potential of HDAC inhibitors to target important proto-oncogenes including the Leukemia-driving MLL fusion in vitro, these agents should urgently be tested in vivo models and subsequent clinical trials.
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Method: Patterns of skeletal 123I mIBG uptake were assigned numerical scores (Mscore) ranging from 0 (no metastasis) to 72 (diffuse metastases) within 12 body areas as described previously. Anonymised, paired image data sets acquired at diagnosis and at completion of Rapid COJEC induction chemotherapy were reviewed, constituting a representative sample of 1602 children treated prospectively within the HR-NBL1/SIOPEN trial. Pre-and post-treatment Mscores were compared with bone marrow cytology (BM) and 3 year event free survival (EFS).

Results: Results 224/271 patients showed skeletal MIBG uptake at diagnosis and were evaluable for MIBG-response. Complete response (CR) on MIBG to Rapid COJEC induction was achieved by 66%, 34% and 15% of patients who had pre-treatment Mscores of < 18 (n = 65.9%), 18–44 (n = 95.42%) and > 44 (n = 64.28%) respectively (chi squared test p < 0.0001). Mscore at diagnosis and on completion of Rapid COJEC correlated strongly with BM involvement (p < 0.001). The correlation of pre score with post scores and response was highly significant (p < 0.001). Most importantly, the 3 year EFS in 47 children with Mscore 0 at diagnosis was 76.8% (90.07), by comparison with a median of 0.42 (A0.05), 0.35 (A0.05) and 0.25 (A0.06) for patients in pre-treatment score groups < 18, 18–44 and > 45, respectively (p < 0.001). An Mscore threshold of 45 at diagnosis was associated with significantly worse outcome by comparison with all other Mscore groups (p = 0.029). The 3 year EFS of 0.53 (A0.07) of patients in metastatic CR (mIBG and BM) after Rapid COjic (33%) is clearly superior to patients not achieving metastatic CR (0.24 (A0.04), p = 0.005).

Conclusion: SIOPEN scoring of 123I mIBG imaging has been shown to predict response to induction chemotherapy and outcome at diagnosis in children with HR-N.

O103

BULSUPHAN-MELPHALAN IS THE SUPERIOR MYELOABLATIVE THERAPY (MAT) FOR HIGH RISK NEUROBLASTOMA: RESULTS FROM THE HR-NBL1/SIOPEN TRIAL.

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Purpose: The HR-NBL1 trial of the European SIOP Neuroblastoma Group randomised 2 MAT regimens to demonstrate superiority based on event free survival (EFS). The HR-NBL1 trial randomised (296 BuMel, 302 CEM). The median age at randomisation was 3 years (1.2–4.1) day*. *reduced if GFR < 70 mg/m²/day. 

Results: Results of 605 patients with evaluable for MIBG-response. Complete response (CR) on MIBG to Rapid COJEC induction was achieved by 66%, 34% and 15% of patients who had pre-treatment Mscores of < 18 (n = 65.9%), 18–44 (n = 95.42%) and > 44 (n = 64.28%) respectively (chi squared test p < 0.0001). Mscore at diagnosis and on completion of Rapid COJEC correlated strongly with BM involvement (p < 0.001). The correlation of pre score with post scores and response was highly significant (p < 0.001). Most importantly, the 3 year EFS in 47 children with Mscore 0 at diagnosis was 76.8% (90.07), by comparison with a median of 0.42 (A0.05), 0.35 (A0.05) and 0.25 (A0.06) for patients in pre-treatment score groups < 18, 18–44 and > 45, respectively (p < 0.001). An Mscore threshold of 45 at diagnosis was associated with significantly worse outcome by comparison with all other Mscore groups (p = 0.029). The 3 year EFS of 0.53 (A0.07) of patients in metastatic CR (mIBG and BM) after Rapid COjic (33%) is clearly superior to patients not achieving metastatic CR (0.24 (A0.04), p = 0.005).

Conclusion: SIOPEN scoring of 123I mIBG imaging has been shown to predict response to induction chemotherapy and outcome at diagnosis in children with HR-N.

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ADVANCING DIAGNOSIS AND TREATMENT OF NEUROBLASTOMA FOR CHILDREN IN LOW INCOME COUNTRIES (LIC) VIA WEB-BASED TUMOR BOARD PLATFORM

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Purpose: Outcomes in children with neuroblastoma (NB) have steadily improved in developed nations, however, 85% of the world’s children live in low-income countries (LIC), where significant challenges remain. Literature reviews report wide global differences in treatment strategies for neuroblastoma. Project aims: 1. Establish a web-based tumor board (WTB) facilitating clinicians in LIC to discuss challenging patients with neuroblastoma in real time. 2. Assess the needs/limitations of care for children in LIC. 3. Foster global dialogue & collaboration to help develop clinical standards and research in LIC.

Method: A monthly, WTB was set up using the www.cure4kids.org platform. Participating institutions present their patients for discussion. Patient demographics, diagnostic evaluations, pathology review, initial treatment considerations, alteration in management based on WTB discussions, resource limitations, and prospective follow-ups are recorded.

Results: Within our first year, participation has increased from 7 to 62 members, from 25 countries. To date, 15 cases have been presented. Median participation/conference was 10. In 60% of cases no N-MYC data was available. Additional challenges identified were: infrastructure limitations for supportive care, nutrition support, and treatment options due to cost/viability of medications. Collaborative discussions regarding research projects have begun via this forum.

Conclusion: To date, we are able to show that a multidisciplinary WTB has resulted in refining treatment plans for numerous patients with NB. We are prospectively identifying limitations in specific low-income locales and have initiated dialogue to plan research projects in an international setting. A developing project in India will standardize testing for N-MYC amplification and provide treatment guidelines based on this critical risk factor. Future plans include working with SIOP-PODC in developing graduated intensity treatment guidelines for low/intermediate and high risk NB in LIC.

O105

DATA FROM AN ITALIAN OBSERVATIONAL STUDY ON PERINATALLY DIAGNOSED SUPRAARENAL LESIONS (JANUARY 2008–DECEMBER 2009)

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Purpose: To study frequency, features and clinical outcome, according to a “wait and see” initial approach, of pre/perinatal expansivne supraparenal lesions, diagnosed by rising alpha fetal protein (AFP) levels and ultrasound surveillance.


Conclusion: BuMel was demonstrated to be superior to CEM and hence is recommended as standard treatment.
and/or metabolic symptoms requesting early surgery, no neuroblastoma stage 4–S, parents’ informed consent.

**Results:** Thirty-eight cases were recruited from 16 centers: 65.7% males, 52.6% prenatal diagnosis, 57.9% left adrenal gland, max Ø 50 mm (range 8–50). US diagnosis was made in all cases. TC was performed in 11 patients, RMI in 8, MIBG in 9 (6 positive). Biochemical pathological values were: urinary catecholamines in 3/32 patients, LDH in 9/29, Ferritin in 12/25. In 6 cases associated pathologies were diagnosed. All but one patient completed 30th week follow-up. We observed complete spontaneous vanishing in 17 cases (range 4–30 weeks, med. 15 w) and partial regression in 14 patients, with stable lesion (max Ø < 15 mm) at 30th week. Six cases went through surgery for disease progression (5 NB, 1 splenic cyst). All patients are alive, with 21 months median follow-up (range 12–34 months).

**Conclusion:** ‘‘Wait and see’’ approach reduces diagnostic and surgical invasive procedures in the first months of life, for small lesions with a tendency to spontaneous regression and generally benign behaviour also in case of neuroblastoma. Radiological criteria are still unable to discriminate lesion type: images centralization advisable to identify regression predictive criteria, if any.

**0106**

**ESTHESIONEUBROBLASTOMA IN PEDIATRIC AGE. A REPORT FROM THE TREP PROJECT IN COLLABORATION WITH THE ITALIAN NBL AND STS COMMITTEES**

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**Purpose:** Esthesioneuroblastoma (ENBL) is a rare tumor accounting for 3–4% of all intranasal tumors with two peaks of incidence at 11–20 and 50–60 years old. It seems more aggressive in children, who have advanced disease at presentation more frequently than adults. As treatment is based mainly on experience gathered in adults, we retrospectively analyzed a series of patients treated at the AIEOP centers.

**Method:** From 1980 to 2010, 11 pediatric patients were treated for ENBL, but data were only available for 9 (6 males, age 0.9–18 years, median 9.9). All tumors were located in the sinonasal region, with one erosion extending intracranially (3 pts) or intraorbitally (3 patients). The Kadish stage was C in 7 patients and B in 2.

**Results:** Chemotherapy was based mainly on the ifosfamide/cyclophosphamide combination plus doxorubicin and vincristine. A major tumor reduction was evident after initial chemotherapy in 4/6 evaluable cases. Only one patient underwent complete tumor resection. Radiotherapy (48.5-60 Gy) was delivered to all children (but only after relapse in one very young child). With a median 13.4 years of follow-up (range 9 to 22.9) 7 patients are alive in 1st and in 2nd complete remission. One patient presented disease progression and the child died 9 months after diagnosis.

**Conclusion:** We confirm that ENBL has aggressive characteristics in pediatric age, but a multimodal approach, based mainly on chemotherapy and radiotherapy, can cure most patients. Our results are encouraging but more data are needed to optimize strategies for pediatric ENBL in terms of both survival and treatment morbidity.

**0107**

**NORDIC RECOMMENDATIONS ON FERTILITY PRESERVATION FOR BOYS AND YOUNG MEN**

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**Purpose:** Unfortunately, fertility preservation for patients with newly-diagnosed cancer is a neglected issue. Boys, who are facing treatments associated with a very high risk of infertility, could be offered the experimental procedure of testicular biopsy cryopreservation. At present, there are no methods to ensure fertility after such procedures, thus further research is warranted. Since the patient number is limited, the cryopreservation and research should be centralized.

**Conclusion:** NA
Conclusion: We demonstrate that appreiant administered to children older than 10 years is safe. Appreiant is effective in preventing or reducing CINV in teenagers receiving moderate/high dose chemotherapy. This improved the care of patients with paroxysmal dysphoria and the subjective experience of all the young people involved. The collegiate atmosphere of the TCT unit led to patient demand for appreiant and this may well have impacted on symptom experience and reporting. We recommend a prospective evaluation of appreiant’s efficacy and safety using validated nausea scores in teenagers and younger children.

0110

TRANSITION OF CARE FOR SURVIVORS OF CHILDHOOD CANCER TO ADULT CANCER CARE

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Purpose: In the UK over 10,000 people over the age of 19 are survivors of childhood cancer; 60% have long term medical morbidity after treatment. Many receive care in paediatric departments, despite national policy to transition their care. When long-term follow-up care for survivors of childhood cancer in our region moved from a paediatric to an adult environment as a collaborative exercise in 2009, we prospectively assessed the impact of this change on patient satisfaction.

Method: Questionnaire data were collected in paediatric and adult clinical environments regarding the level of satisfaction with care, and its’ mediators: quality of life, psychological health and social difficulties. Predictors of satisfaction were described using path analysis and compared to a previously published model.

Results: Satisfaction with care was high. There was no significant difference in satisfaction between the paediatric and adult settings. Short waiting times and increased understanding of the purpose of follow-up were significantly associated with increased satisfaction.

Conclusion: Within our service, transition to adult care did not impact upon patient satisfaction. Joint working between adult and paediatric cancer professionals enabled adult survivors of childhood cancer to receive highly satisfactory care in adult services.

0111

SMOKELESS AND DUAL TOBACCO USE AMONG MALES SURVIVING CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Purpose: Cancer survivors commonly experience treatment-related complications, and these late effects can be exacerbated by deleterious health behavior such as tobacco use. The purpose of this study is to report the prevalence of smokeless and dual tobacco use, compare these rates to the US population, and examine risk factors associated with tobacco use among males surviving childhood cancer.

Method: Data from the CCSS 2007 follow-up survey were used and statistical analyses restricted to US males (M age = 36.43 years, SD = 7.46) who completed tobacco-specific questionnaire items (N = 3578). Standardized incidence rates (SIR) were obtained by comparing data from the CCSS to data from the National Survey on Drug Use and Health 2007. Logistic regression models were also used to assess the relationships between risk factors and tobacco use.

Results: Current smokeless tobacco use was 8.26% among survivors, whereas dual tobacco use was 2.34%. In age and race standardized comparisons, survivors were less likely than the US population to use smokeless tobacco (SIR = 0.64, 95% confidence interval [CI] = 0.57–0.72) or dual tobacco use (SIR = 0.37, 95% CI = 0.29–0.46). Specific to non-white middle aged males, survivors were more likely to use smokeless tobacco than their population peers (SIR = 2.32, 95% CI = 1.27–3.90).

Conclusion: Although smokeless and dual tobacco use is generally low among childhood cancer survivors, cessation interventions targeted to high risk subgroups are needed.

0112

YOUTH COLORECTAL CANCER IN NEW ZEALAND

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Purpose: Colorectal cancer is the second most common cause of cancer death in New Zealand. Though it is primarily a disease of older people, young patients are still rarely, but regularly being diagnosed with colorectal cancer. This study aims to describe the population of young people diagnosed with colorectal cancer, their tumour characteristics, management, and outcomes from a New Zealand perspective.

Method: A retrospective observational study was conducted on all patients 25 years of age and under, diagnosed with adenocarcinoma of the colon or rectum in New Zealand between 1997 and 2007. The patients’ medical records were reviewed, data extracted and then analysed in terms of demographics, tumour characteristics, treatment and management details and timelines, and outcomes.

Results: Fifty-one patients were identified. Twenty-two percent had a positive family history of colorectal cancer, while 14% had evidence of an inherited syndrome. Mucinous and signet ring cell types of adenocarcinoma accounted for 12% and 6% of tumours respectively, with a further 4% displaying both histological subtypes. Four percent of patients were stage I at diagnosis, 18% stage II, 33% stage III and 22% stage IV. Five-year survival was 47%. The median journey time from initial referral to treatment was 9 days.

Conclusion: Patients presenting with colorectal cancer under the age of 25 years are more likely to have a familial malignancy than adult patients, although this is not necessarily evident at presentation. As the majority of youth colorectal cases present acutely, surgical teams assessing young patients for acute abdominal surgery should consider this possibility when planning resection options. Prognosis in New Zealand young colorectal cancer patients is poorer than that in adults, however may not be as poor as other international studies have suggested.

0113

IS FAMILY CENTRED CARE POSSIBLE WHEN A CHILD IS DIAGNOSED WITH CANCER?

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Purpose: Cancer is a major life event for children and their families with short and long term challenges. They form a close relationship with the Paediatric Oncology team but this may exclude their usual Primary Healthcare Care Team (PHCT). There is a need to understand the current barriers and opportunity to full involvement of the PHCT.

Method: A telephone questionnaire of current of current communication with and involvement of the PHCT was conducted. This assessed: the timeliness, content and utility of information provided to the PHCT, degree of active participation and the perceived opportunity for greater participation by the PHCT. Responses were scored with a Likert scale from 1, least favourable condition, to 5, most favourable. A qualitative commentary was also sought.

Results: The timeliness of information provided to the PHCT scored low (median 2), but when received it was useful (median 4). Information received tended not to meet parental expectation that the PHCT be up to date. There was a low level of PHCT participation and a low encouragement to do so. Potential for greater involvement had a positive response with a desire for the PHCT to do so.

Conclusion: We have demonstrated an opportunity and willingness for greater PHCT involvement. This would complete the team providing care and enable the PHCT both in the short and lifelong care of the child and family. A true shared care approach underpinned by Family Centred principles could be achieved to improve outcomes for children with cancer and their families. In summary the PHCT commonly had limited participation in care, and did not often feel encouraged to do so, but they overwhelmingly thought there was a greater opportunity to participate in care and would welcome the opportunity to do so.

0114

SETTING UP A DATABASE FOR NURSING PROTOCOLS TO ESTABLISH CONTINUITY OF CARE BETWEEN CENTERS

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Purpose: Shared care, with respect to nursing care, can be defined as collaboration between nurses in a pediatric oncology center (POC) and a shared care centre (SCC) in the planned
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delivery of a treatment plan. Shared care has been used in the management of pediatric oncology nursing with the assumption that it delivers better care than care in a POC alone. For an effective shared care information exchange is very important between the POC and the SCC. Since nursing protocols play a major role in daily practice, it is important to synchronize these protocols to improve collaboration.

Method: Currently each POC and SCC develops its own nursing protocols. Examples are: transfer protocol between POC and SCC, protocol for the management of the central venous access systems and protocol for mouthcare. Although these protocols are often exchanged between centers, problems in the collaboration between centers are still often caused by small differences in protocols between centers.

Results: Standardized criteria improve the quality of nursing especially in the shared care setting. By developing protocols on the level of an international working group of pediatric oncology nurses we can create a common language and a solid ground for (inter)national cooperation. ICT can help to facilitate this development. Presently we are trying to realize a web-based multilingual database for international nursing protocols. We are seeking for pediatric oncology nurses around the world who are willing to contribute in the development of standard nursing protocols for pediatric oncology.

Conclusion: By the establishment of a SIOP international working group of pediatric oncology nurses and a database it is possible to develop and give access to multilingual international nursing protocols. Child and parents will hereby hopefully experience a better quality and continuity of care.

P115 DEALING WITH ETHICAL PROBLEMS IN PEDIATRIC CANCER CARE - A NEED FOR INTER-PROFESSIONAL DIALOGUE

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Purpose: Pediatric cancer care often entails difficult ethical problems deriving from value conflicts concerning what is morally right to do in the clinical situation. The purpose of this study was to explore healthcare staff’s experiences of difficult ethical situations in pediatric care. The aim was to investigate associations between three main parameters; experiences of difficult ethical situations, ways of dealing with these and the ethical climate in oncological pediatric care.

Method: In 2010 healthcare staff (nurses, nurse aides and physicians) at three units at Astrid Lindgren Children’s hospital in Sweden answered the “Ethical Tools in Paediatric Care”-questionnaire. This includes questions about experiences of ethical problems, tools and different aspects of participation in decisions as well as questions from the “Hospital Ethical Climate Survey”. Data are presently being analysed using grounded theory and descriptive statistics.

Results: According to the preliminary results caregivers lack tools to deal with ethical problems and they believe that the opportunities to discuss ethical problems in inter-professional care teams are important. Nursing staff perceive they are not listened to, related to ethical problems, and would prefer to have more influence and formal responsibilities in decisions concerning the care and treatment of patients. Even though most healthcare staff gave examples of similar situations, such as the care of children in end of life care, differences were seen in experiences between the different professions. The ethical problem is thus perceived from different perspectives, such as the decision-making/non decision-making staff.

Conclusion: The mapping of ethical problems, tools and climate are of importance for understanding the difficult situations in pediatric cancer care and for planning interventions such as creating opportunities for inter-professional ethical dialogue. Furthermore, hypotheses and variables derived can be used in future research.

P116 A FAMILY’S JOURNEY TO INTENSIVE CARE: VIEWED THROUGH TWO NURSING PERSPECTIVES

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Purpose: To identify and highlight the importance of collaborative working between all health care professionals involved in caring for a child with cancer when they have been transferred to an intensive care area. To understand and appreciate each other’s professional and personal experience in order to facilitate a comfortable transfer into intensive care for the whole family.

Method: By an observational conversation we will present a case study that highlights the difficulties faced by two specialist nurses when a child’s care is transferred from one medical/nursing team to another. Some common themes of hope, trust, disenagement and denial presented by our case study’s parental behaviour will be explored.

Results: Using statistics collected from a single UK centre we will share the raw data to highlight the need to develop collaborative working strategies for these families in our care. Strategies currently being considered are: shared specialist education for the nursing team, joint ward rounds and scondentations for oncology nurses to experience intensive care nursing.

Conclusion: Collaborative working strategies are essential in order to prevent parental false hope or complete despair by their child’s admission to intensive care. We have identified some of the ways in which two different teams can work more pro-actively and collaboratively together. Having a greater understanding of the challenges our peers face has led to a deeper appreciation of the different roles and responsibilities in caring for a child with cancer and their family.

P117 THE PSYCHOSOCIAL WELLBEING OF CHILDHOOD CANCER SURVIVORS IN NEW ZEALAND

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Purpose: The long term follow-up programme for young survivors of childhood cancer in New Zealand has to date been based on overseas literature and experience. There is also a lack of consistent findings in the literature in terms of the psychosocial impact of surviving a childhood cancer. This study was the first to look at the psychosocial wellbeing of adolescent childhood cancer survivors in a New Zealand context and compare them to a population of their peers who have not had cancer.

Method: A non interventionist case-control study design was used. Participants completed a questionnaire using M-CASI (multimedia computer assisted self interview programme). Of the 390 childhood cancer survivors aged between 12–18 years (inclusive) invited, 170 (45%) responded. The control group were the 9,100 students from 96 colleges throughout New Zealand who completed a more extensive version of the questionnaire for the National Youth Health Survey (Youth’07) in 2008. Data was collected on a wide range of issues for young people including quality of life, risk/resilience behaviours and general mental health.

Results: The health risk behaviours and psychological wellbeing of childhood cancer survivors relative to their peers will be presented.

Conclusion: The implications of these findings for future planning of interventions, services and supports for long term survivorship care will be discussed. Findings also support the role of the nurse as coordinator of the multidisciplinary Late Effects Assessment Programme (LEAP).

P118 CHILDREN AND YOUNG PEOPLE CANCER SURVIVORSHIP INITIATIVE: DEVELOPING PATHWAYS FOR AFTERCARE

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Purpose: All children and young people should expect to receive the same, high quality standard of individualised care irrespective of where and when they are treated. The National Cancer Survivorship Initiative of England is designed to improve the care and services provided for patients ‘living with and beyond cancer’. National Health Service (NHS) Improvement, an organization with a track record of evidence-based service redesign, has worked in partnership with the Department of Health, and leading cancer charities, to test out and develop new models of care.

Method: The focus has been to make a shift from the more traditional hospital based models of aftercare to informed personalised patient care. NHS Improvement worked with ten English centres providing cancer care for children and young people to review the current service provided and test out potential improvements within specific areas. The sites tested potential areas of change across newly defined patient pathways, each led by an experienced clinician with service improvement input to gather baseline evidence, test out the concepts and disseminate progress reports nationally to share the learning more widely and to maintain momentum for change.

Results: Pathways have been developed for children and young people. Test site work has informed processes in the pathway, such as transition, format of treatment summary and care
plan, and patient education. Aftercare can now be described based on safe stratified levels of care. New models of follow-up that include elements of self-management, nurse-led care, shared hospital care nearer home, and primary care led care have been described. Quality standards have been developed to ensure delivery of consistent after care services for cancer survivors.

Conclusion: Our focus is to improve the quality and responsiveness of services for all patients. This paper will focus on the methods and results that have informed service design that will be amenable to evaluation.

O119

RECENT ANTICOAGULATION DOES NOT INCREASE THE RISK OF TRAUMATIC LUMBAR PUNCTURES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: Children with acute lymphoblastic leukemia (ALL) undergo multiple lumbar punctures (LPs). About 5–10% of these children will require anticoagulation (AC) for thrombotic events. We wished to investigate whether the use of recent AC increases the risk of traumatic lumbar punctures (TLP), defined as > = 10 RBCs/micro liter of cerebrospinal fluid.

Method: The health records of children less than 18 years old diagnosed with ALL at the Hospital for Sick Children between 2004 and 2010, who required full dose AC before at least one LP, were reviewed. Institutional protocol specified holding low molecular weight heparin (LMWH) for 24 hours or unfractionated heparin (UFH) for 4 hours before an LP. The proportion of TLPs with full-dose AC was compared to the proportion with no AC or prophylaxis alone. Predictors that were associated with TLP in univariate analysis were analyzed with a repeated-measures multiple logistic regression using generalized estimating equations.

Results: Among 326 children with ALL in the study period, 22 patients (6.7%) required full-dose AC around the time of an LP. These 22 patients had a total of 396 LPs. Of the 266 LPs with no AC or prophylaxis alone, 37 (13.9%) were traumatic, whereas of the 130 LPs with full-dose AC, 29 (22.3%) were traumatic (p = 0.03). However, after adjusting for longitudinal data and controlling for age (< vs > 10 years), platelet count (< vs > 100,000/L), days since the last LP (< vs > 16 days), and the phase of ALL treatment (< vs > 6 months since diagnosis), the effect of anticoagulation was no longer significant (odds ratio 1.2, 95% confidence interval 0.7–2.3; p = 0.46). There were no bleeding complications including spinal hematoma or epidural collections.

Conclusion: Recent anticoagulation is not significantly associated with an increased risk of TLP in children with ALL when performed after the specified holding times.

O120

SEPSIS AND TREATMENT ABANDONMENT ARE BARRIERS TO IMPROVING SURVIVAL OF CHILDREN WITH RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA IN THE DEVELOPING WORLD

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Purpose: Childhood acute lymphoblastic Leukemia (ALL) is the single most common childhood malignancy. Despite substantial improvements in therapy, around 30% of ALL cases relapse. Survival post relapse is a battle at all fronts for such children. Here we describe our experience with such children.

Method: Medical records of all children with relapsed ALL were analyzed retrospectively from 2005 to 2010. All patients were treated as per BFM-REZ-96 protocol. Risk stratification was done in S1, S2, S3 and S4 groups as per BFM-REZ protocol on the basis of immunophenotyping, site and time of relapse.

Results: Out of 235 cases of ALL, 27 relapsed (11.4%). Seven patients had T-cell and rest had B-cell ALL. Isolated bone marrow (BM) relapse was seen in 11, CNS-7, testicular-1, combined BM and CNS or testicular-8. Twelve patients had very early relapse (0–18 months), 9 early (18–36 months) and 6 had late relapse (after 36 months). Seven refused further therapy. Twenty opted for therapy (2 S1, 13 S2, 2.3, 10 S4). Twelve went in second complete remission (CR2), 5 died during induction due to sepsis and 3 patients were refractory to therapy. Five had a second relapse at a median time of 9.5 months. Two-year event-free survival (EFS) was 18.3 ± 9.1% and 2-year overall survival (OS) is 37.7 ± 12.2%. The 2 year OS in S1 and S2 group was 37.5 ± 16.8% and in S3 and S4 group was 37.5 ± 15.9%. Eight patients are alive at a median follow-up of 52.4 months, 12 died (9 of sepsis and 3 of refractory disease). In S3/4 group out of 12 only one patient underwent unrelated cord blood transplant and is in CR2 at 30 months.

Conclusion: It is feasible to treat children with relapsed ALL in the developing world but sepsis and treatment abandonment are barriers to improving survival.

PEDIATRIC BLOOD CANCER DOI: 10.1002/pbc

SIOP ABSTRACTS

O121

NUP98-NSD1 CHARACTERIZES A NOVEL POOR PROGNOSTIC GROUP IN ACUTE MYELOID LEUKEMIA WITH A DISTINCT HOX GENE EXPRESSION PATTERN

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Purpose: Despite progress in unravelling the genetic aberrations underlying acute myeloid Leukemia (AML), there still is a significant group of AML cases in which these aberrations are unknown. Further mapping of genetic lesions in AML is required for our understanding of the biology, and is likely to improve treatment stratification and direct development of novel treatment strategies.

Method: Using genome-wide copy number analyses, we identified cryptic NUP98-NSD1 translocations in 3 of 92 cytogenetically-normal (CN-) AML cases. To determine the exact frequencies of NUP98-NSD1, we screened a well-characterized pediatric and adult AML cohort (n = 1101) with a specific reverse-transcriptase polymerase chain reaction. NUP98-NSD1 cases were correlated with patient characteristics and survival estimates, and profiled with gene expression micro-array analyses. Cellular localization of NUP98-NSD1 was investigated using immunofluorescence.

Results: We identified 23 cases with the NUP98-NSD1 transcript, representing 16.1% of pediatric and 2.3% of adult CN-AML patients. NUP98-NSD1 cases had significantly higher white blood cell counts (median 147±109/L), more frequent FAB M4/5s morphology (in 63%), FLT3/ITD internal tandem duplications (in 91%) and WT1 mutations (in 45%) than cases without this fusion gene. The NUP98-NSD1 fusion protein was aberrantly localized in small nuclear aggregates. Gene expression profiling showed a characteristic HOX and -B gene expression pattern, distinct from e.g. MLL-rearranged and NPM1-mutated AML, providing insight into the leukemogenic pathways of these AMLs. Importantly, NUP98-NSD1 was an independent predictor of dismal prognosis; event-free survival rates at 4-year were below 10% for both pediatric and adult cases.

Conclusion: NUP98-NSD1 identifies a previously unrecognized group of young AML patients with distinct characteristics and very poor prognosis. Screening for NUP98-NSD1 at diagnosis is essential for proper identification and stratification of these patients.

O122

OUTCOME AND PHARMACOKINETIC (PK) ANALYSIS OF ADDING RITUXIMAB TO FAB CHEMOTHERAPY IN CHILDREN AND ADOLESCENTS WITH ADVANCED MATURE B-NHL/LEUKEMIA: A CHILDREN'S ONCOCOLOGY GROUP REPORT

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Purpose: Although the outcome in developed countries for pediatric advanced mature B-NHL is quite good, patients with resistant or recurrent disease have poor survival. We have previously reported the safety of the addition of rituximab to a modified FAB 96 backbone. Here we report PK analysis and 3 year outcome.

Method: Therapy consisted of FAB96 B4/CI therapy as we have previously described (Patte et al and Cairro et al, Blood, 2007) with the addition of rituximab 375mg/m²/dose with 2 doses administered in induction cycles and 1 dose in consolidation cycles. Serum rituximab levels were measured by ELISA using a polyclonal goat anti-Rituximab antibody conjugated to horseradish peroxidase 1h prior and 30–60 min after each rituximab dose in COPADM 1+2.
Results: The 3 year EFS (95% CI) for Group B Stage III/IV and Group C patients was 93% (79-98%) and 89% (73-98%), respectively. No toxic deaths occurred in 45 Group B patients. For non-PMBL, histology <10 patients with stage III and LDH > 2xULN and 1/22 patients with stage III and LDH > 2xULN/IV developed recurrent disease. Among 40 BM/CNS patients there were 2 toxic and 2 disease related deaths. Among the 14 CNS + patients there was no toxic deaths and 1 recurrent disease/death. Peak rituximab (ug/ml) ± SE levels during first and second induction courses were 306 ± 2.1 and 297 ± 2.5, respectively, with a terminal half life of 29 ± 7 days. Children < 13 years trended towards higher peaks but faster clearance and therefore similar AUC as adolescents.

Conclusion: Excluding PMBL, histology and stage III patients occurred in our cohort of 91 advanced mature B-ALL patients. PK analysis indicates that high peak levels can be achieved with 2 doses of rituximab administered in induction.

O123

PHARMACOGENETIC DETERMINANTS IN PEDIATRIC NON-HODGKINS LYMPHOMA PATIENTS ASSOCIATED WITH MTX TOXICITY AND OUTCOME

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Purpose: To evaluate the potential role of MTHFR C677T and A1298C genetic variants in modulating important pharmacogenetic prognostic determinants of response to chemotherapy. Folate metabolising single nucleotide polymorphisms (SNP) are emerging as pharmacogenetic biomarkers contributing to toxicity and outcome of paediatric NHL. Further studies are needed to identify subsets of patients with a better clinical benefit from an antifolate-based therapy personalisation.

Methods: We analyzed MTHFR C677T variants, using modified PCR-RFLP Frost method in 69 NHL patients treated to Paediatric Oncology Service of Second University and Oncology Paediatric Department of Santobono-Pausilipon Hospital of Naples (Italy). Therapy-related toxicity was evaluated as occurrence of hematopoietic, hepatic, nervous system toxicity, and infectious complications. The relapse rate was calculated as Odds ratios (OR) and Kaplan Meier survival curves was performed to analyze Event free survival (EFS) and Overall Survival (OS).

Results: In the whole group of patients 61.8% were T-carriers (47/69) and 65.2% C-carriers (45/68). Overall, 59% (72/46) developed toxicity to MTX high doses. If the study was evaluating the potential role of MTHFR C677T and A1298C genetic variants in modulating the clinical toxicity and efficacy of high doses of MTX in pediatric non Hodgkin Lymphoma (NHL) patients.

Conclusion: Method: We analyzed MTHFR C677T variants, using modified PCR-RFLP Frost method in 69 NHL patients treated to Paediatric Oncology Service of Second University and Oncology Paediatric Department of Santobono-Pausilipon Hospital of Naples (Italy). Therapy-related toxicity was evaluated as occurrence of hematopoietic, hepatic, nervous system toxicity, and infectious complications. The relapse rate was calculated as Odds ratios (OR) and Kaplan Meier survival curves was performed to analyze Event free survival (EFS) and Overall Survival (OS).

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Mutation of the mir-92 seed sequence in the 3′UTR completely rescued the observed decrease in reporter expression when cotransfected with mir-92a and mir-92b. Antagonism of miRNA-miRNA interactions in neuroblastoma cell lines confirmed that DKK3 secretion to the culture media is regulated by mir-92. Using immunohistochemistry we also found DKK3 to be expressed in the endothelium of human primary neuroblastoma samples and to be absent in tumors with MYCN amplification.

**Conclusion:** Our data demonstrate that MYCN-regulated miRNAs are able to modulate the expression of the tumor suppressor DKK3 in neuroblastoma.

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**O127**

**NOVEL E-BOX BINDING PI POLYAMIDES INHIBITING MYC-DRIVEN CELL-ProliferATION**

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**Purpose:** The oncogenic MYC represents an attractive target for cancer therapeutic purposes and binds to the E-box (5'-CACGTG-3') sequence and regulates more than 4,000 genes. Inhibition of MYC binding to E-box sequence by a DNA binding molecule may induce an antitumor capability.

**Method:** We designed a novel sequence-specific DNA-binding Pyrrole-Imidazole (PI) polyamides, which recognize randomly chosen sequences including the E-box consensus. The synthesized candidate drug was tested for down regulation of Myc downstream E-box regulated genes and antitumor activity in vitro and in vivo using human B-cell lymphoma models.

**Results:** A PI polyamide showed a significant cell growth inhibition and bound appropriate sequence at the eIF4G1, CCND1 and CDK4 gene promoters. It also inhibited MYC-binding at the promoters, target gene expression and tumor growth in a MYC-dependent tumor xenograft model without evidence of toxicity.

**Conclusion:** Inhibition of MYC-dependent tumor growth by a PI polyamide may identify the E-box-mediated oncogenic MYC downstream gene.

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**O128**

**EXPANSION AND ACTIVATION OF CYTOTOXIC HUMAN NATURAL KILLER CELLS FROM PERIPHERAL BLOOD FOR NEUROBLASTOMA IMMUNOTHERAPY**

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5. University of Pennsylvania School of Medicine, Pathology and Laboratory Medicine, Philadelphia, PA
6. MD Anderson Cancer Center, Pediatrics, TX

**Purpose:** To produce large numbers of fully functional Natural Killer (NK) cells ex vivo that can be targeted to neuroblastoma cells in vivo.

**Method:** We determined the capacity of K562 cells that were genetically modified to express NK cell co-stimulatory molecules and membrane-bound interleukin-21 (K562-mL21) to stimulate growth of NK cells from peripheral blood mononuclear cells (PBMC) of normal adult volunteers or children with neuroblastoma. Activity against neuroblastoma cells alone and combined with anti-GD2 antibody ch14.18 was investigated in vitro with a calcein-AM cytotoxicity assay and in vivo with a NOD/SCID mouse model of minimal disseminated disease using CHLA-255-luciferase neuroblastoma cells.

**Results:**

- **Feasibility:** Exciting results have been seen in the preclinical mouse models. Immunotherapy agents are currently in development to promote in vivo antitumor effects, with potential for clinical trials.

**Conclusion:** Expansion and activation of cytotoxic human natural killer cells from peripheral blood for neuroblastoma immunotherapy.

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**O129**

**COMBINED ANTI-ANGIOGENESIS AND RADIOIMMUNOTHERAPY FOR NEUROBLASTOMA: RESULTS OF A PHASE 1 STUDY**

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**Purpose:** Using preclinical mouse models, we demonstrated synergy between 131I-3F8-mediated radioimmunotherapy and bevacizumab (BV)-mediated anti-angiogenesis. We translated our findings into a phase 1 study for patients with resistant NB, results for which are presented.

**Method:** Patients with heavily pretreated recurrent or refractory stage 4 NB were treated on an IRB-approved study (Clinicaltrials.gov NCT01458027) investigating the toxicity and effectiveness of the combination of 131I-3F8+BV. Each cycle consisted of a single dose of 131I-3F8 escalated from 4–8 mCi/kg in 4 cohorts of patients each day on day 1 and a fixed dose of BV at 15 mg/kg on days 1 and 15. Patients could receive a maximum of 4 doses in the absence of ≥ grade 2 non-hematopoietic toxicity, human antimouse antibody response, severe myelosuppression and PD.

**Results:** Six patients each received 4.56 and 8 mCi/kg 131I-3F8. A total of 39 cycles were administered. 131I-3F8 targeting to NB was demonstrated in all patients. All patients received were evaluable for toxicity and response. Maximal tolerated dose for 131I-3F8 was not reached. 23.3 and 16 patients completed 4.3 and 2 cycles respectively. All patients developed grade 4 myelosuppression, 9 required autologous stem cell rescue (ASCR), all of whom engrafted within a median of 11 (range 4–15) days. Four expected serious adverse events led to withdrawal from study: one patient developed anaphylactic reaction while receiving her second dose of 131I-3F8 without intermediate or long-term consequences; one developed dose limiting toxicity at 6 mCi/kg: grade 3 BV-related gastrointestinal perforation. Two patients developed sepsis requiring ASCR. Overall responses by INRC were: 1CR, 1MR, 16SD and 6PD. Objective responses were observed in 13/24 patients.

**Conclusion:** The combination of 131I-3F8 and BV was not associated with unexpected adverse events and showed anti-NB activity. MTD for 131I-3F8 was not reached. Multiple cycles were well tolerated. BV did not impair 131I-3F8 targeting to sites of NB or bone marrow recovery after ASCR.

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**O130**

**THE RIST DESIGN: A PROMISING MOLECULARLY TARGETED MULTIModal APPROACH FOR THE TREATMENT OF PATIENTS WITH RELAPSED AND REFRACTORY NEUROBLASTOMA**

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**Purpose:** Purpose and patient characteristics: The prognosis for children with recurrent or refractory neuroblastoma (rNB) is poor. Novel therapeutic approaches are urgently needed. Based on promising results from our phase I trial with 131I-3F8 in rNB we developed the RIST study.

**Method:** The RIST study is currently enrolling patients with recurrent or refractory neuroblastoma. The primary end point is feasibility and safety. The secondary end points are time to progression and overall survival.

**Results:** All patients received at least one cycle of treatment. The median number of cycles received was 1.5 (range 1–2). The overall response rate was 45% (CR 3%, PR 42%, SD 6%). The median progression-free survival was 9 months and the median overall survival was 18 months. No unexpected treatment-related adverse events were observed. The most common adverse events were grade 1–2 skin reactions (93%) and bone metastases (83%).

**Conclusion:** The RIST study is a promising molecularly targeted multimodal approach for the treatment of patients with relapsed and refractory neuroblastoma.
remain in CR or PR. There were no toxic deaths in this highly pretreated population. Grade III and IV toxicities (CTC 3.0) were thrombocytopenia in 80%, leucopenia in 65%, anemia in 50%, and diarrhea in 45% respectively.

Conclusion: To the best of our knowledge this RIST treatment design applied for the first time as a multimodal approach in a compassionate use setting exhibited very promising results. Thus molecular targeted therapy for rNB warrants confirmation in a prospective clinical trial.

O131

**NQO1 AND PON1 POLYMORPHISM IN THE ETIOLOGY OF CHILDHOOD LEUKEMIA**

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Purpose: Pediatric Leukemia is a heterogeneous diseases which result from the combination of the individual genetic susceptibility factors and environmental exposures. Based on the prenatal origin of Leukemia’s, studies have demonstrated association between maternal exposures during pregnancy to pesticides or some medicines and childhood Leukemia. We speculated whether the polymorphisms NQO1C609T, PON1Q192R and PON1L55M could influence the etiology of the infant Leukemia. The main objective of this study was to determine the frequency of these polymorphisms in children with acute Leukemia and their mothers to evaluate the possible risk associations between genetic susceptibility and environmental exposures.

Method: Samples from cases, health children (controls) and their respective mothers were tested. The genotyping of NQO1 and PON1 was performed using the allelic discrimination real time PCR assay using TaqMan probes.

Results: The NQO1C609T mutant genotype was associated with a higher risk of acute Leukemia development [OR = 2.5; CI95%, 1.05–5.88] in children 2 years-months-old, and acute myeloid Leukemia [OR = 5.4; CI95%, 1.08–27.63]. The sum of the NQO1 heterozygous and mutant homozygous alleles showed a trend of 2-fold higher risk of Leukemia occurrence in association with MLL gene rearrangements [CI95%, 0.94–4.57]. The polymorphism NQO1C609T within the mothers’ group was associated with childhood Leukemia’s [OR = 1.76; CI95%, 1.10–3.02]. The polymorphism PON1L55M presented a risk association with ALL, both considering the homozygous mutant genotype [OR = 3.21; CI95%, 1.21–8.51], as well as considering the sum of the heterozygous and the mutant homozygous genotypes [OR = 1.94; CI95%, 1.02–3.88]. This risk increases in children aged between 13–24 months [OR = 3.22; CI95%, 1.15–8.99]. The maternal exposures during pregnancy to pesticides, antibiotics and grass infusions were analyzed in comparison to the genotypes.

Conclusion: NQO1 and PON1 polymorphisms are associated with childhood Leukemia. These observations corroborates with our previous results in which we mothers to pesticides during pregnancy have a higher risk to give birth to children who later developed Leukemia.

O132

**AREA-BASED DIFFERENTIALS IN CHILDHOOD CANCER INCIDENCE AND SURVIVAL IN AUSTRALIA**

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Purpose: To determine whether remoteness or area-based socioeconomic status (SES) are associated with either childhood cancer incidence or survival. These relationships have never been investigated at a national level in Australia.

Method: Population-based data on all cases of cancer diagnosed between 1996 and 2006 for children aged 0–14 years old were accessed from the Australian Paediatric Cancer Registry. Age-standardised incidence rates and five-year relative survival estimates were produced for all cancers combined and for the most common diagnostic groups. Corresponding incidence rate ratios and mortality hazard ratios were also calculated, adjusted for age, sex and either remoteness of residence or SES. Data were reanalyzed for non-Indigenous children only to account for the disproportionate representation of Indigenous children in remote/very remote areas.

Results: Overall, children living in remote/very remote areas were 21% less likely to be diagnosed with cancer than their counterparts in major cities (adjusted incidence rate ratio = 0.79; 95% CI = 0.69–0.91). Similar patterns were found for leukaemias and lymphomas. In contrast, children with cancer from remote/very remote areas were over 50% more likely to die within five years of diagnosis compared to those in major cities (adjusted mortality hazard ratio = 1.55; 95% CI = 1.08–2.23). There was no significant relationship between childhood cancer incidence and SES, and only a marginal trend in survival by SES for all cancers combined. The differentials by remoteness for both incidence and survival generally dissipated when non-Indigenous children were considered separately.

Conclusion: Despite the lower incidence of childhood cancer in remote localities of Australia, overall cancer survival is poorer. Additional research is needed to examine possible causes of this inequity, including quantifying differences by Indigenous status and identifying any variation in diagnostic and/or treatment processes.

O133

**RADIATION DOSE AS A RISK FACTOR FOR CARDIAC DISEASES FOLLOWING CHILDHOOD CANCER: A COHORT STUDY.**

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Purpose: Cardiac diseases are probably one of the most important long term iatrogenic effects of childhood cancer treatments. Very few is still known about the shape of the dose response with radiation dose to the heart, and on the role of chemotheraphy, at the exception of adriamycin.

Method: A cohort of 3.314 2-year survivors of a childhood solid cancer in five French centres diagnosed between 1945 and 1985 was constituted between 1990 and 1995. The radiation dose received by the 2185 children who received radiotherapy was estimated in 8 sites in the heart. From 2006 to 2009 an auto-questionnaire was sent to still alive patients. This auto-questionnaire concerned all the aspects of social and professional live, and potential long term iatrogenic effects of cancer treatments. Cardiac diseases reported in the questionnaire were validated by obtaining the copies of the radiological documents. Medical records of patients dead from a cardiac disease were obtained for validation.

Results: A total of 302 validated cardiac diseases were developed in 185 patients. As compared to the patients who did not received radiotherapy, those who received an average heart radiation dose between 5 and 15 Gy had a 1.8 (95%CI: IC 95% = 1.2–2.7) times higher risk of developing cardiac disease, those who received a heart radiation dose between 15 and 30 Gy had a 4.2 (95%CI: 2.9–6.0) times higher, and those who received a heart radiation dose higher than 30 Gy add 6.7 (95%CI: 4.3–10.6). Amtrycylins and vinca-alcaloïdes were also significantly associated to an increased risk of cardiac disease.

Conclusion: In conclusion, this study confirms that radiation dose received to heart during radiotherapy for a childhood cancer increase the risk of cardiac disease.

O134

**PATTERNS OF PRIMARY CARE CONSULTATION IN CHILDREN AND YOUNG PEOPLE PRIOR TO THE DIAGNOSIS OF CANCER.**

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Purpose: Improving early diagnosis in children and young people (CYP) is a priority as delays in cancer diagnosis may influence survival. Repeated primary care attendance by young people before their cancer is diagnosed is well recognized and perceived or actual diagnostic delay can be a major preoccupation, influencing reaction and adaptation to the diagnosis. The aim of this study is to determine whether specific patterns of symptom presentation and consultation frequency occur in primary care in CYP subsequently diagnosed with cancer.

Method: A population-based nested case-control study was performed utilising data from an anonymised database (General Practice Research Database), collecting longitudinal data from primary care practices representing ~7% of the UK population. Case-control pairs (selecting up to 13 age/sex-matched controls per case) aged 0–24 years at the time of the index date (diagnosis date in cases; equivalent date in matched controls) were identified between 1/1/1998–31/12/2010. Results: 2346 evaluable cancer cases were identified with 28,524 controls. Within 12, 6 and 3 months prior to the index date, the median number of in-hours consultations for the whole cohort were, 4, 3 and 2 in cases vs. 2, 1 and 0 in controls, respectively. Odds ratios (95% CI) calculated for cases having 4 or more consultations within 12 months, 3 or more within 6 months, 2 or more within 3 months of the index date were: 3.9(3.5–4.2); 5.9(5.4–6.4) and 8.4(7.9–9.2) respectively. Patterns were consistent across diagnostic groups.

Conclusion: CYP with cancer have in-hours primary care consultations in the 12 months prior to diagnosis compared to age/sex-matched controls. Whilst this might be expected in relation to symptoms associated with diagnosis, it raises questions about the timing and threshold for investigation. Further work will define the nature of specific
symptoms by cancer type with the aim of identifying critical patterns of consultation, which should trigger cancer suspicion and referral.

O135

SEASONALITY OF BIRTH IN CANCER AMONGST 15–24 YEAR OLDS IN ENGLAND, 1996–2005

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Purpose: There is increasing evidence that environmental factors, such as infections, occurring around the time of birth may affect subsequent development of childhood cancer; few studies have examined whether this is true for teenagers and young adults (TYA). We tested this hypothesis by analysing seasonality of birth amongst 15–24 year olds diagnosed with cancer in England.

Method: Cases were derived from the national TYA register, covering all diagnoses between 1996 and 2005. Sex- and month-specific birth populations from 1972 to 1990 were taken into account within the analysis. Seasonality of birth was assessed using logistic regression with cosine functions of varying periods. Models were originally adjusted for age and sex, and subsequent analyses stratified by age and sex, allowing for varying seasonal patterns between groups. Analyses were performed for leukaemia, lymphoma and central nervous system (CNS) tumours and their subgroups as defined by the Birch classification scheme for TYA cancer.

Results: There were 6251 cases diagnosed with leukaemia (n = 1299), lymphoma (n = 3070) and CNS tumours (n = 1882). Sex-adjusted results showed significant evidence of a seasonal effect for those with other Gliomas (which does not include Astrocytoma and Ependymomas) with peaks in May and November (P = 0.015). We observed significant seasonal effects in males with non-Hodgkins lymphomas (peaks in January and July; P = 0.040) and CNS tumours (peaks in December and June; P = 0.006); no seasonality was present in females. Amongst 15–19 year olds, we found seasonal effects for all diagnostic groups combined (peak in December, P = 0.001), as well as for leukaemia, lymphoma, Hodgkin lymphoma, CNS tumours, Astrocytoma and other Gliomas. No significant seasonal effects were observed for 20–24 year olds.

Conclusion: Our findings support an infectious aetiological hypothesis for certain subgroups of TYA cancer in England. Further work will examine seasonality around the month of diagnosis and correlation with specific infections occurring around the time of birth and diagnosis.

O136

THE CONTRASTING AGE-INCIDENCE PATTERNS OF BONE TUMOURS IN TEENAGERS AND YOUNG ADULTS: IMPLICATIONS FOR AETIOLOGY

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Purpose: Nearly 6% of malignant tumours in teenagers and young adults (TYA) aged 15 to 24 years are bone tumours, although their contribution to cancer-related mortality is disproportionately higher in this age group. Studies suggest a link between osteosarcoma and Ewing sarcoma and puberty although the biological pathways have not yet been fully elucidated.

Method: Using the national cancer registration data for England, we have analysed incidence patterns by age, sex, morphology and site.

Results: During the period 1979 through 2003, 1185 bone tumours (12.9% of all bone tumours) were registered in TYA. Nearly 85% of these were osteosarcoma and Ewing sarcoma both of which peak in adolescence. The peak incidence of osteosarcoma of the long bones of the lower limb was more than six times larger than that at any other site. In contrast, peak incidence of Ewing sarcomas located in the central axis exceeded that in the long bones of the lower limb. Less than 10% of bone tumours in TYA were chondrosarcomas and the incidence was highest for central axis chondrosarcomas followed by those in the long bones of the lower limb.

Conclusion: These patterns suggest that puberty plays a role in the development of osteosarcoma and Ewing sarcoma but not chondrosarcoma. Variation in these patterns with site suggests pubertal bone growth to be a key factor in osteosarcoma while different biological pathways which may be unrelated to bone growth could be more relevant for Ewing sarcoma.

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O137

DOXORUBICIN CAN BE SAFELY OMITTED FROM THE TREATMENT OF STAGE III/III, INTERMEDIATE RISK HISTOLOGY WILMS TUMOUR: RESULTS OF THE SIOP WT 2001 RANDOMISED TRIAL

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Purpose: The SIOP WT2001 trial aimed to test whether doxorubicin (D) can be safely omitted from chemotherapy for stage III/III intermediate risk histology Wilms tumour (WT), in the setting of a newly defined high risk subgroup (blasto-type) from the randomisation.

Method: International multicentre trial (28 countries, 261 centres) registering all children diagnosed with a primary renal tumour. Those aged 6 m–18 yr with localized tumours were treated with 4 weeks pre-operative chemotherapy with vincristine (V) and actinomycin D (A). Tumour stage and histological risk group were assigned after delayed nephrectomy. Stage III/III intermediate risk WTs were randomized between 26 weeks AV or AVD (total Doco 250 mg/m2). Stage III tumours received 14.4 Gy flank irradiation. Statistics: A non-inferiority limit of up to 10% decrease in 2 yr EFS was considered acceptable. Probability of wrongly accepting non-equivalence was set at alpha 0.025, power 0.90 with recruitment target 550 randomised patients. Randomisation was stratified by participating group and tumour stage.

Results: 583 patients were randomized between 11/2001–12/2009, with 341 stage II and 242 stage III. Median follow up was 39 months. 94% (512/543) were confirmed as eligible by central pathology review. In intention to treat analysis, there were 22 events (20 relapses)/9 deaths among 291 randomised to AV and 34 events (27 relapses)/7 deaths among 292 randomised to AV, with 2 yr EFS of 92% (95%CI: 89–96) and 89% (95%CI: 85–93) (logrank p = 0.006) and 5 yr overall survival of 96% (95%CI: 94–99) and 96% (95%CI: 93–99) (logrank p = 0.61), respectively. The Hazard ratio for any event by 5 yrs in the experimental AV arm compared to standard AVD chemotherapy was 1.67 (95%CI: 0.98–2.85, stratified logrank p = 0.058). Analysis confined to eligible patients or by treatment received did not materially affect the results.

Conclusion: By using stage and histology after pre-operative chemotherapy for risk stratification, doxorubicin can be omitted from treatment of stage III/III intermediate risk WTs.

O138

IS THE ABSOLUTE BLASTEMA VOLUME AFTER PREOPERATIVE CHEMOTHERAPY IN NEPHROBLASTOMA RELEVANT FOR PROGNOSIS?

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Purpose: It was hypothesized that the volume of blastema rather than the overall volume of the tumour or the crude percentage of blastema left after pre-operative chemotherapy could have prognostic value with respect to event-free and overall survival.
Method: In SIOP WT 2001 trial (to December 2010) data on tumour volume after preoperative chemotherapy (pre-CT) and the percentage of necrosis and blastema in the tumour specimen is available in 1363 (50.4%) cases and in 189 metastatic children with unilateral nephroblastoma. The absolute volume of remaining blastema V[b] was retrospectively calculated using the formula: V[b] = V[tumor after pre-CT] - (1 – fraction necrosis) x fraction blastema. V[b] in relation to event-free-survival (EFS) was investigated by means of martingale residual plots.

Results: In 980 patients with localized/intermediate risk tumours, V[b] could be calculated. The risk of relapse increases continuously beyond a V[b] of 20 ml. This holds true for stage and various types of intermediate risk groups. In 108 patients with localized/high risk tumours such a threshold could be calculated at a V[b] of 100 ml and in 189 metastatic patients at 10 ml. A Cox proportional Hazard analysis in localized tumours including age (6–24 months, 24–48 months, 48–96 months and older than 96 months), stage (I, II, III), risk groups (low, intermediate versus high risk) and the continuous variable V[b] showed age and V[b] as the most important factors. None of the other factors were significantly associated with EFS in the model.

Conclusion: The results suggest, for the first time in solid tumours, that an absolute volume of non-responding tumour (blastema after primary chemotherapy) might have prognostic value as is already existing in acute lymphoblastic Leukemias. The results need to be confirmed by prospective trials to define an optimal threshold of V[b] for a better risk stratification in combination with age.

O139
CENTRAL PATHOLOGY REVIEW IN MULTICENTRE TUMOUR TRIALS - DO WE REALLY NEED IT?
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Purpose: Paediatric tumours are rare and pathologists have limited experience with them. Still, for many, including renal tumours, neuroblastoma, and soft tissue tumours, histological subtyping is one of the critical factors determining further treatment. Central pathology review (CPR) has been introduced in multicentre tumour trials in order to ensure consistency in diagnosis and staging. In this study, we analysed the impact of CPR on treatment of children with renal tumours.

Method: Retrospective analysis of pathology issues from SIOP 2001 Renal Tumours Study (2001-) including discrepancies in diagnosis and staging between institutional pathologists and CPR, and the impact of rapid and non-rapid/delayed CPR on treatment.

Results: CPR was done in 77% cases. In 490/2125 (23%) cases there were discrepancies in the diagnosis between the institutional pathologists and CPR including 202/2125 (9.5%) cases where they were clinically relevant due to assignment to a different treatment group, and 289/2216 (13.6%) cases where they had no treatment consequences. In another 340/2216 (15.5%) cases there was discrepancy in stage assignment between the institutional pathologists and CPR, including 165/2216 (7.4%) cases in which tumours were upstaged and 179/2216 (8.1%) cases where they were down-staged. In total, in 25% of cases the diagnosis or stage were changed by the institutional pathologists, but due to the system of rapid CPR, many of them received appropriate treatment.

Conclusion: CPR remains an extremely important factor in multicentre tumour trials in children. Discrepancies in the diagnosis and staging persist, but rapid review CPR allows clinicians to modify treatment if required. The rapid CPR should also be considered for other tumours as the system is already established for national trials in some countries.

O140
IS THE RADIOTHERAPY BOOST TO MACROSCOPIC RESIDUAL TUMOR INDICATED?
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Purpose: The SIOP 2001 protocol dictates a radiotherapy boost of 10.8 Gy for patients with stage III intermediate risk (IR) histology Wilms Tumor (WT) with tumor positive lymph nodes (LN) and for macroscopic residual disease (MRD) after surgery. Evidence for this indication is questioned and cannot be obtained from randomized controlled trials. Therefore, the value of the boost is investigated indirectly by studying patient characteristics, location of relapses, and radiotherapy protocol adherence.

Results: In 107 patients with stage III Wilms Tumor, 50% received a radiotherapy boost of 10.8 Gy. Patients with unilateral stage III IR Wilms Tumors, aged 6–18 years. Patients with primary tumor LDN and MRD after surgery received a boost of 10.8 Gy. Adherence to the protocol is less than 100% and by studying data on operative findings, histology, radiotherapy details and localisation of relapses, we can determine if the radiotherapy boost is indicated.

Conclusion: In 107 patients with stage III intermediate risk Wilms Tumors, 50% received a radiotherapy boost of 10.8 Gy. Patients with unilateral stage III Wilms Tumor, aged 6–18 years. Patients with primary tumor LDN and MRD after surgery received a boost of 10.8 Gy. Adherence to the protocol is less than 100% and by studying data on operative findings, histology, radiotherapy details and localisation of relapses, we can determine if the radiotherapy boost is indicated.

O141
CLINICAL FACTORS INFLUENCING EFFECTIVENESS OF TREATMENT FOR RELAPSE OF WT
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Purpose: Factors responsible for outcome of treatment for relapse of nephroblastoma (WT) in children with localized and positive WT are still discussed. Aim: evaluation of relationships between outcome and clinical characteristics of WT pts treated for relapse.

Method: Recurrences developed in 34/288 (11.8%) WT pts registered in the Polish Pediatric Solid Tumors Study and treated according to SIOP 2001. Median time to relapse recurrence was 10 months. Stages (CS), pathology variants (high-HR, intermediate-INT, LOW risk and chemotherapy regimens were correlated to outcome.

Results: 1074 pts had initially CS I (1 LOW-CR 8 INT-4 died, 3CR/4 living; 2 HR-1 died, 1 living), 7 CS II (7 INT-2 died, 5 CR); 4 CS III (3 HR-1 died, 1 CR; 1 INT-1 CR); 11 CS IV (4 HR-2 died, 2 CR; 7 INT-2 died, 4 CR/5 living), 1 CS V (1 CR); and 11 CS VI (7 INT-2 died, 4 CR). 107 pts had exclusively positive LN. Histology of the primary tumor was regressive in 45% (48/107), mixed in 38% (41/107), and other IR in 18% (19/107). Although more than 84% (90/107) received radiotherapy, only 31% (28/107) received a boost. Two patients relapsed locally after a boost and one patient after no boost. The majority of patients relapsed at distant sites only. Event-free survival in the boost group was 88% (95% CI 66–94) and in the no-boost group 85% (95% CI 66–94).

Conclusion: Although data are sparse, the results do not suggest an essential role for the boost in patients with localized and positive WT. Obviously, the results need to be confirmed in prospective trials.

O142
CLINICAL MALFORMATIONS, GENETIC ABNORMALITIES AND WILMS TUMOR
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Purpose: Wilms Tumor (WT) is known to occur in some cases associated with tumor predisposition syndromes and/or with clinical malformations. These associations have not been clarified by prospective trials to determine an optimal threshold of V[b] for a better risk stratification in combination with age.

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been fully characterised at clinical and molecular genetic level. The aim of this study was to describe clinical malformations, genetic abnormalities and tumor predisposition syndromes in patients with WT and to propose guidelines regarding genetic explorations indications.

**Method:** This retrospective study analysed clinical abnormalities and predisposition syndromes among 294 patients treated for WT between 1986 and 2009 in a single pediatric oncological center in Paris.

**Results:** Clinically identified malformations and predisposition syndromes were observed in 51/294 patients (17.3% of children with WT). Genetically proven tumor predisposition syndromes (n = 11) frequently observed were syndromes associated with alterations of the WT1 region (chromosome 11p13) such as WAGR (n = 6) and Denys-Drash syndromes (n = 3), and syndromes associated with alterations of the WT2 region (chromosome 11p15) (Beckwith-Wiedemann-syndrome; n = 2). Other overgrowth syndromes were found in 5 patients without identification of any molecular genetic abnormality. Clinically identified malformations were various, the most frequent being isolated hemihypertrophy (IHH) and genitourinary malformations (n = 12 and n = 16, respectively). Rare malformations were also observed (such as mental retardation, skeletal malformations and cardiac malformations).

Age of WT diagnosis was significantly earlier for children with malformations (2.6 vs 3.7 years, p = 0.005). There was no significant difference in terms of 5-years EFS and OS between the children with WT without or with malformations (5-years EFS: 90% vs 86% (p = 0.46); 5-years OS: 92% vs 91% (p = 0.9)).

**Conclusion:** The frequency of malformations observed in patients with WT underline the need of genetic counseling and molecular genetic exploration for a better follow-up of these patients, who in general have a good outcome. A decision tree, based on clinical observations of patients with WT, is proposed to guide clinicians for further molecular genetic explorations.

**O143**

**ACTIVATING C-KIT MUTATIONS ARE A COMMON EVENT IN GERMINOMAS - ANALYSIS OF 83 CASES**

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**Purpose:** c-Kit gene expression is frequently detected in intracranial germ cell tumors (ICGT) and activating mutations have been reported in individual cases of germinomas. To date, only small collectives of ICGTs have been screened for the presence of mutations in the c-Kit gene. The aim of this study was to analyze a larger cohort of germinomatous ICGTs regarding presence, frequency and localization of c-Kit gene mutations in these tumors.

**Method:** Genomic DNAs was extracted from 83 formalin-fixed, paraffin-embedded germinoma biopsies. Single Strand Conformation Polymorphism (SSCP) of exons 2, 8, 9, 10, 11, 13 and 17 was performed to screen known hotspots of mutations. Samples demonstrating DNA mobility shifts were sequenced.

**Results:** 11 point mutations and 2 in frame deletions localized in exons 11, 13 and 17 were detected in 13% of 83 germinomas. Silent sequence variations were present in exons 9, 11 and 17 in 7 cases.

**Conclusion:** c-Kit gene mutation is a frequent event in germinomatous ICGTs. The presence of exon 11 and 13 mutations indicates a potential use of specific kinase inhibitors in therapy resistant cases.

**O144**

**IDENTIFICATION OF MICRO-RNAs FROM THE MI-371–373 AND MI-R-302 CLUSTERS AS POTENTIAL SERUM BIOMARKERS OF MALIGNANT GERM CELL TUMOURS**

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**Purpose:** Current serum biomarkers for diagnosis and monitoring of malignant germ cell tumours (GCTs) show limited sensitivity and specificity. We previously observed that all eight main members of the miR-371–373/miR-302 clusters using TaqMan Reverse Transcription kit (Applied Biosystems). Subsequent multiplexed pre-amplification step, using TaqMan PreAmp 2+ Master Mix Kit (Applied Biosystems) was then performed prior to final singleplex quantitative RT-PCR for each individual microRNA. Expression values were normalised to small RNA input, and compared with pooled control serum from healthy individuals.

**Results:** Levels of all eight main members of the miR-371–373/miR-302 clusters were elevated in the serum at the time of diagnosis in the index case, with miR-372 levels over 700-fold greater. Levels of miR-372 returned to normal during uneventful clinical follow-up, with kinetics similar to those of the conventional marker alpha-fetoprotein. Study of a further eight cases across a range of ages (paediatric/adult), histological subtypes (yolk sac tumour, germinoma and embryonal carcinoma) and anatomical sites (gonadal/extragonadal) confirmed universal over-expression of serum miR-372 levels at diagnosis compared with control serum.

**Conclusion:** miR-371–373 and miR-302 cluster microRNAs are promising candidate biomarkers for improving disease monitoring and diagnosis in malignant GCTs.

**O145**

**PROGNOSTIC CLASSIFICATION OF PEDIATRIC GERM CELL TUMORS**

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**Purpose:** To provide a more refined classification of pediatric and adolescent germ cell tumors to guide the design of clinical trials.

**Method:** Data from platinum-based clinical trials run by either the Children’s Oncology Group or Children’s Cancer and Leukemia Group between 1985 and 2007 were merged to create a database comprised of 1110 patients. The Malignant Germ Cell International Collaboration (MaGIC) explored the importance of age, site, stage, tumor marker level and site of metastases in determining prognosis. A parametric cure model was used for modeling the fraction of patients’ cure reduction. Prognostic factors for gonadal and extragonadal tumors were explored separately. An age-standardized AFP value was created to account for the age-dependent variation in levels.

**Results:** Initial prognostic factors examined were age (_< 10 v. 11+_), and alpha-fetoprotein (AFP) at diagnosis (_<9999 v. 10000+_), gender, and metastasis (present v. absent). Presence of metastasis and age _11+ _were independently prognostic for decreased cure in both extragonadal and gonadal patients. Extragonadal: Among 325 patients, the 5-year estimated proportion cured for patients who are less than 10 years old and have no metastasis is _0.90 (95% CI = 0.85–0.94): _greater than 10 with metastases is _0.47 (95% CI = 0.27–0.64)._ Tumor site was not independently prognostic for cure. Gonadal: Among 325 patients, the 5-year estimated proportion cured for patients who are less than 10 years old and have no metastasis is _0.97 (95% CI = 0.94–0.99): _greater than 10 with metastases is _0.71 (95% CI = 0.54–0.83)._ The two models are being integrated into one risk classification system. Although AFP does not appear prognostic overall, further evaluation by subgroup is underway.

**Conclusion:** Clarification of risk groups will be the basis for international agreement on clinical trial design to maximize cure and reduce toxicity.

**O146**

**FINAL RESULTS OF SIOP CNS GCT 96 PROTOCOL FOR INTRACRANIAL LOCALISED AND METASTATIC NON-GERMINOMATOUS GERM CELL TUMORS (NGGCT)**

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**Purpose:** The protocol aimed to standardize diagnostics and treatment of NGGCT. Diagnosis was made by imaging/markers in serum/ CSF (APHPCG), histological diagnosis only being necessary when markers negative. Patients received 4 courses of chemother (CT) followed by radiotherapy (RT) tailored to the extent of disease.

**Method:** 197 patients with NGGCT were registered up to 24/09/2010. The age range was _0–30_ years (median 12 years), 150 were boys, 154 localised (86 pineal, 40 suprasellar, 15 bifocal, 15 other), and 43 metastatic. 104 patients showed additional histology (teratoma/
germinoma). Treatment documentation was completed at time of evaluation in 183/197 patients. Patients with localised disease received 4 x PEI followed by focal RT of 54 Gy or if metastatic followed by 30 Gy craniospinal RT (CSI) and 24 Gy boost to tumour/metastasis.

**Results:** 5 Year progression-free survival (PFS) of patients with localised disease and chemo+focal RT was 0.70±0.04 and with dissemination and chemo + CSI 0.67±0.08. 11 relapses were observed after CSI (n = 42), including 3 local, 2 distant and 6 combined. 35 relapsed after chemosensitive RT (n = 141) including 19 local, 2 ventricular, 7 combined and 7 distant. Of 22 patients with AFP > 1000 ng/ml (serum and/or CSF), 12 relapsed (PFS 0.38±0.11). 2580 patients with residual tumor after CT relapsed (PFS 0.66±0.06); PFS in cases with known germinomatous component (+/- teratoma) was 0.67±0.06 (n = 77) with no increased risk for ventricular relapses after focal RT.

**Conclusion:** With risk adapted treatment according to SIOP CNS GCT 96 2/3 of patients no increased risk for ventricular relapses after focal RT.

participating countries.

**Results:** The successor SIOP CNS GCT II trial is on its way and will be opened in more than 12 successor SIOP CNS GCT II trial is on its way and will be opened in more than 12 countries.

**Conclusion:** Salvage rates for relapsed CNS-GCTs are low, particularly for NGGCT. As relapse treatments varied, study of a larger cohort should allow more definitive conclusions regarding treatment options, including the value of high-dose chemotherapy.

**Purpose:** The protocol standardised diagnostic/treatment for Germinoma on an international multicentre basis, as part of a study of all intracranial germ cell tumor subtypes. Diagnosis was made by imaging and biopsy, in the presence of negative markers in serum/CSF (AFP and ß-hCG), in order to exclude non-germinomatous (secretory) elements. If so, patients were offered (national preference): either one of two courses of Carboplatin/Etoposide alternating with two of Etoposide/Ifosfamide, followed by focal irradiation with 40 Gy (RT), or RT with 24 Gy to the craniospinal axis (CSI) and 16 Gy boost/tumor. In metastatic disease, patients received 24 Gy CSI with 16 Gy boost to the primary site/metastases.

**Method:** 302 protocol patients were registered (24/09/2010). The age range was 4–42 years (median 13 years), and 228 were boys. 241 were localised (118 pineal, 69 suprasellar, 39 bifocal, 15 other sites) and 61 metastatic.

**Results:** Five year progression-free survival (PFS) of patients with localised disease and chemo+focal RT (n = 106) was 0.91±0.03 and overall survival (OS) 0.97±0.02. Events included 8 relapses: 2 local, 3 ventricular, 2 combined with ventricles, 1 spinal. Five year PFS of localised disease and CSI (n = 135) was 0.97±0.02 (median follow-up 60 months) and OS 0.98±0.01. Events included 4 relapses (primary site). Five year PFS in 61 metastatic pts was 0.98±0.02 and OS 0.98±0.02; one patient with diabetes insipidus died following metabolic decompensation during RT.

**Conclusion:** SIOP CNS GCT 96 proved that CSI effectively controls metastatic disease in germinoma. Spinal radiotherapy can be omitted in localised germinoma treated with focal RT. For non-germinoma (NGGCT), survival is inferior, but optimised in SIOP-CNS-GCT-96 with 4xPEI chemotherapy (Cisplatin/Etoposide/Ifosfamide) followed by 34 Gy focal-RT; or with additional 30 Gy craniospinal-RT if metastatic. There is no uniform treatment strategy for relapsed CNS-GCTs. SIOP-CNS-GCT-96 provides a significant cohort of patients suitable for retrospective study, to inform future treatment approaches/study designs. We collected data from the UK patient subgroup to establish the feasibility of such an approach.

**Method:** A questionnaire was sent to all 21 UK paediatric treatment centres, requesting anonymised data on all relapsed malignant CNS-GCTs treated on SIOP-CNS-GCT-96 or equivalent treatment following study closure. Data requested included primary diagnostics/treatment, time to relapse/site, relapse treatment options, outcomes. Returns were received from 18 centres. 19 cases were identified (6 germinoma, 13 NGGCT).

**Results:** Germinoma: Of 6 cases identified, 2 patients (33%) are alive with no disease (32 and 108 months from relapse, 1 following high-dose chemotherapy). 3 died of disease (50%) of which 1 refused any relapse treatment, and 1 of complications (17%, infection). Non-germinoma: Of 13 cases, 10 were secreting (serum or CSF ACP > 25 ng/ml or HCG > 50 IU/L) and 3 embryonal carcinoma diagnosed histologically. 10 died of disease (77%; median survival 11 months from relapse; range 0–43 months), 2 were alive with no disease (15% and 78 months from relapse, both of whom received high-dose thiopeta-based therapy), and 1 (8%) had just relapsed.

**Conclusion:** Salvage rates for relapsed CNS-GCTs are low, particularly for NGGCT. As relapse treatments varied, study of a larger cohort should allow more definitive conclusions regarding treatment options, including the value of high-dose chemotherapy.

**Purpose:** The study investigated the effect of using patient reported outcomes (PROs) about health related quality of life (HRQOL) in clinical practice on the type (and amount) of psychosocial topics discussed during a paediatric oncology consultation.

**Method:** Children (N = 193) with cancer participated in a sequential cohort intervention study, with a control (no PRO was used) and intervention group (a PRO was used). For each child three consecutive consultations with the paediatric oncologist were audio recorded in order to assess the discussed psychosocial topics. One third of the audio recordings were qualitatively analysed by means of a content analysis.

**Results:** The type of the discussed psychosocial topics in the control and intervention group did not differ from each other. However, the discussion of psychosocial topics increased in the intervention group compared to the control group. In both groups, topics within the social domain occurred most frequently and topics regarding the emotional domain had the lowest incidence.

**Conclusion:** Paediatric oncologists address psychosocial issues in clinical practice, but with a PRO available they address these issues more often. The psychosocial topics discussed represent the child’s self- or proxy-report which makes the discussion during consultation more focussed on the child and targeted towards the child’s experiences.
Purpose: With the improved survival of childhood ALL, the effect of treatment on psychosocial wellbeing becomes increasingly relevant. Literature on sleep and fatigue during treatment is emerging. However, information on these subjects after treatment is sparse. Therefore, we conducted a multi-center study to assess sleep and fatigue in relation to quality of life (QoL) after treatment.

Method: Sleep, fatigue and QoL were evaluated by parent-proxy and child-self reports of the Children's Sleep Health Questionnaire, the Pediatric Quality of Life (PedsQLTM) multidimensional/fatigue scale and the Child Health Questionnaire. The Children's Depression Inventory was included for the potential modifying effect of depression. All total scores were compared to Dutch norms.

Results: Sixty-five children were included, being 45 ± 33 months after finishing treatment. Mean age was 10.1 ± 3.8 years, 52% were boys. Patients rated the ALL survivors as having more disturbed sleep (total score: 44.10 (ALL) vs 40.45 (norms), P < 0.002), more fatigue (74.25 vs 81.0, P = 0.004) and lower physical QoL (47.69 vs 56.4, P < 0.001). Time after treatment did not affect these scores. ALL survivors themselves reported less sleep problems (31.70 (ALL) vs 35.04 (norms), P = 0.005) and less depressive symptoms (females: 4.94 vs 9.01, P < 0.001, males: 5.22 vs 8.80, P = 0.016). Fatigue and QoL did not differ. More time after treatment correlated with better scores. Significant associations between sleep, fatigue and QoL were found.

Conclusion: According to parents, but not to children, sleep, fatigue and QoL were substantially impaired after treatment for childhood ALL. Sleep and fatigue were negatively correlated with QoL, indicating a possibility for intervention to improve psychosocial health. Differences in parental and self ratings might be explained by worried parents and/or an adaptive style of the children. Present findings emphasize the need for objective measurement of sleep and fatigue after childhood ALL, e.g., using actigraphy.

**O151 QUALITY OF LIFE AS A POPULATION HEALTH OUTCOME EVALUATION**

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Purpose: The measurement sensitivity of the Pediatric Quality of Life (PedsQL™), a health related quality of life (HRQOL) tool, was assessed in its application to long term survivors of pediatric cancer. Sensitivity was determined by comparing survivors with other populations.

Method: HRQOL of survivors was compared to established clinical cohorts of healthy patients, patients with chronic rheumatic disease, cancer patients, and cancer survivors. Eligible participants were greater than 2 years post-active cancer treatment and were receiving follow-up care. HRQOL was measured with the PedsQL™ Cancer, Core, and Fatigue Modules. Patients and parent proxies reported.

Results: 142 survivors (58% female, 42% male) participated; disease groups included 12% CNS, 24% Leukemia, 10% lymphoma, 54% solid tumor. Average age was 7 years at diagnosis (SD = 5), 24 years at study participation (SD = 10, ranging from 4 to 53), and 17 years post-treatment (SD = 9). Groups were compared using two sample t-tests. Long-term pediatric cancer survivors had lower Core Module HRQOL grand scores than healthy patients (p < 0.05), yet higher HRQOL grand scores than patients with chronic rheumatic disease (p < 0.005) and a combined sample of cancer patients/ survivors (p < 0.005). When compared with a younger sample of pediatric cancer survivors (ages 2–18 years) off treatment for >12 months, HRQOL grand scores were not statistically different. Fatigue Module total scores were significantly higher (reflecting greater fatigue) for the cancer survivors, as compared with healthy patients (p = 0.01). Cancer Module total scores were significantly better for the older patient sample with more years post-treatment, excepting pain and treatment anxiety scores.

Conclusion: The Pediatric Quality of Life (PedsQL™) was sensitive in detecting differences between long term survivors of pediatric cancer and other populations. Fatigue, pain, and treatment anxiety may be causal indicators of HRQOL in long-term survivors of pediatric cancer.

**O152 CAN PARENT-REPORTED PERCEIVED COGNITIVE FUNCTION BE USEFUL IN PEDIATRIC ONCOLOGY CLINICS?**

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Purpose: Survivors of childhood cancer are recommended to receive periodic screening of cognitive function during long-term follow-ups. Current research suggests that parent-reported pediatric perceived cognitive function item banks (pedsPCF), with psychometric properties supported by Item Response Theory (IRT). In this study, we evaluated whether the pedsPCF could be a useful screening tool for pediatric cancer patients.

Method: 356 parents of pediatric cancer patients aged 7–21 (mean age = 13.5 ± 3.5 years) were recruited from pediatric hematology/oncology clinics in Chicago, Memphis and Boston. Of these patients, 53% had a brain tumor; 34% received radiation therapy, 72% chemotherapy and 71% surgery. Average years since diagnosis were 5.7 with 20% < 1 year, 11% 1–2 years, 23% 2–5 years and 46% > 5 years. PedsPCF scores were converted into IRT-based T-scores (mean = 50, SD = 10) using normative data drawn from 1,409 parents of the US pediatric general population.

Results: Significantly lower pedsPCF T-scores were found for children with brain tumors (versus non-brain tumor; t = 5.7, p < 0.001) and years since diagnosis > 5 years (versus other age groups; F(35,158) = 5.7, p < 0.001). Median groups defined by radiation exposure (yes/no) did not differ significantly. Children who received craniospinal or whole brain radiation (n = 53) had lower T-scores than the norm and their scores correlated with years since diagnosis (r = −0.44, p < 0.01).

Conclusion: PedsPCF scores discriminate patients with brain tumor versus other forms of cancer. Consistent with the literature, pedsPCF identified pathology is related to time since diagnosis, particularly for those who received whole brain radiation. Future plans include comparing the pedsPCF to performance on neuropsychological testing batteries.

**O153 BIRDS OF A FEATHER: FRIENDSHIP CHARACTERISTICS AND SOCIAL ACCEPTANCE IN CHILDREN WITH CANCER**

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Purpose: The purpose of this study was to examine differences in patterns of peer affiliation between children with cancer and their non-chronically ill peers.

Method: This study compared 84 children with cancer, ages 8–15 years, to 84 behaviorally similar, gender-, race- and sex-matched, non-chronically peers, with regard to differences in patterns of peer affiliation, social acceptance and friendships. Sociometric data (Like Rating Scale, Revised Class Play, 3 Best Friends) were collected in children’s classrooms from peers. Children with cancer were undergoing treatment for a non-primary-CNS malignancy. Consistent with the literature, pedsPCF identified pathology is related to time since diagnosis, particularly for those who received whole brain radiation. Future plans include comparing the pedsPCF to performance on neuropsychological testing batteries.

**O154 EMPIRICALLY DERIVED PSYCHOSOCIAL STATES AMONG INDIVIDUALS DIAGNOSED WITH CANCER DURING ADOLESCENCE DURING THE ACUTE, EXTENDED, AND PERMANENT PHASE OF SURVIVAL**

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Purpose: To, during the acute, extended and permanent phase of survival, identify psychosocial states among individuals diagnosed with cancer during adolescence and to analyze these in relation to demographic and clinical characteristics, cancer-related negative and positive consequences, coping strategies, and self-reported symptoms of depression.

Method: Individuals participated at 4–8 weeks (n = 61), 6 (n = 56), 12 (n = 50), 18 (n = 48) months, and 2 (n = 38), 3 (n = 42), and 4 (n = 39) years after diagnosis. I-states as Objectives of Analysis was used to identify a finite set of psychosocial states based on three dimensions: vitality, mental health (SF-36), and anxiety (Hospital Anxiety and Depression Scale). Cluster analysis was carried out by Ward’s method.

Results: Three psychosocial states were identified: poor (state A), inappropriate (B), and good (C) psychosocial function. Shortly after diagnosis more individuals than expected by
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chance were found in states A and B and fewer in state C. Over time individuals moved from state A to state C. Four years after diagnosis 77% were found in state C. 8% in state B, and 15% in state A. Female gender, having divorced parents, and use of distraction shortly after diagnosis were related to state A. Contrary, a more positive view of life and absence of bodily concerns were related to state C. A diagnosis of lymphoma was related to state C.

Conclusion: The findings provide support for subgroups of individuals whose level of vitality, mood, anxiety and efficacy differ during the acute, extended, and permanent phase of survival. Most adolescents diagnosed with cancer move from poor to good psychosocial function over time from diagnosis. Clinical interventions tailored to the level of impairment as determined by the clusters may result in better psychosocial outcomes.

O155

NEW FRONTIERS: THE PEDIATRIC NURSE AS A FERTILITY PRESERVATION CONSULTANT

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Purpose: The evolution of the nurse as a fertility preservation consultant at a pediatric hospital will be discussed and the role of nursing as the patient’s advocate for fertility preservation explored. Services which may be provided by the pediatric health care team will be examined, along with the expertise supplied by the adult reproductive experts. The collaboration between the pediatric institution and the adult fertility preservation specialty services will outline key elements to successful programmatic development.

Method: Descriptive poster

Results: The pediatric nurse practitioner has established the role of the pediatric oncology nurse as a fertility preservation consultant by developing expertise in fertility preservation, advocating for patients and families to be given the option of fertility preservation, assessing patient appropriateness for fertility preservation, cultivating a relationship with adult fertility preservation specialists, exploring the potential for fertility preservation to include other pediatric subspecialties such as rheumatology or genetics and promoting fertility preservation research across institutions and disciplines.

Conclusion: Fertility preservation in the pediatric and adolescent patient is gaining recognition as an important component of patient care. Many pediatric oncologists and oncology nurses are not well versed in the topic of fertility preservation. Fertility preservation physicians and nurses often do not have the experience or training to work with pediatric and adolescent patients and families. Pediatric oncology nurses and nurse practitioners are uniquely qualified to provide the following components when advocating for fertility preservation: educating patients and families regarding the risk of infertility and options, providing developmental care sensitive to the cultural and religious background of the family, as well as coordinating care between pediatric specialists and fertility preservation experts.

O156

YOUNG PEOPLE TALK ABOUT CANCER: A VIRTUAL ETHNOGRAPHY STUDY

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Purpose: Adolescents with cancer experience multiple problems associated with cancer treatments. They experience side effects on a daily basis and often live with unrelied symptoms. They develop strategies to help manage changes in the social and functional aspects of their lives. Research that explores the unique perspective and experience of young people can provide a rich information source for people affected by cancer as well as for those caring for them. The aim of this virtual observation study is to use an Internet site, Jimmteens.tv, to explore the kinds of stories young people chose to share.

Method: Jimmteens.tv is a site where young people describe their experiences from diagnosis to living with and beyond cancer. A team of four researchers watched and coded a film series from 15 young people: total 3,669.79 minutes of video recording. Data analysis and interpretation proceed in tandem, with interpretation starting early and returning to the field to re-watch videos as required. Data were transformed through dialogue in the research team and the production of mind maps into a typology of types of stories.

Results: Data reveals four kinds of stories, around treatment and relenting side effects, rehabilitation and getting back on with life, relapse, facing more treatment and coming to terms with dying. In all these stories there were consistent messages of advice about managing effects of therapy, keeping up with friends, goal setting, the importance of family, and getting on with life. Stories about experiences of care were also a feature.

Conclusion: Our study illuminates some of the strategies young people use to gain mastery over their illness, and the types of stories they choose to tell. This presentation will focus on methods used and the findings as we begin to describe patient and professional education materials and research priorities based on patient’s stories.

O157

BURDEN OF LOCAL THERAPY IN SURVIVORS OF HIGH RISK NON-METASTATIC RHABDOMYOSARCOMA AND RELATED DIAGNOSES IN SIOP MMT95

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Purpose: 457 high risk (incompletely resected rRMS). UDS. 1967, pNET at all sites except parasternal/vagina/uterus; and all aRMS patients diagnosed 1995–2003, median age 5.5 years, were randomised between IV (ifosfamide/vincristine/actinomycin D) and 6 drugs (IVA + carboplatin/epirubicin/toposide) delivered over 27 weeks. Cumulative doses2, ifosfamide54 g (both arms), epirubicin 450 mg, etoposide 1350 mg (6 drug). Initial surgical approach was conservative and RT was determined according to site and response to chemotherapy ± surgery. There was no significant difference in 5 year OS between IVA 74% (68–79%) and 6 Drugs 74% (67–79%) Toxicity was significantly greater (infection, myelosuppression, mucositis) for the 6 drug arm. This analysis explored the overall burden of local therapy in long term survivors at median follow up 8.6(0–14.2) years.

Method: All functionally/cosmetically unimportant surgery, or brachytherapy was defined as conservative local therapy. Conservaive surgery was further defined to identify more significant procedures without predicted functional or mutilating consequences as 'large' surgery. All other surgery and external beam RT (all sites, any dose) was classified as significant local therapy.

Results: 312 patients were considered cured (277 in 1stCR, 35 in 2ndCR > 24 months from last relapse). 36/4(112/308 - detailed surgical status was unavailable in 4) received conservative local therapy. 52%(164/312) had external RT and 4%(14/312) brachytherapy. 14%(42/308) underwent mutilating surgical procedures (none at diagnosis) of whom 10 also had RT. 32%(99/308) patients were cured without mutilating surgery or any form of RT (including 3 in 2ndCR) of whom 20 had only undergone conservative initial surgery or biopsy but had no further local therapy; 61 had conservative second surgery after initial biopsy and chemotherapy; and 16 had ‘large’ surgery as first or second procedure.

Conclusion: Care without significant local therapy was achieved in 36% of high risk RMS. As the majority of similar patients in contemporaneous studies would have systematically received RT, strategies to selectively determine the place of RT (in particular) merit continuing attention.

O158

LOCAL THERAPY IS CRITICAL IN LOCALIZED PELVIC RHABDOMYOSARCOMA: EXPERIENCE OF THE INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY MALIGNANT MESENCHYMAL TUMOR (SIOP-MMT) COMMITTEE

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Purpose: Localized pelvic rhabdomyosarcomas (pRMS) are rare tumors with poorer prognosis than the majority of RMS. This study analyzed patient outcome according to the type of local therapy delivered and the effect of disease related factors on prognosis.

Method: 97 children with localized pRMS were enrolled in the SIOP MMT-84, 89 and 95 studies between 1984 and 2004. After primary surgery or biopsy, all children
received ifosfamide/actinomycin/vincristine-based (IVA) chemotherapy (CT). Radiotherapy and surgery were planned in patients failing to achieve complete remission (CR).

**Results:** Median age at diagnosis was 52 months (5 months-18 years). IRS staging was I for 5 patients, II for 15 and III for 77. Patients had embryonal RMS (N = 41), alveolar RMS (N = 29), botryoid RMS (N = 3), or not otherwise specified RMS (N = 24). Outcome: 87 patients achieved local control (90%), 37 relapsed, mainly locally (84%). With a median follow-up of more than 10 years (4-22 years), 5-year OS was 66% (95% CI: 56%-75%) and EFS was 52% (95% CI: 42%-61%). Among the 18 IRS-II patients treated without radiotherapy, 15 survived. Seven out of the 20 IRS-III patients treated without local therapy died. On multivariate analysis, IRS staging, age greater than 10 years and lymph node involvement had a negative impact on overall survival whereas gender, tumor size and histology did not. Perineal/perianal locations had a trend towards a worse prognosis.

**Conclusion:** Preliminary still have a relatively poor prognosis. Radiotherapy or brachytherapy is necessary for all IRS-III patients including those with radiological CR after neoadjuvant CT with or without surgery. Radiotherapy may be withheld in IRS-I patients and children under 3 years with IRS-II (pRMS).

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**O159**

**MUSCLE-SPECIFIC MICRORNA: A NOVEL BODY FLUID BIOMARKER FOR DIAGNOSIS OF RHABDOMYOSARCOMA**

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**Purpose:** Presently, there is no body fluid biomarker of rhabdomyosarcoma (RMS). Several studies have shown that expression profiles of microRNAs in tumor and serum vary among tumor types. To exploit this difference, we evaluated the feasibility of using a muscle-specific microRNA, miR-206, as a biomarker of RMS.

**Method:** Total RNA was extracted from 21 tumor specimens (7 RMS, 14 non-RMS), 48 serum specimens (8 RMS, 23 non-RMS and 17 healthy volunteers), 10 cerebrospinal fluids (1 RMS, 9 non-RMS), 3 pleural fluids (1 RMS, 2 non-RMS) and 2 ascitic fluids (2 non-RMS). microRNAs were extracted from 200μL of body fluids and quantified by real-time quantitative RT-PCR. The expression levels of miR-206 were normalized to miR-16 in tumor and serum specimens and their absolute values were determined in cerebrospinal, pleural and ascitic fluids.

**Results:** Expression of miR-206 in RMS tumors was significantly higher than the expression in non-RMS tumors (p < 0.01). The normalized serum miR-206 expression level could be used to differentiate between RMS and non-RMS tumors, with a sensitivity of 1.0 and a specificity of 0.913. The serum expression level of miR-206 decreased after treatment and increased at relapse. Further, the expression level of miR-206 in cerebrospinal, pleural and ascitic fluids was higher in RMS patients than in non-RMS patients.

**Conclusion:** Our study indicates that serum miR-206 measurement makes it possible to make a correct preoperative diagnosis of RMS and to plan a surgery based on RMS surgical guidelines. miR-206 can be detected not only in serum but also in other body cavity fluids including cerebrospinal, pleural and ascitic fluids of RMS patients. The miR-206 expression levels in body cavity fluids could aid diagnosis of RMS tumors, such as brain metastasis, that are difficult to biopsy. Measurement of miR-206 in serum and body cavity fluids could also be used to monitor disease activity.

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**O160**

**CONGENTIAL SOFT TISSUE SARCOMAS: A CLINICAL REPORT FROM THE ITALIAN SOFT TISSUE SARCOMA COMMITTEE**

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**Purpose:** Soft Tissue Sarcomas (STS) account for about 7.5% of all pediatric malignancies. Histotypes differ depending on age. We analyzed congenital STS in order to better understand tumor characteristics in this age-group.

**Method:** We analyzed patients with histologically confirmed STS, enrolled in three Italian Protocols (1979-2005), diagnosed before 6 weeks of age and therefore considered congenital. They represented 1.7% of all cases: 28/1632 patients.

**Results:** Rhabdomyosarcomas (RMS) were 11/28 (39% vs 56% in the whole population). Embryonal histotype were 6/11; Alveolar RMS was less represented than in the whole population (9.1% vs 31.4%). One patient was staged as IRS II (microscopic residual), 9 IRS III (7 biopsies, 2 excisions with macroscopic residuals), 1 IRS IV. All patients received CT; 8 underwent initial or delayed surgery; 1 received also brachytherapy. Non RMS STS (NRSTS): 17/28 (61%). Infantile Fibrosarcomas represented the most frequent histotype (58.8% vs 10.8% of the whole population); other STS were less frequent than in the entire series. Site: 12 extremities, 5 other sites. Six cases were IRS I, 2 IRS II, 8 IRS III (7 biopsies, 1 initial excision with macroscopic residuals). 1 IRS IV: 12/17 patients received CT. Initial delayed excision was attempted in 14 cases. One patient with pNET presented nodal involvement and distant metastases. One with Fibrosarcoma underwent foot amputation at delayed surgery. Outcome in the whole population was different by histotype. Survival rate for RMS was worse than that of patients < 1 year (27.3% vs 47.6%). Survival of NRSTS was 82.3% 2235 (90%). For chemotherapy-related toxicity.

**Conclusion:** Treatment of congenital STS is a challenge. Chemotherapy must be carefully tailored. Local control is based upon surgery, because radiotherapy cannot be administered. Outcome in the RMS-group was poorer than in the whole population; in NRSTS, instead, it was improved by the high rate of Fibrosarcomas.
CONSERVATIVE TREATMENT OF INTRACULAR RETINOBLASTOMA: A PROSPECTIVE PHASE II RANDOMIZED TRIAL OF NEOADJUVANT CHEMOTHERAPY FOLLOWED BY LOCAL TREATMENTS AND CHEMOTHERMOTHERAPY

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Purpose: Intracircular retinoblastoma treatments often associate chemotherapy and focal treatments. The protocols vary and may combine two or three drugs, and different number of cycles associated to the ocular treatments. A first prospective protocol of conservative treatments in our institution showed the efficacy of the use of two courses of chemoreduction with etoposide and carboplatin, followed by chemothermotherapy with a single agent: carboplatin. In order to decrease the possible long term toxicity of chemotherapy by etoposide a prospective protocol of chemo reduction using vincristine and carboplatin vs etoposide carboplatin was initiated.

Method: Monocentric phase II randomized study for children needing chemoreduction for intracircular retinoblastoma before ocular treatments using vincristin carboplatin or etoposide carboplatin, and followed by local treatment including chemothermotherapy with carboplatin only. Primary endpoint was the need for secondary enucleation or EBRT not for intraocular retinoblastoma before ocular treatments using vincristine carboplatin or etoposide a prospective protocol of chemo reduction using vincristine and carboplatin vs etoposide carboplatin was initiated.

Results: 55 children, 65 eyes were included in the study (May 2004–August 2009). 31 eyes (26 children) were treated conservatively in the arm etoposide-carboplatin and 34 (29 children) eyes in the arm vincristin carboplatin. At one year after treatment 26/34 (76.5%) eyes were treated and salvaged without EBRT or enucleation in the arm vincristin-carboplatin and 28/31 (90.4%) in the arm etoposide and carboplatin.

Conclusion: Neoadjuvant chemotherapy by two cycles of vincristine and carboplatin followed by chemothermotherapy with carboplatin alone achieves good local control. Final statistical analysis is planned two years after the end of treatment.

NEOADJUVANT CHEMOTHERAPY IN STAGE 3 RETINOBLASTOMA AS PER INTERNATIONAL RETINOBLASTOMA STAGING SYTEM: A PROSPECTIVE STUDY

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Purpose: Extracircular retinoblastoma accounts for 20–50% of retinoblastoma cases in resource-challenged countries due to delayed diagnosis and late presentation. Computed tomography (CT) of orbits, magnetic resonance imaging (MRI) of orbits and brain and bone scan are standard imaging modalities in extracircular retinoblastoma. There is no data on role of positron emission tomography (PET) combined with CT (PET-CT) in extracircular RB. The purpose of the study was to evaluate role of PET-CT in stage 3 retinoblastoma as per international retinoblastoma staging system (ISS) at baseline and for response assessment after 3 cycles of neoadjuvant chemotherapy (NACT).

Method: We prospectively enrolled 30 patients with ISSG stage 3 retinoblastoma patients from May 2009–May 2010. All patients received 3 cycles of neoadjuvant chemotherapy (NACT) consisting of vincristine 1.4 mg/m2 and carboplatin 750 mg/m2 on day 1 and etoposide 150 mg/m2 on day 1 and 2 every 4 weekly, followed by surgical excision, external beam radiotherapy (45 Gy) and adjuvant chemotherapy for 9 more cycles. PET-CT scans and MRI orbits and brain were done at baseline (PET-1) and after 3 cycles of NACT (PET-2). All patients also underwent bone marrow biopsy and CSF evaluation for metastatic disease.

Results: 27/30 patients underwent PET-1 and 23/30 patients PET-2. No additional disease sites were diagnosed on PET-CT. Response to NACT was seen in all 23 patients who underwent PET-2; 19/23 had complete response (CR) and 4/23 had partial response (PR). Microscopic tumor was identified in the enucleated specimens of all 23 patients who underwent PET-2. The overall survival for patients with CR in PET-2 was 63.16% and for those with PR in PET-2 was 75% (P = 0.99).

Conclusion: PET-CT does not offer any additional benefit when compared to standard imaging modalities for staging and prognostication in ISSG stage 3 retinoblastoma patients.

THYROID CARCINOMA IN CHILDHOOD AND ADOLESCENTS: A 45-YEAR REVIEW OF CASES IN NORTHERN ALBERTA

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Purpose: Thyroid carcinoma constitutes 0.5–3% of all childhood malignancies. These tumors are rare, affecting 1 in 1 million children per year in the United States, with a similar incidence in Canada. Objective data to guide management is lacking. We report the management and outcome of 53 cases of thyroid carcinoma in children and adolescents over the last 45 years in northern Alberta.

Method: Charts were reviewed for 53 cases of pediatric thyroid carcinoma. We stratified patients based on disease extent at presentation and examine the use of total thyroidectomy versus hemithyroidectomy and its effect on recurrence, survival and long-term side effects. In some patients, post surgery radioiodine therapy was used to ablate residual normal thyroid tissue and to treat functioning metastases. External beam radiotherapy was employed in some patients who developed recurrence.

Results: Pediatric thyroid carcinoma presenting between 1961 and 2006 were reviewed. There were 40 girls and 13 boys. Mean age at diagnosis was 14.5 years (range: 5 years to 17 years) and mean length of follow-up was 11.5 years (range: 4 months to 28 years). All patients were alive at time of last follow-up. Six patients were lost to follow-up. 39 patients had papillary carcinoma, 9 mixed papillary and follicular thyroid carcinoma, 2 follicular carcinoma and 3 medullary carcinoma. Tumor was limited to the thyroid gland in 22 cases, 26 loco-regional disease and 5 loco-regional metastases and distant metastases. We also consider the use of radioactive iodine ablation and its effect on recurrence, overall survival and adverse effects in the pediatric population.

Conclusion: Prognosis for thyroid carcinoma in children and adolescents is excellent, and we advocate total, 4/5 patients and modified neck dissection as initial treatment strategy. We currently routinely ablate residual thyroid tissue and feel this is a reasonable and safe approach.
SIOP ABSTRACTS

**0168**

**ASSOCIATION OF POLYMORPHISMS OF CYTOKINE GENES WITH THE RISK AND CLINICAL COURSE OF CHILDHOOD LAGHERANS CELL HISTIOCYTOSIS**

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**Purpose:** A dysregulation of cytokines may play an important role in the pathogenesis and clinical course of Langerhans cell histiocytosis (LCH). Since it is well known that variant alleles (polymorphisms) of cytokines may influence functional characteristics and/or serum concentration of the molecule, polymorphisms within genes encoding pro- and anti-inflammatory factors.

**Method:** Genetic polymorphisms of interleukin (IL)-6 (G-174C), IL-8 (A-352T), IL-1α (G-308A) were assessed in 202 patients with confirmed LCH and associated with risk and clinical course of the disease.

**Results:** A total of 82 girls and 120 boys (median age: 24 months) were included in the study. The patients presented with single-system (n = 113) or multi-system LCH (n = 89). 56 and 33 patients with and without involvement of risk organs, respectively. Compared to healthy individuals, we found a significant over- and underrepresentation of the homozygosity genotypes of the IL-6 and IL-8 promoter polymorphisms in patients with LCH, respectively (P = 0.0026 and P < 0.0001, respectively). Whereas no polymorphism analyzed was associated with age or gender, the C-allele of the IL-6 G-174C polymorphism was significantly overrepresented in multi-system as compared to single-system LCH (P = 0.0005); this difference was also seen in the subgroup of patients with involvement of risk organs. In addition, heterozygotes for the IL-8 (A-352T) genotype polymorphism were significantly overrepresented in patients reaching a non-active disease status, both at the first follow-up at 6 weeks and over time (P = 0.027 and P = 0.03, respectively).

**Conclusion:** The results of this analysis on the largest cohort of LCH patients published to date suggest that specific cytokine polymorphisms may affect susceptibility to and clinical course of LCH and may ultimately help to design treatment protocols tailored individually for each patient.

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**0169**

**ORAL VORICONAZOLE VERSUS INTRAVENOUS LOW DOSE AMPHOTERICIN B FOR PREMATURE ANFUNGAL PROPHYLAXIS IN PEDIATRIC ACUTE LEUKEMIA INDUCTION: A PROSPECTIVE, RANDOMIZED, CLINICAL STUDY**

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**Purpose:** Invasive fungal infections (IFI) are a major cause of infection-related mortality during induction chemotherapy of acute Leukemia (AL) patients. Data on antifungal prophylaxis (AFP) in children is limited by retrospective design, small sample size and variability of chemotherapy phases having different risk of IFI. There is no data comparing voriconazole versus amphotericin B (AmB) as AFP in either adult/pediatric AL. The present study compares efficacy and toxicity of amphotericin B (AmB) and voriconazole as AFP in pediatric AL patients.

**Method:** As a pilot study, total 100 children (U15 years) with denovo AML and ALL were randomized to either oral voriconazole or low dose intravenous AmB as AFP during induction chemotherapy.

**Results:** Failure of prophylaxis occurred in 14/50 patients in voriconazole arm (1% mucormycosis, 1% IPI, 11 empirical antifungal therapy and 1 withdrawal due to hepatotoxicity) and 17/50 patients in AmB arm (3 possible IPI, 13 empirical antifungal therapy and 1 withdrawal due to difficult venous access) (P = 0.066). Of the 29 patients who had failure of prophylaxis unrelated to drug toxicity, CT chest showed infiltrates in 10 patients with 3/18 in voriconazole arm and 7/16 in AmB arm (P = 0.43). Drug-related serious adverse events were 6% versus 30% in voriconazole and AmB arms respectively (P < 0.01). Further, total number of toxicities per patient in AmB arm were significantly higher as compared to voriconazole arm (P < 0.0001).

**Conclusion:** This is the first randomized study comparing voriconazole with AmB in pediatric AL patients as AFP during induction chemotherapy; our results showed that oral voriconazole appears to be comparable with AmB with less toxicity and more convenience.

(ClinicalTrials.gov identifier: NCT00624143)

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**0170**

**CLINICAL PRESENTATION, OUTCOME AND POTENTIAL ROLE OF ORAL RIBAVIRIN IN MEASLES INFECTION IN CHILDREN WITH CANCERS**

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**Purpose:** To assess clinicoradiological features, outcomes and therapeutic benefit of oral ribavirin in children with cancer who developed measles on chemotherapy.

**Method:** A retrospective audit of paediatric patients with measles was undertaken at Tata Memorial Hospital from January to December, 2010. Patients with measles had survived. Comparatively, the case fatality rate in the present series was 70% in various studies. The morbidity and mortality have decreased with the use of tachycardia and respiratory distress; 6 subsequently required mechanical ventilation. Median lymphocyte count was 800X10⁹/L. 6 patients had lymphocyte count below 500X10⁹/L. 5 of them required ventilatory support. Chest radiographs showed interstitial pneumonia in 6. Severe encephalitis in 1 and normal radiograph in 3 patients. 9 patients were treated with oral ribavirin since intravenous and inhalational ribavirin was unavailable. The dose used was 80 mg/kg/day with tapering after 5 days and the median duration was 10 days (range 6–17 days). 6 pts required ventilation and had progressive respiratory dysfunction with sepsis and expired. These patients were also treated with methyl prednisolone (5–20 mg/kg) and IVIg, along with Vitamin A and Zinc supplements. Overall, four patients recovered with average duration of 6 days since rash. One patient developed subacute encephalitis after a month and is currently neurologically stable.

**Conclusion:** Case fatality rates in severe measles in immunocompromised patients range from 30–70% in various studies. The morbidity and mortality have decreased with the use of intravenous and possibly inhalational ribavirin. Prior to using oral ribavirin, none of our patients with measles had survived. Comparatively, the case fatality rate in the present series was 60%. Patients with respiratory distress requiring ventilation and lymphocytes below 0.5X10⁹/L, had especially poor outcomes. To conclude, oral ribavirin appears to have therapeutic benefit and should be explored as an option where intravenous and inhalational ribavirin are unavailable.

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SIOP ABSTRACTS

O171

CENTRAL VENOUS CATHETERS AND CATHERETIC LOCKS IN CHILDREN WITH CANCER: A PROSPECTIVE RANDOMIZED TRIAL OF TAUROLIDINE VERSUS HEPARIN

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Purpose: Central venous catheters (CVCs) are a major risk factor of bloodstream in children with cancer. Taurodine, a derivative from the aminosulphonic acid taurinamide, has shown efficacy in preventing catheter-related bloodstream infections (CRBSI) in adult patients. The purpose of this study was to determine if taurolidine used as a catheter lock can reduce the number of CRBSI in tunneled CVCs in pediatric patients with cancer.

Method: During a study period of 34 months, 129 newly placed tunneled CVCs in 112 patients were randomly assigned to standard lock with a heparin solution or experimental lock with a taurolidine solution (ClinicalTrials.gov Identifier NCT01073881).

Results: Sixty-five CVCs were included in the standard group and sixty-four CVCs in the experimental group. The two groups were comparable regarding patients’ characteristics except that there were more boys in the experimental group. A total number of 64 bloodstream infections of which 26 were CRBSIs were observed among 31,666 CVC-days. A lower rate of CRBSIs (0.3 per 1,000 CVC-days) was observed in the experimental arm compared with the standard arm (1.4 per 1,000 CVC-days, incidence rate ratio (IRR) = 0.22; 95% confidence interval (CI) 0.07 to 0.61; p = 0.001). A lower rate of total bloodstream infections (1.5 per 1,000 CVC-days) was also observed in the experimental arm compared with the standard arm (2.6 per 1,000 CVC-days, IRR = 0.56; 95% CI 0.32 to 0.95; p = 0.02). Median interval from catheter insertion until first CRBSI was significantly lower in the standard group (140 days, range 12–542) compared with the experimental group (246 days, range 12–811; p = 0.04). Premature removal of the CVC due to infection and overall CVC survival were similar in the two study groups. No adverse effects were observed in the group locked with taurolidine.

Conclusion: Locking of long-term tunneled CVC with taurolidine is efficacious and safe in reducing catheter-related bloodstream infections in children with cancer.

O172

ACUTE PSYCHIATRIC EPISODES DURING INTENSIVE TREATMENT COURSE IN ADOLESCENT CANCER PATIENTS

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Purpose: High dose of chemotherapy may lead to acute somatic complications. Some patients may encounter intensification of fear and depressive reactions as well as acute psychiatric episodes. The purpose of the study was to assess the incidence of acute psychiatric episodes during treatment course in adolescent cancer patients.

Method: This study covered history of 125 consecutive adolescent cancer patients diagnosed between Jan, 2007 - March, 2011 in single pediatric onco-hematology ward. The mean age was 14.9 yrs. Planned psychosocial support program was designated to all patients. The psychiatric episodes during treatment course in adolescent cancer patients. Some patients may encounter intensification of fear and depressive reactions as well as acute psychiatric episodes. The purpose of the study was to assess the incidence of acute psychiatric episodes during treatment course in adolescent cancer patients.

Results: During observation period 41 of 125 (32.8%) patients had shown disadaptive reactions with various level of intensity. The most often noticed behaviors were regressive one that were manifested with depressed mood, crying, stubbornness and withdrawal from the activity. In 5 of 125 patients (4%) had noticed 10 acute psychiatric episodes. Six of those episodes with increased consciousness disorder, delusions, extremely intensified fear and touchiness. In all cases Pancrvalidis was diagnosed. Other episodes occurred in patients who took dexamethasone and during antifungal treatment (one patient with fungal infection in CNS). Duration of disorders was from 3 to 17 days. Patients required several psychiatric consultations and intensive pharmacological treatment.

Conclusion: Symptoms of disadaptive reactions occurs in high percentage of cancer adolescents. In 9 of 10 acute psychiatric episodes, acute somatic complications co-occurred. During Pancrvalidis occurrence of acute neuropsychiatric disorders is particularly often.

IPS0 ABSTRACTS

IPS001

SURGERY AT THE WILMS TUMORS WITH THROMBOSIS

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Purpose: The iSA Platform aims to develop a free web-based environment that enables communication for second opinion, pathology and medical imaging reviews or case referrals, among primary care centres and hospitals of reference. The platform provides also clinical case teaching archive for academic institutions. The iSA Project seeks to impact on the quality of medical care at hospitals in Cooperation Partner Countries (emerging communities) for patients diagnosed with cancer and severe infection diseases.

Method: The iSA network of hospitals is divided into two main groups: 1: The iSA leading team in charge of providing specialized expertise, that includes four Spanish hospitals (University Hospital Son Espases-Palma, Instituto Valenciano de Oncología-Valléncia, Hospital Vall d’Hebron-Barcelona, Hospital San Joan de Deu-Barcelona). 2: The requesting centers: Hospital Regional Docente de Trujillo (Peru), Instituto Nacional de Cancerología (Mexico), Centro Estatal de Cancerología de Colima (Mexico), Hospital Regional de Bata (Equatorial Guinea), Saint John of God Hospital (Sierra Leone), College of Health Sciences of the University of Nairobi (Kenya), Kenyatta National Hospital (Kenya), CMF Maasai Health Ministries (Kenya).

Results: We analyse interconsultation results by considering indicators: Consultations per month, communication impact (1-Level of diagnostic certainty based on iSA Anatomic Pathology digital imaging review 2. Impact of iSA consultation on clinical decision making 3. Level of patient benefit) and educational and academic achievements. Global statistic (2010): Cases 142 Users 193 Institutions 79 Countries 29.

Conclusion: It has showed evidence to justify investments on human resources, technology and infrastructures in each center. The iSA Clinical Platform may be a feasible tool to make specialized clinical knowledge and biomedical technologies accessible to researchers and health workers in emerging communities where medical expertise and technological resources are deeply needed. This project is supported by a grant of the Seventh Framework Programme of the European Union. www.theisaproject.eu
Purpose: To evaluate surgery at the Wilms tumors with thrombosis.

Method: With 1990 on 2010 47 (2.8%) patients with the Wilms tumors with thrombosis were observed. After neoadjuvant chemotherapy complete or partial tumor regression of intravascular tumor’s component was achieved in 57.9% and 21.1% respectively. 23 children were operated on as nephrectomy and thrombectomy. Thrombus of right renal vein - 6, 5 - left renal vein, subepithelial segment of the inferior vena cava (IVC) was involved in 7 cases and retrohepatic - 5. The boy 2 years: bilateral nephroblastoma; thrombus in IVC (retrohepatic segment); 4 courses of neoadjuvant chemotherapy. Operation: right nephronectomy, thrombectomy with resection of infrarenal segment of IVC. The time of operation - 270 min. 5-months. The patient was discharged for 12 days. After adjuvant therapy remission - 16 months. The boy 4 years: Wilms tumor at the left pT3N0MO, adhesive thrombus IVC (retrohepatic segment) with spread to contralateral renal vein, right hepatic vein and infrarenal segment of IVC. 4 courses of neoadjuvant chemotherapy. Operation: left nephronectomy, thrombectomy with resection of infrarenal segment of IVC, reconstruction of right renal and right hepatic veins. The time of operation - 390 min. Blood loss - 800 ml. The patient was discharged for 12 days. After adjuvant therapy remission - 16 months.

Results: In the whole group of operated children significant surgical complications and deaths were not registered in this group - 52.8%.

Conclusion: This observation shows successful surgical removal of extended tumor thrombus of nephroblastoma without cardiopulmonary bypass in children.
Purpose: Local treatment of youngest patients with soft tissue sarcomas (STS) has well-known age-related limits. Aim of the report is to evaluate local treatment in a group of children under 3 years of age with RMS and RMS-like tumours.

Method: Polish Paediatric Solid Tumour Study Group registered 181 patients with STS staged I-IV treated according CWS 2002 protocol. 11 patients were younger than 3 years (ages 3–33 months). 1 girl and 10 boys) and were treated according to CWS 2002 for stage I-III RMS and RMS-like tumours in centres of Polish Paediatric Solid Tumour Study Group. Pathology variants were embryonal RMS/5, alveolar RMS/1, PNET-EES/1. Locations of primary tumours were: genito-urinary tract not bladder/prostate/5, bladder&prostate/2, others/3, extremities/1. TNM: T1a-3, T2b-1, T2b-3, N0 M0 (in all). Treatment consisted of chemotherapy and primary or secondary resection of tumors/R0-R1, biopsy & radiotherapy. 64% of the risk groups (CWS) were low /2, standard/3, high/6.

Results: 9/11 patients are alive (81.8%), 7 in Int CR (63.6%), 2 in PR (18.1%). 1 pts relapsed (despite primary R0) and died of progression (9.9%), 1 patient died of sepsis (9.9%). Regarding supplementary local treatment, 4 of 11 pts were irradiated on and 3 are in supplementary local treatment, 4 of 11 pts were irradiated on and 3 are in locoregional therapy, 4 pts in CR, 1 died in septic shock.

Conclusion: Favourable outcome in youngest patients seems confirmed. Regarding local treatment, supplementary radiotherapy is probably very effective in this group of pts, however toxicity of this treatment must be taken into account. Maximal efforts shall be focused on surgical local control of the disease: 4/5 pts who had R0 resection are alive.

IPS0005
DIFFERENTIAL EXPRESSION OF INVASION PROMOTING GENES IN CHILLOOD RHABDOMYOSARCOMA
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Purpose: Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma with a poor prognosis especially in patients with metastatic disease. Up to now, mechanisms of metastatic invasion are not completely understood. Expression profiling of RMS tissue samples may offer a deeper understanding of these mechanisms and may allow a systemic search for novel targeted therapies. The aim of this study was to identify mechanisms of metastatic invasion in RMS.

Method: Gene expression analysis using the Affymetrix U133 Plus2 array was performed in tumor samples from 19 patients with RMS treated within the CWS 96- and -2002 trials. Validation of target genes was performed by qRT-PCR. Data were analyzed using Pathway analysis software. Possible invasion promoting genes were evaluated in knock-down experiments using siRNA and invasion assays.

Results: In alveolar RMS samples, 211 of 534 genes were over expressed. In embryonal RMS, 323 genes were over expressed. One group of genes was identified, which was involved in pathways regulating cell growth, morphology and motility. A high expression of transcription factors such as FOXF1 and LMO4 was found in patients with metastatic disease. Knock-down experiments of FOXF1 and LMO4 resulted in a > 10 fold inhibition of invasion.

Conclusion: We could identify a major regulatory process for metastatic invasion in childhood RMS. LMO4 and FOXF1 are potential therapeutic targets for prevention of childhood RMS.

IPS0006
RARITY OF INDICATION FOR SURGICAL TREATMENT FOR INFANTILE HAEMANGIOMAS AFTER INTRODUCTION OF PROPRANOLOL
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Purpose: Since 2008, number of authors advocated the efficacy of propranolol in treatment of infantile haemangiomas (IH). The indications for this treatment, its duration, dosage of propranolol and relationship to other methods (e.g. surgery, laser therapy) applicable, need further studies.

Method: Since 2009 three medical centers cooperated in the treatment of IH with propranolol orally using the same criteria of inclusion and the same scheme of medication. Propranolol were advocated "as so-called ‘critical regions’, very rapid progression and size > 5 cm, ulceration/major cosmetic impairment. Propranolol was administered orally, doses ranged from 1.2 to 3.8 mg/kg/day. Thus far (2009–2011) 203 patients are registered in this study. Fifty-two of them completed the treatment. Primary response was assessed in 151 patients under the treatment, final outcome in those 52 who finished the treatment.

Results: Primary response assessed earliest at 1st week of therapy and was observed in 145/151 (96%) pts, stabilization only - in 6/151 (4%). None of patients progressed under the treatment. Final response was assessed in 52 patients who finished the treatment after 2–17 months of medication. In 39 of them (78%) complete or near complete (over 75%) regression of IH was observed, in 11 (21.1%) regression was moderate (25 to 74%), in 2 pts disease was stable (3.9%). None of IH progressed. Eleven pts were submitted to subsequent surgery: 2 due to lack of response (stable IH) and 9 - due to residual scar/fatty tissue remaining after regression of IH. There were no complications related to propranolol.

Conclusion: Favorable results of propranolol 39/52 (75%) pts, with near complete or complete regression, administered orally for IH, decreased the need for surgical correction to only 11 cases (21%) of those who completed therapy. Note that only critically involved and rapidly progressing/ulcerative IH were qualified for this treatment.
Purpose: To define performance possibility endoscopic surgery in children's oncology.

Method: In Scientific Research Institute of in children's oncology and hematology of N.N.Blohin RAMS endoscopic operations in patients with tumors are regularly performed since 2007. At the present moment the score of performed operations is 2490 of which 112 were laparoscopic and 106 were thorascopic. Operation specter includes biopsies of large formations (92), lung resections (59), nephrectomies (23), adenectomies (18), kidney resections (1), gastric resections (5), hepatic resections (5), hemihematopaties (8), retroperitoneal tumortomies (11), mediastinal tumors (1), perfomed on the organs of minor pelvis (5), appendectomies (1), splenectomies (1). Operated children were aged form 2 month to 18 years (average 8.3 years). Diagnostic operation's average time was 28 minutes. Therapeutic operations took from 30 minutes (in cases of standard adenectomies) to 280 minutes (hemihematopaties). Maximal blood loss was 400 ml in cases of hemihematopaties. Performing endoscopic surgical interventions in children has its specific features: small abdominal cavity volume, lesser sizes of all anatomical structures, and specific features of performing prolonged pneumoperitoneum, it is also impossible to separately intubate selected bronchi when performing thorascopic operations in children under 6 years old.

Results: advantages of using laparoscopy in children with tumors are: earlier possibility of starting specific postoperative treatment, less traumatic operation, minimal blood loss, decreased rate of postoperative complications, earlier recovery of physical activity in operated children, decreased time of staying in the hospital, better cosmetic effect after surgical intervention.

Conclusion: performing endoscopic operations in children with malignant tumors is possible from the age of several weeks without breaking the principles of oncological surgery; in such operations the age of the child is not a limiting factor for performing surgical interventions.

IPS0009

PULMONARY METASTASECTOMY IN PEDIATRIC SOLID TUMORS

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Purpose: To evaluate the surgical management, complications and the outcome of patients who underwent pulmonary metastasectomy for solid tumors.

Method: Case records of solid tumor patients who underwent pulmonary metastasectomy in the period September 2001 to April 2009 were reviewed to evaluate the disease distribution, number of thoracotomies, type of resection, complications and ultimate outcomes. Kaplan Meier survival estimates were obtained for 3 year overall survival (OS) and event free survival (EFS). Results: During this time period, 23 patients (8 Wilms [WT], 6 Osteosarcoma [OSa], 4 Ewing sarcoma [EW], 3 Rhabdomyosarcoma [RMS]), 2 cases of malignant germ cell tumors [MGT], 1 each of malignant mesenchymal tumor [MRT], Ewing sarcoma [EW] and rhabdomyosarcoma [RMS]) underwent a total of 33 thoracotomies (14 unilateral, 8 bilateral and 3 re-thoracotomy) for the mesenchymal tumor [MMT], Ewing sarcoma [EW] and rhabdomyosarcoma [RMS].

Conclusion: performing endoscopic operations in children with malignant tumors is possible from the age of several weeks without breaking the principles of oncological surgery; in such operations the age of the child is not a limiting factor for performing surgical interventions.

IPS0011

EXTRACORPOREAL RADIATED AUTOGONOUS TUMOR BONE GRAFT - A RECONSTRUCTION OPTION FOR DIAPHYSEAL TUMORS

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Purpose: We analyzed our results with Extracorporeal Radiated Autogenous Tumor Bone Graft (ECRT bg) for reconstruction in limb salvage after resection of diaphyseal tumors. Method: 35 cases of diaphyseal tumors (OGS (n = 17) and PNET (n = 18)) were reconstructed with ECRT by between July 2005 to September 2009. The femur was involved in 18 cases, tibia in 11, humerus in 5 and ulna in 1. The average resection length was 21 cm (range 10 to 30). The excised bone was radiated with 50 Gy prior to reimplantation and stabilised with the host bone using plate fixation in 32 cases and an intramedullary nail in 3.

Results: One patient died due to chemotherapy complications. 33 of the remaining 34 patients were available for follow up. The mean follow up was 28 months (range 3 to 69 months). 4 patients had infection necessitating removal of graft. 4 more cases needed additional surgery to augment the reconstruction prior to union. The average time to union was 7 months, with union at metaphyseal ends (5.7 months) occurring quicker than at diaphyseal ends (8.8 months). There were 3 local recurrences, one isolated and two with distant metastasis. All local recurrences were in soft tissue away from the radiated graft. 10 patients died due to disease progression. The mean follow up for survivors was 34 months (range 18 to 69 months). The mean MSTS functional score was 27 (range 22 to 30).

Conclusion: ECRT bg is a convenient and inexpensive technique for limb salvage which avoids the logistic issues involved in allograft procurement and the specialized expertise necessary for microvascular anastomosis. It is an oncologically sound procedure with good functional outcomes in diaphyseal tumors.

IPS0012

PAEDIATRIC DIAPHYSEAL MALIGNANT TUMORS - IS INTERCALARY RESECTION SAFE & OPTIONS FOR RECONSTRUCTION

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Purpose: Bone tumors in the diaphysis are relatively uncommon. In most of these it may be possible to achieve adequate margins without sacrificing the adjacent articular surfaces. We asked whether intercalary resection with preservation of the adjoining joints could achieve satisfactory disease control. We also looked at the options for reconstruction, the complications arising therewith and the functional outcomes.

Method: We reviewed 525 malignant skeletal tumors in patients 18 years and less which were operated at our institute between January 2002 and June 2008. Forty two patients (8%) with lesions located in the diaphysis had undergone an intercalary resection with preservation of the adjoining joints. Age ranged from 2 to 16 years. After resection, various methods of reconstruction were adopted based on tumor size and availability of reconstruction options.
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Thirty seven patients were available for follow up. Follow up duration ranged from 4 months to 86 months (mean 38.3 months).

Results: Oncologic results. There were 3 local recurrences. Two patients died of chemotherapy related complications. An additional 6 patients succumbed to the disease. The follow up duration in the survivors ranged from 25 months to 86 months with a mean of 45.7 months. Results of reconstruction: Overall 7 of 37 patients (19%) had infection. Sixteen patients (43%) of the 38 whose reconstructions were evaluable needed a repeat surgery for complications related to reconstruction. The functional status as determined by Musculoskeletal Tumor Society Score ranged from 18 to 30 (mean 27).

Conclusion: Joint preserving intercalary resections are an oncologically safe option and give adequate local control. Paediatric diaphyseal malignant tumors pose a unique challenge after intercalary resection as regards reconstruction. Repeat surgeries to augment reconstruction are not uncommon but the final functional results are gratifying.

IPS0013

THE RESULTS OF TREATMENT OF CHILDREN WITH METASTATIC WILMS TUMOURS (WT) IN AN AFRICAN SETTING

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Purpose: The impact of liver metastases of WT on survival is controversial. From Africa, where the socio-economic circumstances differ from the developed world, there are no data regarding the influence of liver metastases on survival. Aim: 1) To determine the prognostic value of liver metastases in the African setting. 2) To audit treatment results (survival: OS-EFS, toxicity, abandonment) of metastatic WT.

Method: Fifty four patients with stage IV disease from a cohort of 150 new patients (2002–2011), were included. In all patients the site of metastases and pre-treatment biopsies were obtained. Seven patients with stage V disease and visceral metastases were included in the analysis. Neo-adjuvant chemotherapy following SIOP principles was offered to all and combined with nutritional resuscitation and TB-prophylaxis, anti-helminthics, anti-infective drugs. Neo-adjuvant chemotherapy following SIOP principles was offered to all and combined with nutritional resuscitation and TB-prophylaxis, anti-helminthics, anti-infective drugs.

Results: OS at 5 years was 65% and EFS was 44%. Of the 54 patients, 39 had favourable histology, 9 unfavourable, and in 3 could not be determined. EFS was 30% in unfavourable histology and 55% in favourable histology (p = 0.04), there was no significant influence of histology on OS. Overall liver metastases were present in 19 (35%) patients, but isolated liver metastases only in 4 (7%). There was no significant influence on outcome by the site of metastatic disease. Only 3/19 patients had persistent liver metastases and underwent resection. Despite aggressive supportive care, 2 patients (3.5%) died within the first two weeks of treatment. Two patients died of chemotherapy toxicity and two of complications following biopsy. Loss to follow up was only 6/54 (11%).

Conclusion: Even in the African setting, liver metastases do not worsen the prognosis of children with WT. Despite the poor socio-economic circumstances, survival was comparable to data from other centres. Chemotherapy was tolerable, and fewer patients were lost to follow up than expected.

IPS0014

TOXICITY OF HYPERTERMIC INTRAPEITONEAL CHEMOTHERAPY IN PEDIATRIC PATIENTS WITH SARCOMATOSIS: EARLY EXPERIENCE AND PHASE 1 RESULTS

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Purpose: Intra-abdominal metastasis secondary to soft tissue sarcoma is a rare form of tumor dissemination in children. Complete surgical resection is often deemed impossible and children are frequently offered palliative care only. We adopted an aggressive approach for these cases which includes removal of dozens to hundreds of tumor nodules followed by perfusion of the abdominal cavity with hyperthermic chemotherapy (HIPEC) with a curative intent.

Method: We evaluated the toxicity and outcome of 23 children and young adults undergoing 27 HIPEC procedures using Cisplatin. Disease diagnoses included rhabdomyosarcoma (RMS), Non-rhabdomyosarcoma soft tissue sarcoma, (NRSTS), desmoplastic small round cell tumor, (DSRCT), mesothelioma, Wilms’ tumor, and melanomas, and adenocarcinoma. Patients underwent cytoreductive surgery followed by the delivery of 100 mg/M² of Cisplatin at 40.5-41 degrees Celsius, for 90 minutes in the operating room. A subset of these patients were enrolled on our phase 1 study and as part of the dose escalation cohort received 150 mg/M² of Cisplatin HIPEC. All toxicities were recorded.

Results: In the patients enrolled on the phase 1 study, the maximum tolerated dose was 100 mg/M². The dose limiting toxicity was grade 3 renal failure. Five of 27, 18%, had grade 3 or higher renal failure. One patient developed a subclinical decrease in hearing and there were 2 grade 3 hematologic toxicities, 2 grade 3 hepatic toxicities and one grade 3 ileus. One patient suffered grade 3 cardiotoxicity. There were no operative or perioperative mortalities. Surgical complications occurred in 5/27 (18%) of patients. With a follow-up of 6 to 60 months, 7 patients (26%) had no recurrence.

Conclusion: HIPEC is safe in pediatric patients with extensive abdominal metastasis. The majority of the toxicity is renal. Surgical morbidity was less than that seen in the adult population. More study is needed to determine for which histologies HIPEC is most efficacious.

IPS0015

OUTCOMES OF SURGICAL EXCISION OF EWING SARCOMA OF RIB

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Purpose: To define the characteristics and analyze the results of treatment of patients with non-metastatic Ewing sarcoma of the ribs.

Method: Between January 2004 and January 2011, 44 patients with non-metastatic ES of the ribs received multimodal therapy at a single institute. The patients consisted of 28 males and 16 females with a median age of 13 years (range, 2–20). At diagnosis 29 patients had large tumors (greatest tumour dimension > 3 cm); A radiologically visible pleural effusion was noted in 20 patients and was documented to have malignant cells on cytological examination in 4.

Results: Thirty two patients had multiple and 9 had a single rib resection; 3 patients had inoperable disease at exploration. Five patients required wedge resection of the adjacent lung. Polypropylene mesh was used for reconstruction in 32; mesh and cement in 2; free flap in 1. Primary closure was achieved in 6 patients. A tumour-positive margin after surgery was noted in 6 patients. Histological response after chemotherapy was assessed in 34 patients. After initial control, 17 patients relapsed. The site of the first relapse was local (n = 4), both local and distant (n = 6), or distant only (n = 7). 13 patients died after relapse. Eighteen patients are alive and disease free with a 3 year overall cause-specific survival of 55.6%. Response to chemotherapy was the sole significant prognostic factor (P = 0.04); gender, age at diagnosis, existence of pleural effusion, surgical margin (positive or negative) were not significant.

Conclusion: Ewing sarcoma of the ribs is an aggressive malignancy. The major site of disease relapse is local. Response to initial chemotherapy is an important prognostic marker.

IPS0016


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Purpose: To investigate, in a retrospective study, the epidemiologic, microbiologic and clinical aspects of CVC-BSI in children < 18 years treated at the PHOU.

Method: The 2 long-term access catheters used were Hickman (HC) and port catheters (PC). CVC-BSI rates, pathogens distribution, rates of CVC removal and relationship between CVC-BSI and the microbiologic picture and type of catheter used, its way of insertion (open or closed) and the anatomical insertion site (subclavian or jugular veins), were analyzed.

Results: 93 patients developed 178 CVC-BSI episodes; 56/93 (60%) patients had 1 CVC-BSI episode and the other 22 episodes. 83 (89%) patients were > 1 year of age. Average number of CVC-BSI episodes/1000 days of catheter use was 4.7. More CVC-BSI episodes were recorded among patients with HC than in patients with PC (5.05 vs. 3.57/1000 catheters days, P = 0.059). There were no differences between the CVC-BSI rates in relation to insertion method or anatomical site of insertion. Overall, 228 pathogens were isolated, of them 127 Gram(+) (94 Gram(+) and 7 Candida spp). 1 pathogen was isolated in 139 episodes. More Enterobacteriaceae spp. were isolated in CVC-BSI patients with HC vs. those with PC (40/113, 36%, vs. 106/55, 19%, P = 0.001). More S. epidermidis were isolated in CVC-BSI occurring in patients with PC vs. those with HC (25/65, 38%, vs. 23/103, 22%, P = 0.02). CVC was removed due to BSI in 52/178 (29.2%) episodes. Pseudomonas spp. susceptibility to gentamicin, piperacillin and ceftazidime was relatively low (79–82% of all isolates). No fatalities directly related to CVC-BSI were recorded.

Conclusion: 1) CVC-BSI rates at HOU were low; 2) CVC-BSI rates were higher in patients with HC compared with PC; 3) Enterobacteriaceae spp. were the pathogens most frequently isolated in CVC-BSI in patients with HC while S. epidermidis was the dominant pathogen in CVC-BSI in patients with PC.

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IPS0017

ADRENOCORTICAL TUMOURS IN CHILDREN: AIMS EXPERIENCE

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Purpose: To review the presentation, management and outcome of children with adrenocortical tumours.

Method: Retrospective review of all children diagnosed with adrenocortical neoplasm enrolled in solid tumour clinic from 1992–2010. Presentation, management, pathology and outcome were studied.

Results: A total of 20 children were treated during this period. There were 11(55%) boys and 9(45%) girls. The age ranged from 3 months to 132 months (median 36 months). Five (25%) children were less than 1 year, 6(30%) were 1–5 years and 9(45%) more than 5 years of age at presentation. Thirteen (65%) presented with weight gain (4 had pain in abdomen as well), 2 each with precocious puberty and hirsutism, while 1 each with chest pain, fever and lump in abdomen. The diagnosis was Cushing’s syndrome in 18(90%), of whom 12(60%) had virilisation also. Hypertension was seen in 13(65%) and a mass was palpable in abdomen in 11(55%). Two (10%) had liver metastasis at presentation. Sixteen (80%) children underwent adrenalectomy. Four patients could not be operated upon as three died before intervention, and 1 was lost to follow up before surgery. IVC thrombus was present in 3(15%), out of which two were operated upon and 1 died preoperatively of pulmonary embolism. Two patients with IVC thrombus received chemotherapy, one of them preoperatively. One patient received radiotherapy postoperatively. Histopathology was reported as carcinoma in 9, in 15 patients of whom histology was available. Three (18%) developed local recurrence (one had pulmonary recurrence also). On last follow up 14(70%) were alive (range 1–149 months). Six patients died within 1 to 10 months of diagnosis with or without treatment.

Conclusion: Majority (90%) of adrenocortical tumours in children present with Cushing’s syndrome with virilisation. Though metastasis at presentation is uncommon, locally extensive disease may preclude complete resection and the overall disease free outcome is dismal.

IPS0018

NEUROBLASTOMA: OUTCOME OVER A 14 YEAR PERIOD FROM AIIMS NB 96 PROTOCOL

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Purpose: To evaluate the outcome of children with neuroblastoma (NB).

Method: All children with NB registered from October 1996 through July 2009 were included. INSS was used for staging. All received chemotherapy, radiation therapy and surgery as appropriate.

Results: Of 144 patients with NB enrolled in this study period, there were 12(8.3%) with NB4s. The age at diagnosis ranged from 15 days to 6 months with the age being <1 month in ten (83.3%) children. The primary was in the adrenal in 8(66.7%), extra-adrenal in 8(65.3%) and CR was achieved in 35.7% while for stage 4 the OS was 35.7% [95CI 19.3–69.5]. The OS was 69.7% for those below 12 months of age [95CI 54.0–84.9] and CR was achieved in 54.9% for abdominal tumors [95CI 42.9–65.3] and CR was achieved in 35.7%; while for extra-abdominal tumors the OS was 82.6% [95CI 62.6–92.3] and CR was achieved in 62.5% (p = 0.07). All 6 (100%) patients with stage 1 and stage 2 disease were alive and disease free. The OS was 71.5% for stage 3 [95CI 55.3–82.7] and CR was achieved in 56.9%, while for stage 4 the OS was 35.7%[95CI 19.3–52.4] and CR was achieved in 17.6% (p < 0.001). The OS was 33.3% for 4S [95CI 48.2–95.6] and CR was achieved in 75%.

Conclusion: All of children with stage 1&2 achieved CR and were alive, while 57% of stage 3 could achieve CR and had an OS of 71.5%. The OS (35.7%) and CR (17.6%) for stage 4 was significantly less (p = 0.001).

IPS0019

NEUROBLASTOMA 4S: OUTCOME FROM AIIMS NB 96 STUDY

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IPS0020

EFFICACY AND LONG TERM OUTCOME OF LAPAROSCOPIC ADRENALECTOMY FOR NEUROBLASTIC TUMORS

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Purpose: Previous studies about laparoscopic resection of neuroblastomas concluded to a good efficacy with a short term follow up. The aim of this study was to report on the efficacy and long-term results of laparoscopic resection of adrenal neuroblastic tumors.

Method: Retrospective study of 26 children treated by laparoscopic adrenalectomy for neuroblastic tumor (21 neuroblastoma, 5 ganglioneuromas). These selected cases represented 32% of the overall 82 abdominal neuroblastomas managed in these units during the same period of time. Stage distribution was: 14 stage I, 12 stage II (including 4 Ms). None of the localized tumors underwent preoperative chemotherapy. The median age (range) at surgery was 34 months (2–155). The median largest tumour diameter was 40mm (20–110). Recurrence was performed through peritoneal laparotomy (n = 23) or retroperitoneotomy (n = 3) in lateral or prone position. The specimen was extracted in a bag (25/26) through a trocar orifice or a suprapubic incision (n = 5) depending on the size.

Results: Complete macroscopic resection was achieved in 100% of cases. Pathological examination concluded at microscopical complete resection in 17/26 (65%). No procedure required conversion to open surgery. No tumor rupture occurred. The median duration of pneumoperitoneum was 70 min. (40–200), and the length of hospital stay was 3 days (2–6). An additional procedure was performed during the same laparoscopy in 8/26 children (gastroscopy, Nissen fundoplication, ovarietomy for cryopreservation, liver biopsy). With a median follow-up of 66 months (4–103), no event occurred in the localized tumor group (EFS 100%). In the metastatic group, 3/12 children presented metastatic recurrence or progression (OS 75%) with a median follow-up of 57 months (6–106).

Conclusion: Laparoscopy allows effective long-term local control of the disease in a wide range of clinical presentations of adrenal neuroblastic tumors. In selected cases, complete resection can be achieved in most patients.

IPS0021

UNEXPECTED AND UNEXPLAINED MORTALITY AFTER EXTENDED NEUROBLASTOMA RESECTIONS – A PROPOSAL FOR CONCERTED RESEARCH

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**IPSO023**

**SURGICAL INTERVENTION STRATEGIES FOR PEDIATRIC OVARIAN TUMORS: FROM THE EXPERIENCE OF 60 CASES IN ONE INSTITUTION**

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**Purpose:** Surgical treatments of pediatric ovarian tumors are heterogeneous. This study aims to investigate surgical intervention strategies for pediatric ovarian tumors.

**Method:** The pathological diagnosis, surgical treatment, and clinical outcome were retrospectively analyzed for 60 children with ovarian tumors treated at our institution between 2000 and 2010.

**Results:** Twenty-one of 60 patients were prenatally diagnosed neonatal cases with cystic lesions. Of 21 neonates, surgery included the ultrasound guided aspiration in 14 cases, aspergillus oophorectomy through minimally invasive approach in 7 cases, and salpingo-oophorectomy in 10 cases with torsions. All of 31 cases are alive and cosmetic excellent. For 8 patients with malignant tumors including borderline lesions of mucinous or serous cyst adenoma, surgery included salpingo-oophorectomy in all 8 cases, and the postoperative chemotherapy was administered in 2 yolk sac tumors and 1 dysgerminoma. Only one case of yolk sac tumor with lung metastasis at initial diagnosis died of disease after recurrence.

**Conclusion:** The majority of pediatric ovarian tumors were benign disease, and the patients with malignant lesions had good prognosis. In neonatal cases, salpingo-oophorectomy or cystectomy by umbilical crease incision approach is feasible and excellent cosmesis. In the cases with suspected malignancy, the necessity of salpingo-oophorectomy depends on the frozen pathology of enucleated tumor with ovarian preservation after aspiration of cystic lesion through Rocky Davis incision. We recommend tumor resection with ovarian preservation through minimally invasive approach as the first line treatment in pediatric ovarian tumors.

**IPSO024**

**SURGERY IN PATIENTS WITH TESTICULAR MALIGNANT GERM CELL TUMORS: COMPLIANCE TO SURGICAL GUIDELINES AND RESULTS IN THE ITALIAN COOPERATIVE STUDY**

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**Purpose:** Surgery represents a main and often the only treatment in patients with testicular Malignant Germ Cell Tumors (MGCT). We analyzed the compliance to surgical guidelines and the results in a series of patients with testicular MGCT +/- retroperitoneal node involvement, without distant metastases.

**Method:** 42 patients, observed in 15 Centers were enrolled in the Italian Cooperative Study on MGCT (January 2004-December 2010). 14/42 were younger than 2 y, of age, 28/42 between 13 – 18 y. Treatment was delivered according to COG-Staging-System: St.I patients (complete excision with inguinal orchifunicolectomy+decrease of markers, +/hemiscrotectomy if scrotal involvement) did not receive further treatment; St.II patients (scrotal involvement after hemiscrotectomy and/or retroperitoneal node (RPN) enlargement < 2 cm) received chemotherapy (CT): PE1Gx3; St.III patients (retroperitoneal node involvement, without distant metastases). Results: St.I: 26 patients. 3/26 had a scrotal approach due to suspected testicular torsion: 1/3 underwent hemiscrotectomy, 2 did not receive further therapy after decrease of alphaFP, due to patient’s or physician’s decision respectively. 3/26 were successfully treated for RPN relapse, occurred at 3.69 months after adequate surgery (2 adolescents, 1 infant). St.II: in 4 patients CT was delivered due to slight enlargement of RPN (+persistent alphaFP in 1). St.III: 12 patients received CT and RPND (bilateral in 1). Histology was negative in 11/12. All patients are alive without disease, 39 in St.III, 3 in St.II (a 9-86 months -med:48). 1 St.I patient suffered from postoperative pyothorax. Among patients younger than 2 y, 10/14 had a pure YST, 12/14 had St.I disease; among those between 13-18 y, 27/28 had a mixed histology, 14 were St.II or St.III. In 3 adolescents a testicular prostheses was positioned during primary operation.

**Conclusion:** Outcome was excellent. Regional relapses, observed only in St.I patients, were cured. Surgical guidelines were followed in 40/42 cases. Scrotal approach did not worsen the outcome of patients who did not receive further treatment.

**IPSO025**

**POSTOPERATIVE OBLICTIONS AFTER THYROIDECTOMY AND NECK DISSECTION IN CHILDREN WITH THYROID CARCINOMA**

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**Purpose:** To analyze the rate of complications after thyroidectomy (TE) with lymph node dissection (LND) in children with thyroid carcinoma (TC).

**Method:** 51 children (5–18 years old) have been included in research from 2005 till 2010. All patients were staged using the UICC classification 1997: 1N1M0 - 3 patients; 2N0 - 1M0 - 31, 3N0M1 - 3, 4N1M0 – 14, TE+CLDN (central lymph node dissection) was performed in 18 patients (1N1M0 - 3, 2N1M0 - 14, 3N0M1 - 1), TE+CLDN+ Ipsilateral MND

Pediatr Blood Cancer DOI 10.1002/pbc
Purpose: Salivary gland tumors are uncommon in children, accounting for only 1% of all radiotherapy.

Results: There were postoperative complications which included: 1 case of larynx edema (1.96%) after TE+CLND+bilateral MND (4N10), 4 (7.8%) cases of permanent unilateral recurrent laryngeal nerve paralysis/paresis (4N10 - 2; 4N10 - 1; 2N10 -1 case after TE+CLND+bilateral MND), 1 case (1.96%) of recurrent laryngeal nerve paralysis (4N10 after TE+CLND+bilateral MND), permanent hypoparathyroidism in 21 (41%) patients (2N1-3, 3N1-1, 4N1-3, 4N0-4) which TE+CLND+ipsilateral MND was carried out in 5 cases, TE+CLND-bilateral MND - in 4 cases, and TE+CLND in 12 cases. The chronic hypoparathyroidism revealed in 2 children (3.9%) from which 2 have 4N11 stage, after TE+CLND-bilateral MND.

Conclusion: Postoperative complications were not noted in patients with stage T2-3 No M and stage T1 with metastasis in central lymph node from one side. Complications were registered in 14 (45%) out of 31 patients with T2N1M0 stage and in 1 out of 3 patients with T3N1M0-1 stage. All patients with stage T4N1a-M0 have complications. Persistent postoperative complications were revealed in 5.8% of cases of which chronic hypoparathyroidism was noted in 2 patients (3.9%), recurrent one-sided laryngeal nerve paralysis in 1 patient (1.9%).

IPSO026

MALIGNANT SALIVARY GLAND TUMORS IN CHILDREN

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Purpose: Salivary gland tumors are uncommon in children, accounting for only 1% of all pediatric neoplasms. The rarity of salivary gland tumors makes it impossible for any institution to gain solid experience in their diagnosis and therapy. The aim of this report on therapeutic experience is to present treatment strategies and provide with operation results.

Method: 10 patients with malignant salivary gland tumors in children treated between January 2007 and Jan 2011 were selected from the prospective database.

Results: There were 10 children ranging from 7 to 13 years of age, 2 females and 8 males. Tumors were localized to the parotid gland in 6, submandibular gland in 3 and minor salivary gland of the oral mucosa in 1. The commonest presentation was a painless swelling in the respective salivary gland. The commonest histology was mucoepidermoid carcinoma in 5/10 (submandibular gland: 3, parotid: 1 minor salivary gland 1). One patient had rhabdomyosarcoma of the parotid and two each had metastasis from medulloepitheloma of the eye and cutaneous squamous cell carcinoma of the face arising in xeroderma pigmentosum. The epithelial tumors were treated with surgical excision. Three and one each was intermediate grade and low grade respectively with no lymph nodes metastasis. None of these four patients received adjuvant radiotherapy. One patient with high grade mucoepidermoid carcinoma received adjuvant radiotherapy. Patient with metastases underwent total parotidectomy and spinal pectoralis major myocutaneous flap reconstruction for the skin defect in three. All patients received adjuvant radiotherapy. There were no local recurrence in any patients and all are alive and free of disease till date.

Conclusion: Surgical excision remains the mainstay of treatment of salivary gland tumors in children. Radiotherapy is reserved for high grade epithelial cancer and in presence of lymph node metastasis. Metastatic disease are also effectively treated with surgical excision and radiotherapy.

ICCCPO ABSTRACTS

ICCCPO001

WEB-BASED NEUROBLASTOMA RESEARCH INFORMATION FOR PARENTS: A MODEL FOR INTERNATIONAL COLLABORATION OF PEDIATRIC CANCER NON-PROFITS

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Purpose: Understanding disease and treatment is beneficial for parents who have children with cancer. News of research progress in pediatric oncology is sought after by motivated parents of children with cancer world-wide. Information on clinical trials, cancer biology, and treatment advances presented at scientific meetings and published in journals is in demand, particularly in Europe. This project sought to address this unmet need for parents of children with neuroblastoma (NB).

Method: A collaboration of 6 non-profit foundations from Australia, North America, and Europe supported the NB Globe Neuroblastoma News website project, and provided travel funds for reporting at Neuroblastoma Meetings from June 2010 to April 2011. News curation was accomplished using feeds from clinicaltrial.gov, PubMed, and Google Scholar using the search term “neuroblastoma.” Reports on journal publications, meeting abstracts, trial openings, industry news, and related developments were posted an average of once weekly. Website traffic analysis was performed using Google Analytics.

Results: Forty-one articles on NB-related research were published on nbglom.com and from August 2010 to March 2011 the site had 1290 unique visits per month, with a total of 9038 visits and 33,590 page views. Visitors averaged 3.7 pages and 2:31 minutes per visit, with bounce rate of 1.7%. English-speaking visitors comprised 87%, with remaining visitors using 54 other languages. Of 9038 total visitors, 1574 (17.4%) were from Europe, and 725 (8.0%) were from Asia and Oceania. Over 2700 keyword phrases were used in searches to locate the site, and most terms contained treatment-related agents such as “ch14.18.”

Conclusion: The response to this web-resource suggests there is a demand for disease-specific news of research advances and information on clinical trials, and that an international non-profit collaboration to facilitate this is feasible. This model focusing on neuroblastoma for disease-specific information may be applicable to other pediatric tumors.

ICCCPO002

SONNENINSEL (ISLAND OF SUN) - THE FIRST PSYCHOSOCIAL AFTERCARE CENTER IN AUSTRIA

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Purpose: Every year 250 Austrian children and adolescents develop cancer. There is an increase of requirements of the psychosocial aftercare for the cured children and adolescents, who are concerned with late effects, difficulties with school or finding a job/friends.

Method: The evaluation of the situation and the needs of children and adolescents after cancer shows that more offers are necessary.

Results: The Austrian Childhood Cancer Organization builds a house called “Island of Sun.” It will be a wooden house with four pavilions on the premises of 15,000 sq km. The location is in the surrounding of Salzburg, near a lake. The house is accessible for people with a disability. There is room for 50 people. The aim of this “Island of Sun” is to establish a competence center for children and adolescents after the treatment, LTS, the siblings and parents. Therefore, we offer psychological support through a wide range of events like summer camps for survivors and siblings, meetings or seminars of parents and adolescents, seminars for bereaved parents, camps with special needs (after a brain tumor or palliative care), training courses for Survivors, parents and psychologists. Another aim is to be an advice centre in different topics concerning childhood cancer (job, nutrition, and counselling).

Conclusion: Our understanding of aftercare is how long the LTS, siblings and families need a support. They decide by themselves how long they need a support and in which form. This decision will not be made only by an external person. This offer of our competence center will be open for Austrian people and the neighbouring countries. The “Island of Sun” will make a progress in the long term psychosocial aftercare of children and adolescents after cancer and their family. This will lead a step forward in the support and improve of quality of life for them.

ICCCPO003

PARENTS SATISFACTION IN A DEPARTMENT OF INTEGRATIVE PEDIATRIC ONCOLOGY: A TEN YEAR EXPERIENCE

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Purpose: In the Gemeinschaftskrankenhaus Herdecke (GKH) children and adolescents with cancer are routinely treated with integrative medicine approaches. In addition to guideline-based conventional treatment a multimodal therapy concept is applied which includes anthroposophic pharmacotherapy (particularly mistletoe extracts) and non-pharmacological (e.g. art-therapies, external emobrications). We analyzed the recalled satisfaction of parents of children treated for cancer in the centre for integrative pediatric oncology at GKH from 1999 to 2008.

Method: The parents were anonymously asked to report their satisfaction with treatment and outcome as well as additional items addressing aspects of integrative treatment, using the modified CSQ-8 questionnaire, a validated screening tool for detecting patient satisfaction. Descriptive statistics were gathered.

Results: Of the 98 mailed questionnaires were 58 returned (59%). Mistletoe extracts were used in 57 children (84%); they were useful well by 51 children (90%), while 23% of the parents reported side effects. In February 2010, 54 of the 68 responders (79%) stated a good health status, while 13 children (19%) had died of their tumour; 1 child (1.5%) was still in therapy. Treatment benefit was stated as very high by 58 of the parents (85%). 67% described the quality of care as excellent; 65% of their needs were met in most areas. 72% were very satisfied with the extent of help, 88% would come back if their child needed further help, 85% were very satisfied with the treatment on the whole, and 82.5% stated that their child had received the kind of treatment they wanted. The mean of the overall impression on a scale of 1–10 was very high with 9.3.
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**ICCCPO004**

**MADE TO MEASURE-CONSUMER FEEDBACK CAN DRIVE SERVICE IMPROVEMENT**

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**Purpose:** To develop a consumer feedback tool to help drive the quality improvement process of a state-wide paediatric oncology service.

**Method:** In 2005 the Paediatric Integrated Cancer Service (PICS) initiated an independent consumer satisfaction survey for inpatients and for outpatients, across three major metropolitan paediatric oncology service providers: Royal Melbourne, Peter MacCallum and Health and Peter MacCallum cancer centres. The methodology includes random sampling which is undertaken by an independent organization that also conducts all administrative functions required including sampling, mail distribution and processing of returned surveys. The reporting framework offers state-wide satisfaction levels and sub-grouped data for each facility; it also benchmarks results against established norms and tracks organizational specific trends over time. Surveying has now been conducted annually for the last five years.

**Results:** Results have indicated consistent themes impacting on consumer perceptions of quality, including communication between families and health care providers, waiting times for outpatient appointments and cancer therapies, nutrition and food services, procedural pain management, processes for complaints and access to psychosocial services.

**Conclusion:** Satisfaction measurement championed by strong leadership is a critical factor in building a culture of service excellence. These surveys provide actionable data, and enhance decision-making regarding quality and strategic planning and allocation of resources to match consumer-identified needs. These surveys have been used to underpin specific improvement projects on the three sites and across multidisciplinary teams. This “all in one” patient satisfaction survey could be utilized on a national basis, providing opportunity for national benchmarking across the paediatric oncology sector, which is currently not possible.

**ICCCPO005**

**ENGAGING CONSUMERS: A PAEDIATRIC ONCOLOGY MODEL IN PRACTICE**

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**Purpose:** To build a model of consumer participation to help support health policy development and service delivery.

**Method:** In partnership with the health services, The Paediatric Integrated Cancer Service (PICS) in Victoria, Australia, developed a consumer participation model. It looked at how consumers can, and should, be included in the service’s activities.

**Results:** Major elements of consumer participation include: recognizing the Parents Advisory Group (PAG) as the consumer group for children’s cancer by the Victorian Department of Health; membership of the PAG Chair on the PICS Clinical Advisory Committee; a document from PAG to the Minister for Health in 2009 helping establish funding for five supportive care improvement working parties, each with a PAG representation; evaluating patient satisfaction annually using a validated survey at each of the PICS sites; creating a database for consumers interested in participating in focus groups; including parent feedback to patient information, leaflets, surveys and research projects; an “in principle” agreement for a Community Reference Group, including members from philanthropic and community support groups and the Chair of the PAG.

**Conclusion:** PICS recognizes the valuable role that consumers play in supporting health policy development and service delivery. The experiences of patients and families dealing with a diagnosis of childhood cancer are both challenging and unique. It is important that these experiences are recognized in service planning. PICS will continue to draw upon consumer expertise to provide input into both individual care and broader service development. This model ensures PICS will maintain an organizational culture that values consumer participation.

**ICCCPO006**

**CHALLENGES OF FUNDRAISING IN INDONESIA: A DEVELOPING COUNTRY**

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**Purpose:** Indonesia as one of the largest country with population of more than 220 million people scattered in more than 3000 islands. The Govt authorities looking after cancer has only been set up in year 2006. Childhood cancer is not the main priority of the government. Lack of information about childhood cancer

**Method:** Identify the need for fundraising, find a good media promotion company to help you, prepare a good file and administration and give out progress continuously, give out image that the foundation is accountable and reliable and bring as many companies, groups, communities to work together for a good cause

**Results:** More people know about childhood cancer, more people want to be involved in the program, more media coverage and more people interested to donate

**Conclusion:** Public awareness is one the best tool for fundraising, focus on goal and prepare good proposal and be confident with it.

**ICCCPO007**

**TREATMENT REFUSAL IN PAEDIATRIC ONCOLOGY IN GERMANY**

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**Purpose:** In developing countries treatment refusal and treatment discontinuation are key factors in paediatric oncology treatment failure. There are no published data from developed countries in this regard. About 1800 newly diagnosed children and teenagers with cancer between birth and 15 years are treated almost exclusively in paediatric oncology centres per year.

**Method:** This study aims to investigate the problem of treatment refusal in paediatric oncology by means of a survey addressed to all paediatric oncology centres in Germany for the period 2008–2009.

**Results:** Of the 73 clinics approached, 70 responded to the questionnaire and a total of 17 treatment refusals were registered within a given 2-year period (annual incidence 0.5%). 35% of parents initially refused treatment for their children, 53% discontinued during the course of treatment, and in 12% of cases a statement in this regard could not be procured. The mean age of patients was 12.1 years and mean survival time was 6 months. There were no diagnosis clusters. In 5 cases paediatric patients were treated and survived following withdrawal of custody. The reasons given for refusal or discontinuation of treatment were mostly related to parents’ personally held beliefs. At the time of the survey 35% of patients had died, 41% were still alive and the current status of 24% of patients was not known.

**Conclusion:** Whereas in developing countries financial, logistical and educational factors play a primary role in treatment refusal or abandonment, in Germany it seems that parents’ personally held beliefs and coping strategies are the main influencing factors. This investigation highlights the importance of sustaining a functioning and mutually communicative physician–parent–patient relationship as well as psychosocial intervention and accommodation at diagnosis and throughout the course of treatment. A united approach amongst physicians and legal representatives in the case of treatment refusal should be brought into discussion.

**ICCCPO008**

**FOLLOW UP OF CHILDHOOD CANCER SURVIVORS: EXPERIENCE FROM A DEVELOPING COUNTRY**

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**Purpose:** Progress in therapy has made survival into adulthood, a reality for most of children & adolescents diagnosed with cancer today. Notably this growing population remains vulnerable to variety of long term therapy related sequelae. Systemic ongoing follow up of these patients therefore, is important for providing early detection of & intervention for potentially serious late onset complication.

**Methodology:** The methodology based on data collected retrospectively from medical records includes all cases of cancer among 0-15 years diagnosed from 2001–2005 with patient demographics, diagnosis & therapy details (including cumulative dose of medications).
THE REMEMBERED LEGACY OF CANCER: CANCER-RELATED MEMORIES AND POST-TRAUMATIC OUTCOMES IN CHILDHOOD CANCER SURVIVORS AND THEIR FAMILIES

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Purpose: Evidence suggests that patients and families experience intrusive memories following a diagnosis of childhood cancer. However, little research has examined the types of memories they have about the cancer experience years afterwards, and the effects of these memories on their long-term adjustment. This study aimed to examine the characteristics (number, memory strength and valence) of the memories of long-term survivors and their families spanning the cancer experience (from pre-diagnosis to post-treatment). These findings were explored with relation to individuals’ post-traumatic stress and post-traumatic growth outcomes.

Method: Participants were 180 survivors (mean age = 24.9 years; mean time since treatment = 15.4 years), 107 mothers, 70 fathers, and 61 siblings. Participants completed three questionnaires: the Memory of Cancer Experience questionnaire, the Impact of Events scale-Modified, and the Post-Traumatic Growth Inventory. The relationships between these variables were examined using correlational and hierarchical multiple regression analysis.

Results: All family members had some memories of the cancer experience. Parents recalled more memories than survivors and siblings overall (t = 12.04, p < .01), and these were also stronger (t = 9.79, p < .01). Parents had more negative memories than survivors and siblings for the pre-diagnosis (t = 2.73, p < .01) and diagnosis (t = 2.20, p < .05) periods. Siblings had more negative memories for the diagnosis (t = 2.51, p < .05) and post-treatment (t = 2.89, p < .01) periods than did survivors. Having more memories, which were stronger, and more negative, correlated with more severe post-traumatic stress symptoms (r range = .26–.44, p < .01), as well as greater post-traumatic growth (r range = .26–.67, p < .01).

Conclusion: Despite their different roles and ages during the cancer experience, all family members had cancer-related memories. Parents’ and siblings’ memories were in some cases more negative than survivors’, emphasizing the need to better conceptualize their role in family adjustment during and after cancer. The relationship between strong, negative cancer-related memories and post-traumatic stress and growth highlights the complex duality of family adjustment after cancer.

ICCCPO009

EVALUATING THE EFFICACY AND NEED FOR AN ONCOFERTILITY PRESERVATION PROGRAM IN THE PEDIATRIC POPULATION

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Purpose: The continued increase in survival rates among male pediatric cancer patients emphasizes the long-term implications of cancer therapy on infertility. Current guidelines recommend discussing fertility preservation options with all cancer patients and providing sperm cryopreservation (SCP) referrals as needed. To improve patient access to SCP we initiated a formal fertility preservation program in 2007 at Children’s Memorial Hospital (CMH). The program’s progress was measured against a well-established oncology program at Northwestern Memorial Hospital (NMH).

Method: For 2008–2010, the total number of fertility consults and the subsequent number of patients undergoing SCP were identified using a systematic chart review of all pediatric cancer patients at CMH. At NMH these criteria were collected electronically using the Enterprise Data Warehouse (EDW). To ensure pediatric patients were capable of sperm production, a minimum inclusion age of 13 was used at CMH. These patients were compared to 18–35 year old male cancer patients from NMH.

Results: Of the 86 male cancer patients meeting study criteria at CMH, a total of 22 were given fertility consults and 16 banked sperm, a SCP yield of 73%. This compares to the 130 NMH consults that resulted in SCP yields of 75% and 74% for ages 18–26 and 27–35 respectively. Moreover the CMH program demonstrated an improvement in SCP yield from 67% in 2008 to 86% in 2010. Of the 16 patients who banked sperm, 9 had a hematologic malignancy and 4 had a neurologic malignancy. No significant age difference was found between patients banking sperm and those not banking sperm (p = .137).

Conclusion: The rapid growth in the number of fertility consults and high percentage of counseled patients agreeing to sperm bank demonstrates a demand for fertility preservation in the pediatric population that is comparable to the adult population.

ICCCPO010

20 YEARS OF PRIMA KLIMA - A CAMP FOR CHILDHOOD CANCER PATIENTS IN GERMANY

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Purpose: In 1991 six childhood cancer patients from Stuttgart, Germany (all between 16 and 18 years old) participated at “Camp Good Days and Special Times” in Rochester, USA, together with two staff members of the psychosocial team of the “Olgahospital”, the hospital in Stuttgart. Together they had the idea to establish a camp for childhood cancer patients in Germany and implemented PRIMA KLIMA (name of the camp) in 1992. Since then, they arrange the camp PRIMA KLIMA for childhood cancer patients and now, in 2011, we celebrate our 20th anniversary!

Method: Each year 45 (former) cancer patients aged 8 to 15 participate at the camp. The staff consists of one doctor, two nurses, one psychologist, one social worker and other personnel of the hospital in Stuttgart and around 10–15 former childhood cancer patients aged 17 to 37 (some were former participants of PRIMA KLIMA). Each year we have a special motto at PRIMA KLIMA. During the 5 days on camp we do a lot of activities together.

Results: Our aims are: to provide contacts from childhood cancer patient to (former) childhood cancer patients, to strengthen the self-esteem of childhood cancer patients, to enhance motivation for the strenuous cancer therapy, to consolidate confidence in coping with the cancer disease, to gain a positive attitude to the cancer diagnosis and last but not least: to stabilize hope for healing!

Conclusion: 20 years of PRIMA KLIMA show that it is possible to establish a camp for childhood cancer patients just with the beginning of having an idea. Now we are well organized and an established institution at the Olgahospital in Stuttgart. A total of about 500 kids went to the camp and enjoyed a nice stay there. I am proud to be one of the six teenagers in 1991 at Camp Good Days. Now I am 36 and psychologist.

ICCCPO012

UGAM- VICTORS OF CHILDHOOD CANCERS: STRENGTH, CHALLENGES & OPPORTUNITIES

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Purpose: Childhood Cancer Survivors attending After Completion of Therapy (ACT) Clinic at TMH came together on 7th June 2009 to form voluntary support group called ‘Ugam’ under Survivorship Programme of ICS. Ugam means to rise, underscoring determination to rise above all obstacles & be victors. Programmes undertaken by Ugam: Counseling of survivors and parents, self-empowerment of young survivors, helping children undergoing treatment, social awareness and re-bonding with society and newsletter on annual survivor’s day.

Method: Two members of Ugam on rotational basis conduct counseling session on Tuesdays for survivors of childhood cancers attending ACT clinic at TMH. Data collected identifies the challenges & helps to understand how survivors can start life afresh exploring new opportunities by providing role model. They motivate survivors to become Ugam’s members. Chatai clinic is conducted every Saturday to counsel & give psychosocial support to parents whose children are undergoing treatment at TMH.

Results: Ugam has 96 committed members and 20 peers. They have counselled 185 cancer survivors since June 2009 & intervened in following areas: Motivating survivors to overcome

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Somatic deformities & get integrated in society. Educational and career related assistance and guidance to survivors who had disruptions due to treatment and then lose interest because of psychosocial & financial problems. Helping in overcoming social fears and hindrances regarding matrimonial problems arising from their cancer experience. Ugam members have been participating in Chatas clinic since May 2010. They help parents of active patients to get accommodation at free/concessional boarding centers.

Conclusion: Ugam has many challenges ahead such as insurance protection for cancer survivors, overcoming job & matrimonial discrimination. Ugam would like to collaborate and disseminate date and enquires to collaborate with survivor groups at national & international level for advocacy issues in larger sociopolitical processes.

ICCCPO015

PSYCHO-SOCIAL REHABILITATION COURSES: ENHANCING ADAPTATION AND HEALING IN PEDIATRIC ONCOLOGY PATIENTS AND THEIR FAMILIES

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Purpose: The pediatric oncology department together with the parents association organizes courses for families of children with cancer. These courses are funded by the Social Insurance Institution of Finland and are free of charge for the participants. The institution determines strict rules and standards for what is to be included in the rehabilitation programs of the courses. The goals of the rehabilitation programs are to help all family members adapt to living with cancer.

Method: These state funded courses have been running since 1985. They are held at a recreation and camp center which is owned by the parents association. Five courses are held yearly. There are separate courses for patients with leukemia, solid tumors and brain tumors. There is also a course for patients who have undergone an allogeneic stem cell transplant. The courses run from 3 days to a week and they are all family courses for up to ten families. Families are given information about the disease, treatment and possible late-effects. Psychosocial issues are also addressed and families are supported in many different ways. The courses are run by a multiprofessional and experienced team, out of whom many work on the oncology ward.

Results: The effectiveness and realization of the rehabilitation programs are followed up by evaluations and reports. The information and support families have received during the courses have helped them find normalcy in life after the acute phase of treatment. It has been shown that one of the most important gains of these courses is peer support. It is very rewarding for all family members to share experiences with others who are in a similar situation.

Conclusion: During the past two years the Social Insurance Institution has required more evidence based research and evaluation of the rehabilitation courses in order to make sure that the requirements of high quality rehabilitation are met.

ICCCPO014

SURVIVORETOG, THE ENHANCEMENT OF DISSEMINATION OF INFORMATION REGARDING SEQUELAE AFTER CHILDHOOD CANCER THROUGH UTILISATION OF SOCIAL MEDIA

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Purpose: To develop SurvivorNet by improving dissemination of good clinical practice, patient information and effective communication employing the World Wide Web further optimisation, through utilisation of the new social media.

Method: A standard. org domain was used to publish an HTML-based website integrating optimisation, through utilisation of the new social media.

Results: Traditionally and evolving marketing and public relations techniques can be successfully exploited to optimise delivery of information to parents, their families and medical professionals via utilisation of the numerous possibilities of the Internet.

Conclusion: Dissemination of certified medical information through social media contributes efficiently to meeting the information needs of Childhood Cancer Survivors and other interested parties.

ICCCPO015

SUPPORT INTERVENTIONS FOR PARENTS OF CHILDREN WITH CANCER: A REVIEW OF EFFECTIVENESS REDUCING PARENTAL DISTRESS

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Purpose: The aim of this review was to explore structured intervention programs for parents/ families of children with cancer. The efficiency of programs in reducing parental distress was particularly paid attention to.

Method: Literature searches was conducted from February 17th to April 15th 2008, using Ovid search (Medline, Psychinfo, and Cochran Library) - keywords being: parents and children and cancer (110 results); parents and childhood cancer and intervention (1 result); parents and children and cancer and therapy (9 results). The following inclusion criteria were utilized: (a) intervention targeted parents of children with ongoing or completed cancer treatment; (b) adjustment and psychological distress/symptoms was part of the design; (c) contact with a professional (e.g. therapist) should be a crucial part of the intervention; (d) the study had been published in a peer-re-viewed journal, and; (e) was presented in English.

Results: Of totally 25 evaluated studies, 9 met the criteria for inclusion in the review. As two articles reported the results of the same study, one was excluded. The final review thus covers 8 separate IV programs. Concerning program effectiveness, the results ranged from a no-effect to a small effect for some participants.

Conclusion: Most of the programs were not effective in reducing parental distress. The heterogeneity of the target groups and intervention programs made it difficult to generalize the effect of the programs. Many of the intervention programs were built on Cognitive behavioral theory which may not be optimally suitable for working with parents experiencing having a child with cancer, while this theory is based on targeting dysfunctional thinking patterns and trying to change them. It is important to have in mind that having a child with cancer is an existential life crisis and intervention programs might be more effective if they are flexible, aiming at normalizing and respecting individualized distress symptoms among parents.

POSTERS

PA001

ADOLESCENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA: ABANDONMENT, TOXICITY AND SURVIVAL AT A TERTIARY CARE CANCER CENTER IN DELHI, INDIA

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Purpose: Age remains one of the important poor prognostic factors in acute lymphoblastic leukemia (ALL). The objective of this study was to study the demographic profile, pre-treatment characteristics, toxicity and treatment outcome of adolescents with ALL.

Method: A retrospective analysis of a consecutive cohort of 68 children 10–18 years of age with a proven diagnosis of ALL from October 1997 to October 2007 was performed. The treatment included a moderately intensive protocol with a 4-drug induction. Prophylactic cranial radiotherapy was planned for all patients excluding girls with non-T cell ALL and white blood count (wbc) less than 50000/cmm.

Results: The median age at diagnosis was 13 years (range 10–18 years) and 73.5% (50/68) were male. The median wbc at diagnosis was 76700/cmm (range 1200–6700000/cmm). Immunophenotyping (available in 64 patients) revealed pre-B phenotype in 39 (61%), T phenotype in 25 (39%). Molecular genetic abnormalities included bcr-abl (3/39) and MLL translocation (3/39). Sixty one (90%) patients achieved complete remission, 3(4%) abandoned treatment, 2(3%) had refractory disease and there were 2(3%) induction deaths. Significant induction toxicities included infections, hepatitis, and hyperglycemia. The primary reason for abandonment was socioeconomic. There were 22 relapses and median time to relapse was 11 months. Of these 3/22 are in second complete remission. Site of relapse was mediastinal in 18(isolated 10 and combined 8), and extramedullary in 4(isolated testicular 1, isolated CNS 3). Five year overall survival (OS) was 57% (25 deaths and 4 abandonments), and event free survival (EFS) 48.5% (35 events, include abandonments 7, relapse 22, refractory 2, toxic death 4). The EFS for children 1–9 years during the study period was 70%.

Conclusion: Adolescents with ALL had higher abandonment and toxicity and lower EFS when compared to younger children treated with the same protocol during the study period.

PA002

THE UTILITY OF END-OF-TREATMENT BONE MARROW ASPIRATES IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A QUALITY IMPROVEMENT PROJECT

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Purpose: Several studies have concluded that end-of-treatment bone marrow aspirates (EOTBMAs) are ineffective for detecting subsequent relapse in acute lymphoblastic leukemia (ALL). Nonetheless, many centers routinely perform EOTBMAs. Our first
Purpose: We assessed survival and toxic death rates before/after cases/year. Twinning with a higher income country program began in 2004, focused on 1Universidade de Sao Paulo, Sao Paulo, Brazil
2Hospital Infantil Robert Reid Cabral, Oncology, Santo Domingo, Dominican Republic
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92Guillermo Rawson Hospital, Hematology, San Juan, Argentina
10Hospital Infantil Robert Reid Cabral, Hematology, Santa Domingo, Dominican Republic
11University of Sao Paulo, Pediatric Hematology/Oncology/BMT, Aurora, CO
12MRC Holland, Research, Amsterdam, Netherlands
13Maria Arrieta1, Erica Ramis2, Claudio Larrea2, Adriana Cano3, Silvia Brandalise4, Anjo Veerman5, Silvia Brandalise4, Anjo Veerman5
14Low MIR-196B and high MIR-708 expression are associated with a poorer prognosis, using the 2-DDCT method. The expression levels of the miR and the clinical and biological variables were analyzed by Mann-Whitney test.
15Results: All patients received an 8-week interim maintenance with oral prednisone, vincristine, and L-asparaginase. Due to high rates of early death, a less intensive regimen (HIRRC-2008) was introduced in 2008 that consisted of a 7-day prednisone prophase followed by a 3-drug (prednisone, vincristine, and L-asparaginase) induction. Patients received consolidation therapies of different intensity based on risk group, prednisone induction (MLPA).
16Conclusion: The HIRRC-2008 approach using less intensive induction/consolidation therapies was associated with significant decreases in early mortality and improvements in short term survival. Additional follow-up is needed to assess the long-term efficacy of this approach. These results have implications for ALL treatment in other countries with limited resources.

Purpose: To determine the frequency distribution of aneuploidy in Indonesian childhood ALL by multiplex ligation-dependent probe amplification (MLPA).

Method: A multicenter descriptive study was conducted. Samples consisted of bone marrow slides of Indonesian ALL children. The DNA was isolated from stained bone marrow slides by Phenol-chloroform (PCI) methods. MLPA with centromeric probes (P161 and P182) was used to detect aneuploidy from the DNA sample. Prior to the test on samples, the MLPA was validated on hyperdiploidy cell lines (CEM and 8226) and on the DNAs from Dutch ALL children with known karyotype.

Results: All patients received consolidation therapies of different intensity based on risk group, prednisone induction (MLPA).

Conclusion: The HIRRC-2008 approach using less intensive induction/consolidation therapies was associated with significant decreases in early mortality and improvements in short term survival. Additional follow-up is needed to assess the long-term efficacy of this approach. These results have implications for ALL treatment in other countries with limited resources.

Purpose: Low Mir-196B and high Mir-708 expression are associated with a poorer prognosis.

Method: The Hospital Infantil Dr. Robert Reid Cabral (HIRRC) treats 30–improving ALL outcomes. We assessed survival and toxic death rates before/after cases/year. Twinning with a higher income country program began in 2004, focused on.

Results: Of 193 eligible patients between 2000 and 2005, 188 (97%) received EOTBMAs. All patients received an 8-week interim maintenance with oral prednisone, vincristine, and L-asparaginase. Due to high rates of early death, a less intensive regimen (HIRRC-2008) was introduced in 2008 that consisted of a 7-day prednisone prophase followed by a 3-drug (prednisone, vincristine, and L-asparaginase) induction. Patients received consolidation therapies of different intensity based on risk group, prednisone induction (MLPA).

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and turbidity. Quantification of Ig concentrations was performed at diagnosis, during the first year of treatment in patients with more than fifteen months from diagnosis and beyond treatment. We compared the concentration values by IGRS Igs and turbidity.

Results: The concentration of IgG in patients 3 to 8 years, showed a statistically significant decrease. During the first year of treatment the concentration of Ig A, G and M was dissimilated. In patients off treatment, the concentrations of Ig A, G and M were lower than in the control group. The qualitative determination of IgG and Anti Rubella Measles Rubella seronegativity showed (33.3%) for measles interviewed (61.1%) in patients previously vaccinated and who had completed the qualitative determination tratments. La ISM IDR tuberculosis and statistically significant differences were also obtained at high concentrations of Igs.

Conclusion: Chemotherapy may influence the concentration of IgA, IgG and IgM. Regarding the role of antibody-producing-cells, we found that vaccinated patients undergoing chemotherapy were negative in the qualitative determination of IgG and Anti Anti Measles Rubella. Therefore considering the use of hyper-immune human gamma globulin in patients enrolled in severe infectious diseases and re-vaccinating patients once they are restored to normal immunoglobulins.

PA007

ADOPTIVE NATURAL KILLER (NK) CELL IMMUNOTHERAPY AND ROMEDEPSIN, A HISTONE DEACETYLASE INHIBITOR FOR 11Q23 INFANTILE ALL: NOVEL TRANSLATIONAL APPROACH

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Purpose: Infantile ALL, characterized as chemo-resistant cells which may shed NK cell NKG2D-ligands MIC/A/B and escape immune cytotoxicity. Our Objective was to describe a single centre experience of what happens to such children after diagnosis.

Method: A retrospective analysis of medical records of all children who were diagnosed with DS and Leukemia at Sir Ganga Ram Hospital from Jan 2005 to Jan 2011.

Results: Overall, 410 cases of Leukemia (Male/female ratio 3:1) were diagnosed at our centre. However 9 (2.2%) of them also had DS. Male/Female ratio was 2:7 (P value = 0.0001). Eight of these 9 patients were less 2 years of age and 3 were neonates. Type of Leukemia was myeloid in 8 and lymphoid (Pre-B expressing CD10) in 1. None had central nervous system disease. Out of 8 myeloid malignancies, 5 had acute myeloid Leukemia (AML) (M1-2, M7-3), 2 had transient myeloproliferative disorder (TMD) and 1 had Juvenile myelomonocytic Leukemia (JMML). One AML patient was lost to follow-up. Four AML were treated as per COG-A2971 protocol. Two are in first remission (1 and 4 years post completion), one with complex cytogenetics died of refractory disease and one died due to pulmonary hemorrhage during induction chemotherapy. Spontaneous remission was seen in 2 TMD and JMML patient. Only patient with acute lymphoblastic Leukemia died of sepsis during induction chemotherapy as per UKALLXI protocol.

Conclusion: It is feasible to treat children with Down syndrome with Leukemia in the developing world. Spontaneous recovery in Neonates is possible.

PA008

PHARMACOKINETIC OF HIGH DOSE METHOTREXATE (HD-MTX) TREATMENTS IN CHILDHOOD LEUKEMIA

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Purpose: MTX is a widely used antifolate cytostatic agent for the treatment of different childhood malignancies in different dose and manner. The aim of our study was to compare the concentration values by pharmokinetic parameters and toxicity after ALL-BFM-1995 and 2002 protocol.

Method: 43 children were treated with 5 g/m²/4 h MTX and 39 children with 2 g/m²/24 h MTX. The mean age of the patients was 7 to 15 years (0.5–15.7). Totally 283 MTX infusions were analysed. Serum MTX and 7-OH-MTX levels were measured with HPLC at 24, 36, 48 hours, while the MTX concentration in the CSF was determined at 24 hours after the start of MTX infusion. Considering the toxicity of the treatments we measured the serum ALAT, ASAT; bilirubin, creatinine, protein levels before therapy and one day, two days and one week after treatment.

Results: Mean MTX level at 24 hours and 7-OH-MTX level at 36. hours were significantly lower after 2 g/m² courses than after 5 g/m² courses (MTX2: 29.7±17.4 µmol/l; MTX5: 89.5 ± 55.0 µmol/l; 7-OH-MTX2: 4.1 ± 1.7 µmol/l and 7-OH-MTX5: 1.8 ± 1.6 µmol/l; p< 0.00001). In children who were under 5 mg/m² MTX significantly more cases of hepatotoxicity, thrombocytopenia, mucoitis occurred, however these side effects were mild and reversible. Repeated MTX treatments in the same children did not alter the MTX pharmacokinetic: 7-OH-MTX levels showed closer correlation with the toxicity parameters than MTX (p = 0.0004).

Conclusion: 5 g/m² MTX resulted in more reliable therapeutic serum levels with slightly more toxicity. CSF MTX concentrations did not depend on the MTX dose. 7-OH-MTX measurements might be more useful than MTX levels to detect toxicity.

PA009

SHOULD WE TREAT CHILDREN WITH DOWN SYNDROME AND LEUKEMIA IN THE DEVELOPING WORLD?

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Purpose: Leukemias in children with Down syndrome (DS) are characterized by unique clinical and biological features. In a country where cost of therapy is a barrier to care of childhood Leukemia should children with DS and Leukemia be offered therapy? Here we describe a single centre experience of what happens to such children after diagnosis.

Method: It was a retrospective analysis of medical records of all children who were diagnosed with DS and Leukemia at Sir Ganga Ram Hospital from Jan 2005 to Jan 2011.

Results: Overall, 410 cases of Leukemia (Male/female ratio 3:1) were diagnosed at our centre. However 9 (2.2%) of them also had DS. Male/Female ratio was 2:7 (P value = 0.0001). Eight of these 9 patients were less 2 years of age and 3 were neonates. Type of Leukemia was myeloid in 8 and lymphoid (Pre-B expressing CD10) in 1. None had central nervous system disease. Out of 8 myeloid malignancies, 5 had acute myeloid Leukemia (AML) (M1-2, M7-3), 2 had transient myeloproliferative disorder (TMD) and 1 had Juvenile myelomonocytic Leukemia (JMML). One AML patient was lost to follow-up. Four AML were treated as per COG-A2971 protocol. Two are in first remission (1 and 4 years post completion), one with complex cytogenetics died of refractory disease and one died due to pulmonary hemorrhage during induction chemotherapy. Spontaneous remission was seen in 2 TMD and JMML patient. Only patient with acute lymphoblastic Leukemia died of sepsis during induction chemotherapy as per UKALLXI protocol.

Conclusion: It is feasible to treat children with Down syndrome with Leukemia in the developing world. Spontaneous recovery in Neonates is possible.

PA010

THROMBOSIS DURING INDUCTION PHASE OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA- A SINGLE CENTER EXPERIENCE FROM DEVELOPING WORLD

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Purpose: Thrombosis is a known complication during induction phase of treatment of acute lymphoblastic Leukemia (ALL). The risk of thrombosis in children with ALL reportedly ranges between 1% and 37%. L-Asparaginase is a chemotherapeutic agent commonly used during induction phase of treatment of ALL. Thrombotic states during induction phase of treatment of ALL were evaluated.

Method: Thrombotic states were analyzed retrospectively in ALL patients diagnosed between Jan 2005 and Feb 2011. These patients were treated on UKALLXI protocol for standard risk and BFM protocol for high risk. Their fibrinogen levels at the time of thrombosis were also recorded.

Results: Of the 235 patients who received L-asparaginase in the induction phase of chemotherapy, 14 patients (5.96%) suffered a hypercoagulable event during the induction phase. Two patients had seizure and MRI revealed superior sagittal thrombosis in five and infarcts in seven patients. Two patients developed lower limb thrombosis. These two patients had central venous line inserted at the time of thrombosis. Median fibrinogen in these 14 patients was 1 g/l(range 0.9 to 1.4 g/l). Two patients expired during this episode and one went into vegetative state.
Conclusion: Incidence of thrombosis was almost similar to western data. Fibrogenin cut-off level for withholding L-asparaginase or FFP administration should be raised to 1 g/dl instead of 0.5 g/dl recommended.

PA01

TREATMENT AND OUTCOME OF INFANT ACUTE LYMPHOBLASTIC LEUKEMIA IN DEVELOPING WORLD: A SINGLE CENTRE EXPERIENCE

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Purpose: Acute Leukemia is rare in infants. Symptoms are nonspecific, thus early diagnosis and treatment is necessary. It has peculiar biologic features and poor prognosis. It differs from Leukemia in older children with respect to immunophenotype, cytogenetic and molecular genetic features.

Method: 287 cases of diagnosed Leukemia were retrospectively analyzed from January 2005 to March 2011. Ten of these were infants. Their clinical profile, immunophenotype, cytogenetics and treatment outcome were analyzed. Five cases had Acute Lymphoblastic Leukemia (ALL) and 5 had Juvenile Myelomonocytic Leukemia.

Results: Amongst 5 infants with ALL, 2 were Pre B, 1 Pro B, 1 T cell ALL and 1 unclassified as the surface markers could not be done. Male to female ratio was 2:3. Median age of presentation was 7 months (range: 3–11 months). Three presented with fever and abdominal distension and 2 had bleeding. All patients had hepatosplenomegaly and 1 had lymphadenopathy. One had testicular involvement. Median haemoglobin, total leucocyte counts and platelet counts were 7 g/dl (range: 5.8–23.0), 23000/cmm (2200–145000) and 56000/cmm (28000–100000) respectively. Four had L1 FAB morphology and 1 L2. Bone marrow cytogenetics showed trisomy 18 in one, 46Xins(19)(pl11p23) in one and normal in 2. None had CNS involvement. One had MLL rearrangement and none were positive for BCR-ABL or TEL-AML fusion gene. Two refused treatment and 3 were treated as per Interfant 99 protocol. One in complete remission with a follow up of 44 months, 1 relapsed at 18 months and 1 left treatment after induction therapy.

Conclusion: ALL is rare in infancy and though outcome is uniformly poor, treatment with intensive chemotherapy is feasible in India, and results are encouraging.

PA02

INCIDENCE OF VERTEBRAL FRACTURES IN CHILDREN WITH LEUKEMIA AFTER 12 MONTHS OF CHEMOTHERAPY

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14Canadian Pediatric Bone Health Working Group, Pediatrics, Ottawa, Canada

Purpose: Fractures are an important complication of childhood acute lymphoblastic Leukemia (ALL). The frequency of incident vertebral fractures (IVFs) in ALL as well as the surface markers could not be done. Male to female ratio was 2:3. Median age of presentation was 7 months (range: 3–11 months). Three presented with fever and abdominal distension and 2 had bleeding. All patients had hepatosplenomegaly and 1 had lymphadenopathy. One had testicular involvement. Median haemoglobin, total leucocyte counts and platelet counts were 7 g/dl (range: 5.8–23.0), 23000/cmm (2200–145000) and 56000/cmm (28000–100000) respectively. Four had L1 FAB morphology and 1 L2. Bone marrow cytogenetics showed trisomy 18 in one, 46Xins(19)(pl11p23) in one and normal in 2. None had CNS involvement. One had MLL rearrangement and none were positive for BCR-ABL or TEL-AML fusion gene. Two refused treatment and 3 were treated as per Interfant 99 protocol. One in complete remission with a follow up of 44 months, 1 relapsed at 18 months and 1 left treatment after induction therapy.

Conclusion: ALL is rare in infancy and though outcome is uniformly poor, treatment with intensive chemotherapy is feasible in India, and results are encouraging.

PA03

METHOTREXATE TRANSPORTER GENES AS NEW TOXICITY MARKERS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: Acute lymphoblastic Leukaemia (ALL) is the most common childhood malignancy. Although marked advances in chemotherapy have resulted in high cure rates, interindividual differences in drug responses are an important cause of adverse drug reactions. These differences can be due to different factors, including polymorphisms in key genes. An important component of ALL therapy is methotrexate (MTX). Treatment with high-dose MTX often causes toxicity, dose reduction or cessation of treatment being necessary. In the last years, several studies have investigated the relationship between genetic variation and MTX-related toxicity. However, the associations found are not always confirmed. Recently, several polymorphisms in a transporter gene, SLCO1B1, have been strongly associated with MTX toxicity in a genome-wide study by Treviño and collaborators. In the present study, we evaluated polymorphisms in genes of MTX transport as toxicity predictors in pediatric B-ALL, of all them homogeneously treated according to the standardized LAL/SHOP protocol.

Method: DNA was extracted from blood samples of 150 paediatric ALL patients treated with the LAL/SHOP protocol by standard phenol-chloroform method. We analysed the association between the polymorphisms and toxicity using the Fisher exact test (p value < 0.05).

Results: We found an association between MTX plasma levels and SLCO1B1 rs11054879 CC genotype (p = 0.008), confirming the results of Treviño and colleagues.

Conclusion: Our results suggest that polymorphisms in genes involved in MTX transport could be new toxicity markers in pediatric ALL.

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PA04

IMPROVEMENT OF SURVIVAL RATE OF CHILDREN WITH ALL IN KYRGYZSTAN

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Purpose: In Kyrgyzstan before the year 2000, up to 50 children a year die from acute lymphoblastic Leukemia. The introduction of an effective protocol which is a modified version of the ALL-BFM-95 which in Kyrgyzstan has resulted in an increase in the 5 year overall survival from 0% to 70% can serve as a model for improving care for children with ALL in developing countries.

Method: The patients are divided into three groups according to prognostic factors: Standard Risk (SR), Intermediate Risk (IR) and High Risk (HR). Patients were treated on the modified ALL-BFM-95 protocol. The protocol modification consisted of reduction of the “M” dose of methotrexate from 5 g/m2 to 1 g/m2

Results: The study included 521 patients from May 2000 to October 2010. Risk group status was assigned to 332 patients: 264 SR, 21 IR and 57 HR. The 5-year EFS was 67.5% in SR, 68% in IR and 55% in HR. The disease free survival in children with acute lymphoblastic Leukemia in a developing country with a developing economy is a very difficult challenge for physicians. Despite this gradual, step-by-step improvement of available diagnostic and treatment methods and the introduction of modified protocols such as based on the ALL-BFM-95, children with ALL may improve their survival. Kyrgyzstan has been able to improve the overall survival of children with ALL from 0% to 70% at present. This is probably not ideal in terms of survival, but doctors should do everything possible, depending on their capabilities and their resources, to improve the outcome for children with ALL.
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SIOP ABSTRACTS

PA015

COMPLIANCE TO TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose: Identifying the factors that influence compliance to treatment in pediatric patients with acute lymphoblastic leukemia (ALL).

Method: The study was carried out in Children’s Emergency Hospital Sf. Mary Iasi, Oncology-Department, on 201 children with ALL, aged between 0–18 years. Five parameters were analyzed (sex, age, geographical region, relapse, death) to assess compliance to treatment. The methods used were descriptive and inferential statistical analysis. Compliance to treatment was defined as presentation to hospital for treatment according to the sequence protocol, in pediatric patients given that tutors were informed about the benefits of the treatment’s rigor. From the lot were excluded patients who didn’t meet therapeutic discipline reasons other than compliance (e.g., continue treatment at another hospital).

Results: For the 184 patients who received Leukemia treatment (being excluded patients who refused treatment and those who died before initiating treatment) it was found that 20.1% of them were not compliant to treatment, while 79.9% met the therapeutic discipline.

There were no statistically significant correlations between compliance to treatment and demographic parameters, namely sex (r = 0.036, p = 0.632), age (r = 0.054, p = 0.463) and geographical region (r = 0.102, p = 0.168). Non-compliant patients tended to relapse after unfavorable evolution (sample 164 patients with relapse; r = -0.328, p = 0.005) and death (sample 184 patients who died; r = -0.331, p < 0.005) more than patients compliant to treatment.

Conclusion: In the absence of treatment, the evolution of ALL is fatal within a constant alternating days, weeks or months. Compliance to treatment is an essential element for the favorable evolution of leukemic patients. Since the objective demographic factors do not influence compliance to treatment, it is necessary to identify individual factors, namely the psycho-cultural and religious, which influence parents’ decisions on further chemotherapy leukemia patients.

PA016

TOXICITY OF HIGH-DOSE METHOTREXATE THERAPY IN PATIENTS OF ACUTE LYMPHOCYTIC LEUKAEMIA WITH DOWN SYNDROME

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Purpose: In order to examine the reasons of inferiority of treatment results of acute lymphocytic Leukemia (ALL) in patients with Down syndrome (DS), we compared the plasma concentration of methotrexate (MTX) and severity of toxicity in ALL patients with and without DS.

Method: Consecutive patients of ALL with DS (4 cases) and without DS (16 cases) were treated at our Department with TCCSG Protocols 15 (P15) and 16 (P16) which contain 3 courses of high-dose MTX for prophylaxis of central nervous system Leukemia (CNS phase). The plasma MTX concentration was measured using Envi14 Methotrexate Assay and toxicity was graded according to National Cancer Institute Common Toxicity Criteria.

Results: The first course of high-dose MTX in P15 consists of MTX 3 g/m² over 12 hours (Group 2) and other courses of P15 and all courses of P16 consist of MTX 5 g/m² over 24 hours (Group 3). We reduced MTX dosage to 2 g/m² over 24 hours for DS patients (Group 1). Mean plasma concentrations at 48 hours after infusion for the first course were 0.50 ± 0.013 ± 0.13 μmol/L for Group 1, 1.33 ± 0.15 ± 0.32 μmol/L for Group 2 and 0.54 ± 0.06 ± 0.32 μmol/L for Group 3. Toxicity greater than grade 3 was only oral mucositis which was seen only in Group 1.

However, the length of time required to complete CNS phase was longer for Group 1 (43.5 ± 9.2 days) than for other groups (28.6 ± 4.6 days for Group 2 and 31.4 ± 3.4 days for Group 3) (P = 0.015 & 0.013) because of delayed recovery from gastrointestinal symptoms. All patients with DS are alive and disease-free for 2 to 9 years.

Conclusion: MTX clearance tended to be delayed in patients with DS but significant toxicity was only mucositis. If appropriate leucovorin rescue is given, all patients with DS could be treated with the same protocol but minor modification of dosage may be needed.

PA017

DIFFERENTIAL EXPRESSION OF LAMIN B1 IN THE BONE MARROW MONONUCLEAR CELLS OF ACUTE LYMPHOBLASTIC LEUKAEMIA ACCORDING TO INITIAL RESPONSE TO CHEMOTHERAPY

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Purpose: Precursor B lymphoblastic Leukemia is a B-cell lineage neoplasm of lymphoblasts. The initial response to induction-chemotherapy is the most important prognostic factor in ALL patients. Patients with rapid early-response (RER < 5% of blast in bone marrow at day-7 after induction-chemotherapy) have better event-free survival compared to slow-early responders (RER > 25% of blast). The drug sensitivity/resistance of leukemic blasts is mainly determined by specific genetic abnormalities, however, in more than 20% of ALL, the abnormalities remain unclassified, and the treatment outcome persist variable. This study aimed to find plasmable biomarkers of drug sensitivity/resistance in ALL using 2-DE and mass spectrometry.

Method: Proteomic analysis was performed using proteins from BMMCns of Twelve patients (five belong to RER and seven SER groups). Differential protein expressions from both groups were analyzed by PDQuest and identified by matrix-assisted laser desorption/ionization-time of flight/mass spectrometry. Differentially expressed proteins were reconfirmed using Western blot.

Results: The 714 spots in RER and 555 spots in SER were visualized in gels. Of these 28 up-regulated and 25 down-regulated proteins in SER as compared to RER-were identified. Among these protein Lamin-B1, actin and α-tubulin were up regulated in SER (t-test, P value < 0.05) and were further verified by Western blot analysis.

Conclusion: Actin and α-tubulin are associated with microtubules and/or microfilament cytoskeleton. Lamin-B1 is early target for caspase degradation. Further characterization of the altered proteins is now underway to elucidate their roles in drug resistance as a potential biomarker for ALL therapy.

PA018

ZEBULARINE DECREASES CELL PROLIFERATION AND INCREASES APOPTOSIS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA CELLS

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Purpose: Acute lymphoblastic Leukemia (ALL) is the most common hematologic malignancy in childhood and represents a heterogeneous disease regarding its biology and prognosis. Despite the advances in treatment, about 20% of patients relapse and/or die, indicating the need of different therapies for this group. Recently, epigenetic drugs as inhibitors of DNA methyltransferases (iDnmts) have shown anti-neoplastic effects in different tumors. Zebularine (ZB) is a potent inhibitor of DNA methylation and has been associated with induction of apoptosis and enhancing tumor chemo- and radiosensitivity. However, its effects on childhood ALL cell lines has not previously been reported. Herein, this study aimed to evaluate the effects of ZB on cell proliferation and apoptosis of childhood ALL cells.

Method: Functional studies of cell proliferation and apoptosis were performed in triplicate with Jurkat and ReH cell lines. Statistical analysis was made by one or two-way ANOVA and Bonferroni post-hoc. To calculate the doses with 50% inhibition of proliferation (Dm or IC50 values) data were analyzed by the median-effect method (Calcusyn software; Biosoft, Ferguson, MO).

Results: Both cell cultures were sensitive towards ZB treatment (50, 100, 200, 300 μM), showing a concentration-dependent inhibition of proliferation (P < 0.05). It was observed dose- and time-effect difference of proliferation (P < 0.05). The IC50 values were of 102.93 ± 14.01 and 62.15 ± 15.11 μM for Jurkat and ReH, respectively, at 72h. ZB also causes apoptotic cell death in ALL cells, where the percentage of apoptotic cells significantly increased after treatment compared control (P < 0.05).

Conclusion: These results indicate that ZB may be a promising drug for the adjuvant treatment of ALL, since it is reported as a less toxic drug among the others iDnmts. Further studies should be conducted to confirm its potential.
Purpose: Identification of prognostically significant oncogene fusion transcripts like TEL-AML1, BCR-ABL & MLL-AF4 among childhood B-lineage ALL patients of Kerala, using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).

Method: Bone marrow/peripheral blood samples were collected from 215 Keralite children (0–14 years) with newly diagnosed B-lineage ALL treated at Regional Cancer Centre Trivandrum, Kerala from December 2008 to March 2011. Fusion gene transcripts were detected by multiplex nested RT-PCR assay.

Results: Of the 149 RNA samples extracted from 215 newly diagnosed Paediatric B-lineage ALL, 91 yielded analyzable cDNA. Median age was 4.5 years. MF ratio was 1.81:1. 5 were infants and 86 were between 1–14 years. Of 5 infants, 4(80%) were MLL-AF4 positive (20%) was BCR-ABL positive. Of 86 children, 6(7%) were TEL-AML1 positive, 6(7%) were BCR-ABL positive & 15 (17%) were MLL-AF4 positive. Treatment response was favourable among TEL-AML1 children with all of them attaining remission in 4 weeks and no relapse. Among BCR-ABL group though all of them attained remission in 4 weeks, two of them relapsed on therapy & died. Among MLL-AF4 group, one child did not attain remission in 4 weeks & 2 children relapsed on therapy.

Conclusion: The study results so far have revealed a low frequency (7%) of favourable TEL-AML1 and a higher frequency of the unfavorable MLL-AF4 (17%) & BCR-ABL(7%) gene fusions among the Paediatric B-lineage ALL in Kerala. This may be owing to the poor outcome seen in the Indian subcontinent. Study emphasizes the need to include molecular screening of fusion gene transcripts in the routine diagnostic panel of paediatric ALL in Kerala for providing tailored therapy & improving survival.

Purpose: The aim of this study was to evaluate whether the levels of cerebrospinal fluid (CSF) osteopontin is related to central nervous system (CNS) involvement and to determine whether the elevated CSF osteopontin levels are the early decisive marker of CNS involvement before the beginning of the symptoms and signs in children with acute leukemia.

Method: The study’s sample was consisted with the patients that were diagnosed as acute leukemia at our hospital between March 2008 and June 2010. The patients were divided into two groups: children with CNS involvement and children without CNS at diagnosis and follow-up. The CNS involvement was obtained in 3/13 patients at diagnosis and in 10/13 patients at follow-up. Total 6 CSF samples (3/6 at diagnosis and 3/6 at remission period) of the patients with CNS involvement in the diagnosis were taken. The CSF samples of the patients with CNS involvement at follow-up were taken at diagnosis, before relapse, at relapse and remission.

Results: The mean levels of CSF osteopontin of 62 patients with acute leukemia at diagnosis and control group were 32.76 ± 49.22 ng/mL and 14.93 ± 8.4, respectively (p = 0.65). The mean levels of CSF osteopontin of patients with CNS involvement and patients without CNS at diagnosis were 27.68 ± 32.73 ng/mL and 38.4 ± 92.12 ng/mL, respectively (p = 0.50). The mean CSF osteopontin level of the patients with CNS involvement during follow-up at the time of relapse was significantly higher than the patients without CNS at diagnosis (127.4 ± 52 vs 27.68 ± 32.73 ng/mL) (p < 0.001). The CSF osteopontin levels between the periods of diagnosis-before relapse-relapse-remission were significantly different in patients with CNS involvement.

Conclusion: It is shown that high CSF osteopontin levels were associated with the evidence of CNS involvement for childhood acute leukemia patients, and more importantly, the increases in CSF osteopontin levels was associated with early decision of CNS involvement in this study.

Purpose: PHARMACOECONOMY IN PRACTICE OF REGIONAL CHILDREN'S ONCOHEMATOLOGY CENTRE IN RUSSIA

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Purpose: Estimating pharmacoeconomic analysis of different chemotherapy protocols in oncohematology patients in Russian clinic.

Method: Research was conducted from 2003–2006 in Chelyabinsk Regional Center: Cost-effectiveness analysis of treatment with acute lymphoblastic leukemia under Protocol BFM ALL-90(M) N = 84 and cost-effectiveness analysis of treatment with children with Non Hodgkin Lymphoma B-cell under Protocol BFM(M) N = 24. Criteria for cost-effectiveness: level of survival, years of life according quality, duration of “extra” life and etc. Data were analyzed using descriptive statistics and variations around the costs were obtained.

Results: Average cost components comprised: chemotherapy drugs and delivery (44%), management of complications and comorbidities (17%), etc. (7%) Medical efficiency (n = 84) of treatments under of technology BFM ALL-90 (M) by survival rate was OS = 0.75. QALY (quality-adjusted-life-year) in the patients ALL on Report BFM ALL (90) M was from 5.0 to 0.8 even after 5 years of remission does not reach population’s indicator 0.95. Treatment of 77 patients costs the State about 1540 thousand dollars. From them a cost of illness in 6.3 times will exceed expenses. Medical efficiency (n = 24) of treatments under of technology BFM NHL-B cell (M) by survival rate was OS = 0.87. Cost-safety differences-862 QALY years, 32.2 per patient. The sum for remuneration was about 9 times more than ‘cost of illness’. Problems of Health technology assessment in children’s oncohematology has based on the numerous spectrum of adverse events in future life of the patients.

Conclusion: Pharmacoeconomic analysis of BFM (M) protocols ALL and B-cell Non Hodgkin Lymphoma proved the medical, social and economical effectiveness of technology. Pharmacoeconomics could be the basic of country-specific health care delivery systems and decision-making processes for coverage, reimbursement, and pricing decisions for pharmaceuticals and medical device.

Purpose: CLINICAL, BIOLOGICAL AND IMMUNOPHENOTYPIC FEATURES OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA WITH MLL GENE REARRANGEMENTS IN POLISH POPULATION

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Purpose: The incidence of children suffering from ALL with MLL gene rearrangements.

Method: During the period of 2006 in Chelyabinsk Regional Center: Cost-effecness analysis of treatment with acute lymphoblastic leukemia under Protocol BFM NHL-B cell (M) by survival rate was OS/C6 52 vs 27.68/C6 53.48 ± 92.12 ng/mL, respectively (p = 0.50). The mean levels of CSF osteopontin of patients with CNS involvement and patients without CNS involvement were 27.68 ± 32.73 ng/mL and 38.4 ± 92.12 ng/mL, respectively (p = 0.001). The CSF osteopontin levels between the periods of diagnosis-before relapse-relapse-remission were significantly different in patients with CNS involvement.

Conclusion: It is shown that high CSF osteopontin levels were associated with the evidence of CNS involvement for childhood acute leukemia patients, and more importantly, the increases in CSF osteopontin levels was associated with early decision of CNS involvement in this study.

Purpose: OSTEOPONTIN INCREASES IN THE CEREBROSPINAL FLUID PRIOR TO MENINGEAL INVOLVEMENT IN CHILDREN WITH ACUTE LEUKAEMIA

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Purpose: Although the significant improvement in treatment efficacy of childhood acute lymphoblastic Leukemia (ALL) has been achieved, still 20–30% of patients relapse. In order to minimize the relapse rate, identification of new prognostic factors seems to be essential. The ALL gene rearrangements are recurrent genetic abnormalities in ALL. Unfortunately, the importance and prognostic significance of MLL rearrangements are not fully conclusive. Therefore, we aimed at biological, immunophenotypic and clinical characterization of Polish patients suffering from ALL with MLL gene rearrangements.
62 SIOP ABSTRACTS

Method: The clinical data were obtained from 397 children with acute lymphoblastic leukemias treated in the centers of Polish Pediatric Leukemia and Lymphoma Study Group. In all patients, one marrow slides at initial diagnosis were analyzed with MLL split-signal fluorescent in situ hybridization. Furthermore, the long-distance inverse PCR reaction was performed to sequence the breakpoints of MLL gene aberrations. Blast cells immunophenotype was precisely determined with multicolor flow cytomtery. The laboratory and clinical features in two groups were compared using the Fisher's exact test or U-Mann-Whitney test.

Results: MLL gene rearrangements were found in 24 patients with de novo ALL (6%). The most frequent MLL rearrangement was t(4;11), present in 62.5% of MLL+ cases. Patients with MLL-ALL were characterized by significantly lower age at diagnosis (3.6 years in MLL+ ALL vs. 7.1 years in MLL- ALL), higher initial leukocytosis and blast cell count, higher blast cell count at day 8 (worse prednisone response) and more frequent hepatosplenomegaly. In addition, the flow cytometric technique revealed the predominance of CD10-negative NOS pro-MTCL in MLL+ ALL.

Conclusion: The incidence of MLL gene rearrangements in Poland is comparable to data obtained in European and American studies. MLL gene alterations are associated with distinct immunophenotypic and clinical features (predominance of higher aggressiveness and poor response to therapy).

PA025

PREVALENCE OF FAVORABLE PROGNOSTIC CYTOGENETIC MARKERS & ETV6/RUNX1 (TEL/AML1) GENE IN PEDIATRIC B-LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA IN INDIAN PATIENTS

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Purpose: Information regarding certain cytogenetic aberrations assists immensely both in prognosticating and treating children with B-lineage Acute Lymphoblastic Leukemia (ALL). There are geographical and racial variations in the frequency and prevalence of these aberrations. Data from the Indian subcontinent is sparse. Previous studies from this region have shown a low frequency of favorable markers such as TEL(AML1) (0-8.6%) and hyperdiploidy from the Indian subcontinent. Aim: To identify the frequency of cytogenetically important prognostic markers in pediatric B-lineage ALL.

Method: Bone Marrow samples at diagnosis from 106 newly diagnosed ALL patients aged 1–18 years presenting at three centres in North India were analyzed for chromosomal abnormalities with conventional G-banding techniques and interphase fluorescence in situ hybridization (FISH) using locus specific probes to detect cryptic TEL/AML1, BCR-ABL and MLL gene rearrangement.

Results: Of the 106 patients, cytogenetics results were available for 82 (77.5%) patients. The metaphase was not analyzable in 24 (22.5%). Thirty nine (37%) patients had normal diploid karyotypes, diploid hyperdiploid was seen in 14 (13%) patients, hyperdiploid (> 47-50 chromosomes) in 19 (18%) patients and hypodiploid (< 46 chromosomes) in 10 (9.5%) patients. There were a total of 14 (13.2%) structural abnormalities in this group of patients that included t (9;22) in 8 patients, (9;11) in 6 patients, and other translocations and inversions in 2 patients. Of the 106 patients, 63% patients were seen to have hyperdiploidy (>= 35 chromosomes) as the most common abnormality. The median follow up of the study was 18 months and the OS was 52.2%. NOTCH1 complex mutations were associated with better outcome by univariate analysis (p = 0.013).

Conclusion: This report demonstrated that the relevance of NOTCH1 complex mutations associated with outcome in T-ALL overall survival.

PA024

COMPLEX NOTCH1 MUTATIONS AS PROGNOSTIC IMPACT FACTOR IN PEDIATRIC T-CELL LEUKEMIA

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Purpose: Molecular alterations are frequently in T-ALL and controversial issues were raised regarding the real prognostic impact of NOTCH1 mutations. The study aimed to test whether NOTCH1 mutations with additional molecular abnormalities in PTEN and RASS1 would be correlated with T-ALL outcome.

Method: We analysed a series of 138 T-ALL cases. T-ALL subtypes, status of S1T-T1 fusion genes, ectopic expression of HOX11.2, mutations in KRAS, PTEN and NOTCH1 were assembled for overall survival (OS) analysis. Univariate analyses were calculated using Pearson’s test. The log-rank test was used to compare the survival distributions according to molecular aberrations. The OS was determined using the Kaplan-Meier method.

Results: The frequency of NOTCH1 mutation was (43.5%), PTEN (10.5%), KRAS (9.5%), and RASS1 (56.6%) in cases, the coexistence of NOTCH1 mutations and other molecular alterations was observed. No statistical association was disclosed between NOTCH1 mutations compared to any variable analyzed of the T-ALL cases. The median length of the follow-up was 66 months and the OS was 52.2%. NOTCH1 complex mutations was associated with better outcome by univariate analysis (p = 0.013).

Conclusion: The frequency of NOTCH1 mutations associated with outcome in T-ALL overall survival.

PA026

NUTRITIONAL STATUS AS A PROGNOSTIC FACTOR IN RESPONSE TO TREATMENT AND SURVIVAL OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE CENTRE EXPERIENCE

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Purpose: Malnutrition in the context of pediatric oncology is known to be a poor prognostic factor for tolerating chemotherapy. However, in developing countries with widespread malnutrition, there are no definite guidelines for identifying at-risk patients and for early intervention. The purpose of this study was to estimate the prevalence of malnutrition in pediatric acute lymphoblastic leukemia (ALL) patients at initial diagnosis and to correlate it

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with the clinical course. It was also aimed to determine a cut-off percentile of Body Mass Index (BMI) below which early nutritional intervention is advisable.

Method: The present study was carried out from the retrospective review of the medical records of ALL patients diagnosed at Pediatric Hematology Oncology unit, Sir Ganga Ram Hospital, New Delhi, between Jan 2005-Jan 2011. Anthropometric parameters at initial presentation were recorded. Weight for age, height for age and BMI for age were calculated based CDC 2000 growth charts. Major events including induction failure, relapse, serious infections and death were recorded.

Results: The data of 190 patients were available for evaluation. Male: female ratio was 2.5:1. Median age was 4.5 years. (Range: 0.5–19 years). Among the patients in whom immunophenotyping was done, 91% were Precursor B ALL. Weight, height and low BMI for age (< 10th percentile) at initial diagnosis in 39%, 20% and 44.7% of the study group respectively. Patients with low BMI tolerated chemotherapy poorly. More infections occurred during induction therapy in patients with low BMI than others (29% vs 17.2%, p = 0.08). Survival trend was both for serious bacterial infections and deaths in induction period. The 3-year OS was 60.8 ± 6.8% in low BMI vs. 78.9 ± 5.4 in those with normal BMI (P = 0.031).

Conclusion: BMI for age is a sensitive marker of nutrition. Patients with low BMI for age should receive aggressive nutritional rehabilitation along with cancer chemotherapy.

PB001

RAS MUTATION IN CHILDHOOD ACUTE MYELOID LEUKEMIA DOES NOT INFLUENCE CLINICAL OUTCOME: A STUDY OF THE JAPANESE CHILDHOOD AML COOPERATIVE STUDY GROUP

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Purpose: Although mutations in RAS are frequent in AML and seem to contribute to leukemogenesis in a subset of patients, their prognostic significance has not been firmly established. We performed the mutational analysis of RAS in pediatric AML patients who were treated on the Japanese Childhood AML Cooperative Study Group Protocol, AML99, to clarify the clinical significance of RAS mutation.

Method: One hundred fifty-seven pediatric patients with acute myeloid Leukemia (AML) were analyzed for NRAS and KRAS mutation around the hot spot at codons 12, 13 and 61, and correlated the results to cytomorphology, cyogenetics, other molecular markers and prognostic relevance of these mutations.

Results: 18.5% (n = 29) had an activating mutation of RAS. KRAS mutations (n = 18, 11.5%) were more frequent than NRAS mutations (n = 11, 7.0%) in this study as opposed to previous reports. RAS mutation was relatively overrepresented in FAB type M4 and M5 (p = 0.02). There were no significant differences in other clinical manifestation and distribution in cytogenetic subgroups between with or without RAS mutations. The frequencies of overlap genomic alterations such as FLT3 internal tandem duplication (ITD), FLT3 D835 mutation, KIT mutation and MLL partial tandem duplication were not significantly different between with or without RAS mutations. In this cohort of patients, we could not demonstrate any significant prognostic impact of RAS mutations (3-year OS 75% vs 79%, p = 0.60, DFS (59% vs 67%, p = 0.061) between with or without RAS mutation in 134 AML patients excluding those with FAB-M3 and Down syndrome).

Conclusion: The patients were treated with AML99 protocol according to the Japanese Childhood AML Cooperative Study Group including high dose cytarabine improved the outcome, thus the presence of a RAS mutation may not significantly influence clinical outcome.

PB002

FLT3 MUTATIONS IN ACUTE MYELOID LEUKEMIA IN CHILDHOOD

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Purpose: Mutations of FLT3 receptor are involved in the development of hematologic malignancies. Although FLT3-ITD mutations seem to be associated with worse outcome in adult AML, the influence of these mutations in children remains uncertain. Our aims were to analyze the incidence of the two primary types of FLT3 mutations (ITD and TKD) in our AML patients and to assess the association of these mutations with clinical features and outcome.

Method: Samples of 177 AML patients diagnosed between March-2000 to December-2010 were analyzed for the presence of FLT3 mutations. FLT3-ITD and FLT3-TKD were studied by RT-PCR and qRFLP, respectively. Positive samples were sequenced and mutations were characterized.

Results: FLT3-ITD mutations were found in 19 (10.7%) cases, while FLT3-TKD was detected in 12 (6.8%) cases. No patients were positive for both types of mutations. There was no difference between FLT3-mutated and WT cases regarding WBC and Platelet counts. There was statistically significant association between FLT3-ITD and age (p < 0.00001) and AML FAB-M3 (p < 0.00006). Nine of nineteen patients with FLT3-ITD and 4 of 12 with FLT3-TKD remain in complete remission. Only one of 6 patients with normal karyotype who presented FLT3 mutation remains in complete remission with long follow-up. No statistical significant differences were observed when outcome of cases with WT-FLT3 with mutated cases (ITD+TKD) were compared. In addition, when cases with normal karyotype (WT vs. FLT3-mutated) were analyzed separately, no differences in outcome were observed, too.

Conclusion: We confirmed the association of FLT3-ITD mutation with AML FAB-M3 and age. No influence of FLT3 mutations was observed in the outcome in our setting, neither in the total AML cases nor in cases with normal karyotype. However, more cases need to be analyzed for defining the actual impact value of these abnormalities.

PB004

CHARACTERIZATION OF PEDIATRIC ACUTE LEUKEMIAS (AL) OF UNUSUAL IMMUNOPHENOTYPE ACCORDING TO THE NEW WHO GUIDELINES

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Purpose: Most AL are clearly defined and treated accordingly as Lymphoblastic or Myeloblastic considering expression of lymphoid (B/T) or myeloid (My) surface/ cytoplasmic markers. However, rare cases are hard to classify: AL of Ambiguous lineage: Myeloblastic considering expression of lymphoid (B/T) or myeloid (My) surface/ cytoplasmic markers. Possible syndromes that usually manifests in childhood with aplastic anemia, reticulated hyperpigmentation, nail dystrophy, and leukoplakia, we have established two methods to measure telomere length: 1) telomere/centromere-fluorescence in-situ hybridization and 2) quantitative real-time PCR.

Method: Telomere/centromere-fluorescence in-situ hybridization (T/C-FISH) is a FISH-based technique that requires chromosome preparation, using probes against the telomere repeats and, as internal control, against the centromere of chromosome 2. When combined with fluorescence R-banding on metaphases, the telomere length of each individual chromosome arm can be measured (Perner et al. 2003). This was demonstrated in a large study on 78 patients with MDS (Lange et al. 2010). T/C-FISH was validated by comparing the telomere length of 5 healthy controls with published data: the measured T/C values, the standard deviation and the telomere length profile, especially the telomere length expected according to the patient’s age, agreed with Mayer et al. (2000). A quantitative PCR (qPCR) analysis was modified according to Cawthon (2002) and was validated by measuring telomere lengths of four cell lines and five patients and showed a very good correlation of relative telomere length measured by qPCR and T/C-FISH. Therefore, the qPCR will enable fast measurement of large cohorts in the future.

Results: In an analysis of an 11-year old boy suspected of suffering from DC, we were able to detect very short telomeres, a finding supporting this diagnosis. The patient’s telomeres measured 3.97 kb versus an age-adapted normal length of 11.09 kb (according to Mayer et al.). In addition, a DKC1 mutation could be identified in the patient.

Conclusion: In conclusion, telomere length measurement should be implemented as a diagnostic tool to identify patients with DC in the future.
to characterize this group among our population of patients using the newest WHO ’08 guidelines.

Method: From April 1994 to February 2011, 1475 pediatric cases of AL were diagnosed in our Institution, of which 59 had been previously classified as ALAL using the EGIL staging. Standard flow cytometry, cytogentic and RT-PCR techniques were used.

Results: Applying WHO ’08 guidelines for the re-classification, 40 cases with an unusual phenotype were determined: 7 cases of mixed-phenotype with 1q23/MLL abnormalities, 8 B/My, 8 T/My, 10 characterized as infrequent types and 7 without specific Ly/My markers, 3 of which were characterized as DCAL, 3 as undifferentiated (UAL) and 1 remained as unclassifiable. Thus, only 37 cases (2.5%) met the new criteria for ALAL. Within ALAL, abnormalities of chromosome 7 were detected in 6 of 39 patients and of 1q23/MLL in another seven. All 3 DCLAL responded well to ALL protocols. Of the ALAL, 30 patients achieved CR, 3 patients did not respond or switched the lineage and 4 died during induction. Twenty-one patients presented events (16 relapses, 1 switch). Twelve pts remain in CR1 and 2 in CR2.

Conclusion: Expression of CD34 supports transformation taking place on early precursors, its absence in UAL should orientate the evaluation for DCL. Thirteen patients showed unfavorable karyotypes involving genes related to lineage determination. Clinical significance, treatment strategies and differences between pediatric and adult patients have not yet been established for these usual cases. Considering the low incidence of these ambiguous phenotypes, homogeneous multicenter reports should help clarify these issues.

PB006

TARGETED IMMUNOTHERAPY WITH GEMTUCUMOZ OZOGAMICIN DURING CONDITIONING AND POST ALLOGENEIC STEM CELL TRANSPLANTATION IN CHILDREN AND ADOLESCENTS WITH POOR AND AVERAGE RISK AML/MDS

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Background: The prognosis for average risk (CR1 and CR2) and poor risk childhood AML is approximately 20–60% 2-year EFS and 10–20% 2-year EFS, respectively; new therapies are desperately needed. The majority of children and adolescents with AML express CD33. Gemtuzumab Ozogamicin (GO) is an immunotoxin targeted to CD33, has been associated with 30% OR in refractory childhood AML (Sievers et al, JCO, 2001).

Objective: We determined safety and efficacy of GO added to myeloablative conditioning (MAC) and post reduced intensity conditioning (RIC) allologeneic stem cell transplant (AlloSCT) in poor and average risk childhood AML, respectively.

Method: GO was administered on day -14 (3, 4.5, 6.0, and 7.5 mg/m²) with Busulfan (days 7 to 4; 3.2–4.0 mg/m²) and cyclophosphamide (days −3 and −2; 60 mg/m²) followed by AlloSCT (Study A) or following RIC AlloSCT (Fludarabine 30 mg/m²/d x2 and busulfan 3.2–4.0 mg/m² x2) pre AlloSCT for 2 doses wks apart (4.5, 7.5, 7.5 and 9 mg/m²) (Study B).

Results: Study A: 12 poor risk AML (8 IF, 3 Relapse, 1 CR3), median age 3.0 yrs, f/u 1379d, 9/12 UCB, 3 pts at each GO dose level. There were no DLTs related to GO, day +100 TRM 0%, day 30, 60, 180 donor chimerism was 99%, and 5 yr OS was 50%. Study B: 17 average risk AML (10 CR1, 4 CR2, 3 MDS), median age 13 yrs; 5u 812d, 11 related/6 unrelated donors, dose level 1: N = 3, N = 3; 2: N = 3, N = 3; 3: N = 3, N = 2. There were 3 DLTs related to GO, 1 yr donor chimerism was 97% and 1 yr OS 84%.

Conclusion: GO is well tolerated in MAC and following RIC and AlloSCT in the setting of yr donor chimerism was 97% and 1 yr OS 84%.

PB007

PROGNOSTIC SIGNIFICANCE OF ADDITIONAL CYTOGENETIC ABERRATIONS IN 733 DE NOVO PEDIATRIC AML(2Q31-32/MLL-REARRANGED AML PATIENTS: RESULTS OF AN INTERNATIONAL STUDY

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PB008

VALUE OF ROUTINE BONE MARROW EXAMINATION IN PEDIATRIC ACUTE MYELOID LEUKEMIA (AML): A STUDY OF THE DUTCH CHILDHOOD ONCOLOGY GROUP (DCOG)

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Purpose: The outcome of pediatric AML is still disappointing, due to relatively high treatment related mortality and relapse rates (30–40%). Past treatment protocols have called for more screening using bone marrow aspirate (BMA) achieving first Complete Remission (CR1) to detect relapse at an early stage. However, evidence for this policy is lacking in non- FAB type M3 AML patients. We therefore retrospectively studied the clinical relevance of routine BMA in an unselected cohort of all pediatric AML patients in the Netherlands.

Method: Patients were included when they were treated according to DCOG treatment protocols and had achieved CR1 and were excluded when previously diagnosed with Myelodysplastic Syndrome (MDS). Data were analyzed using Chi-square test.

Results: Of 480 patients, data in 349 patients could be included, of whom 148 suffered BM relapse. A total of 1790 BMA had been performed, 1648 (92%) routinely and 142 (8%) on indication when a relapse was suspected. Forty routine BMA showed a BM-relapse (2% of all routine BMAs), while as many as 108 (76%) suspected relapses were confirmed by BMA on indication (P<0.0001). Forty-one routine BMA and only 1.3 BMA on indication, respectively, have to be performed to detect 1 BM-relapse. The sensitivity and specificity of early detection of relapse through abnormalities in clinical examination and blood counts is 73% and 98% respectively; positive predictive value (PPV) is 76%, negative predictive value (NPV) is 98%.

Conclusion: Routine BMA after CR1 did not significantly attribute to early detection of relapsed AML. These results suggest that BMA after achievement of CR1 should only be performed on indication or in the setting of clinical research. We aim to confirm these findings prospectively.
Purpose: We previously showed that outcome of pediatric 11q23/MLL-rearranged AML depends on the translocation partner (TP). In this multicenter international study on 733 children with 11q23/MLL-rearranged AML, we further analyzed which additional cytogenetic aberrations (ACA) had prognostic significance.

Method: Clinical data and karyotypes from 733 11q23/MLL-rearranged patients were collected from 11 collaborative study groups. Karyotypes were centrally reviewed. The 2 or Fisher’s exact test was used to compare differences in proportions of variables among groups. Survival of patients with specific aberrations was analyzed using the Kaplan-Meier method and Gray’s test for competing risks. Multivariate analyses were performed with the Cox proportional hazards model.

Results: ACAs occurred in 344/733 (47%) and were associated with unfavorable outcome (5-year overall survival (OS) 47% vs. 62%; P < 0.001). Trisomy 8, the most frequent specific ACA (n = 130344, 38%), independently predicted favorable outcome within the ACAs group (OS 61% vs. 39%; P = 0.003; Cox model for OS Hazard Ratio (HR) 0.54, P < 0.03), based on reduced relapse rate (26% vs. 49%; P < 0.001). Trisomy 19 (n = 37344, 11%) independently predicted poor prognosis in ACAs cases, which was partly caused by refractory disease (remission rate 74% vs. 89%; P = 0.04; OS 24% vs. 50%; P < 0.001; HR 1.77, P = 0.01). Structural ACAs had independent adverse prognostic value for event free survival (EFS) (HR 1.36, P < 0.001). Complex karyotype, defined as ≥3 abnormalities, was present in 26% (n = 192733), and showed worse outcome than those without complex karyotype (OS 45% vs. 59%; P = 0.003) in univariate analysis only.

Conclusion: In conclusion, like TP, specific ACAs have independent prognostic significance in pediatric 11q23/MLL-rearranged AML, and the mechanism underlying these prognostic differences should be studied.

PB008

CLINICAL AND PROGNOSTIC SIGNIFICANCE OF INV(16) AND EOSINOPHILIA IN PEDIATRIC ACUTE MYELOMONOCYTIC LEUKEMIA - A REPORT OF THE DUTCH CHILDHOOD ONCOLOGY GROUP

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Purpose: The cytogenetic aberrations inv(16)(p13.1q22) and t(16;16)(p13.1q22), usually associated with favorable outcome in childhood AML, were further analyzed which additional cytogenetic aberrations (ACA) had prognostic significance.

Method: ACAs occurred in 344/733 (47%) and were associated with unfavorable outcome (5-year overall survival (OS) 47% vs. 62%; P < 0.001). Trisomy 8, the most frequent specific ACA (n = 130344, 38%), independently predicted favorable outcome within the ACAs group (OS 61% vs. 39%; P = 0.003; Cox model for OS Hazard Ratio (HR) 0.54, P < 0.03), based on reduced relapse rate (26% vs. 49%; P < 0.001). Trisomy 19 (n = 37344, 11%) independently predicted poor prognosis in ACAs cases, which was partly caused by refractory disease (remission rate 74% vs. 89%; P = 0.04; OS 24% vs. 50%; P < 0.001; HR 1.77, P = 0.01). Structural ACAs had independent adverse prognostic value for event free survival (EFS) (HR 1.36, P < 0.001). Complex karyotype, defined as ≥3 abnormalities, was present in 26% (n = 192733), and showed worse outcome than those without complex karyotype (OS 45% vs. 59%; P = 0.003) in univariate analysis only.

Conclusion: In conclusion, like TP, specific ACAs have independent prognostic significance in pediatric 11q23/MLL-rearranged AML, and the mechanism underlying these prognostic differences should be studied.

PB010

ACUTE MEGAKARYOBLASTIC LEUKEMIA IN CHILDHOOD: 15-YEAR EXPERIENCE IN A SINGLE GREEK INSTITUTION

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Purpose: To analyze the clinical and demographic characteristics of children with Acute Megakaryoblastic Leukemia (AMLK) treated in a single centre in Athens, Greece over the last 15 years.

Method: Data was collected by a retrospective review of the records of all 47 patients treated to our unit from 1995 until February of 2010, 8 of whom had AMKL.

Results: The male:female ratio was 5:3. The median age at diagnosis was 12.58 months (1.53–20.63) and the median time from symptom onset to diagnosis 43.5 days (3–318). The median leukocyte count at diagnosis was 16500/μL (4000–83700). At diagnosis, 2 children had moderate hepatosplenomegally and 2 only hepatomegally, 3 infants had subcutaneous nodules, while 3 had CNS involvement, 1 among them with brain chloromas. None of the children had Down syndrome. Seven infants had rare chromosomal abnormalities and 1 MLL rearrangement, but none had the classical for AMKL translocation t(1;22). All children were treated with BFM AML protocols and they were all considered high risk. Five children achieved remission after the 1st course of chemotherapy, 2 after 2 courses and 1 after 3. Six children died in a median time of 9.06 months (5.16–35.76) from diagnosis, 5 from disease progression during treatment and 1 from bone marrow transplant toxicity. The other 2 are alive in 1st remission after allogeneic bone marrow transplant, 14 and 45 months from diagnosis, respectively.

Conclusion: AMKL is a rare AML subtype, which usually affects younger children, even infants who present with leukocytosis and extramedullary disease, like CNS involvement and chloromas. It has a poor overall prognosis, if treated with intensive chemotherapy alone, with early disease progression, which results to death.

PB011

ACUTE MYELOID LEUKEMIA: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS FROM A SINGLE GREEK INSTITUTE

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Purpose: To study the demographic and clinical characteristics of children with Acute Myeloid Leukemia (AML) treated in a single centre in Athens, Greece over the last 15 years.
Method: Data was retrospectively collected by the clinical records of all 48 patients treated to our unit from January 1993 until February 2010. After exclusion of 5 children with secondary AML and 1 child with MDS, 42 children were included in our study.

Results: The male:female ratio was 20/22, while the median age at diagnosis was 5.96 years (0.25–14.90). Regarding FAB classification, 5 children had M0, 6 M2, 3 M3, 12 M4, 8 M5 and 8 M7. The median leukocyte count at diagnosis was 2055/3 (500–4000000). CNS involvement was seen in 4 children. Molecular findings were normal cytogenotype in 5 children, t(8;21) in 2, inversion 16 in 3, t(15;17) in 3, MLL rearrangement in 3, 20 had complex cytogenetics and in 6 children, analysis failed. All children were treated with BFM AML protocols. Totally, OS was 55% and EFS 47.5%, while 30 children were classified as high risk, with 5 having OS < 33.3% (p = 0.011). Twenty-seven children achieved remission after the 1st course of chemotherapy, 11 after 2 or more courses, 2 never achieved remission and 2 died before starting chemotherapy. There was a correlation between courses to remission and OS (p = 0.036). The OS was 41.14% for children below 24 months and 65.22% for older (p = 0.054). The best OS was noticed in M3 (100%) and M4 (72.7%). Regarding BMT, 6 children had an allo-BMT in 1st remission and OS was 66.67% and in 2nd remission with OS 50%.

Conclusion: The M4, M5 and M7 forms are the most common in our population. Children with high-risk disease and slow response to treatment have a worse prognosis.

PB014

OUTCOME OF JUVENILE MYELOMONOCYTIC LEUKEMIA: A DEVELOPING COUNTRY EXPERIENCE

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Purpose: Juvenile myelomonocytic Leukemia (JMLL) is a rare, myelodysplastic-myeloproliferative disease usually presenting in early childhood. JMLL is difficult to distinguish from other myeloproliferative syndromes such as chronic myeloid Leukemia because of the similarities in their clinical and bone marrow findings. We describe a series of 6 patients with JMLL, who had almost similar clinical and laboratory findings.

Method: Records of children presenting with Leukemia from Sep 2006 to Feb 2011 were retrospectively reviewed to analyze the presenting features and treatment outcome of JMLL.

Results: Out of 287 cases of Leukemia diagnosed during the study period, 6 had JMLL. Male to female ratio was 1:1. Median age of presentation was 10 months (range: 2–96). All patients had fever, abdormal distension and massive hepatosplenomegaly. Two had bleeding and 1 lymphadenopathy. Median hemoglobin, TLC platelet count were 7.5 g/dl (range: 5.5–12.2), 305500/mm3 (45700–103000) and 375000/mm3 (15000–66000) respectively. Median of immature granulocyte counts, absolute monocyte count and blast in peripheral smear were 11.5% (range: 5–35), 12586/mm3 (3656–18612) and 5.5% (4–10) respectively. Serum immunoglobulins were raised in 4. Monosomy 7 was present in 1 case and HbF was increased in 3. BCR-ABL was negative in all. Two patients were lost to follow up, one child died due to tumor lysis after receiving one dose of cytarabine. One with Down’s syndrome was simply observed and recovered spontaneously. Two patients were given daily hydroxyurea (50 mg/m2) and in partial remission with a median follow up of 10 months. Their TCL hyperplassemogamy and requirement of blood components decreased. None of the patient reached curative stem cell transplant due to economic constraints.

Conclusion: JMLL has peculiar biologic features and poor prognosis. Most patients do not reach transplant in the developing world due to either economic constraints or death. Though no standard chemotherapy guidelines are present for JMLL, hydroxyurea had valuable role to improve survival.

PB015

IS THERE A ROLE FOR A NOVEL MAINTENANCE THERAPY IN PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKEMIA?

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Purpose: This is a retrospective analysis of pediatric AML patients (non-APL) who received a novel maintenance therapy (MT). The aim was to see if MT helped in decreasing the relapse rate (RR) and improve survival.

Method: 87 children received curative therapy between 2004 & 2009. Induction was mainly Inj. cytarabine 100 mg/m2 CI day 1–7 along with Inj. daunorubicin 60 mg/m2 days 1–3. BM aspiration was done on day 10 & those with blasts > 5% received Inj. Cytarabine 8 mg/m2. This was followed by 2 to 3 consolidations with Inj. Cytarabine 3 mg/m2 q 12 hourly days 1, 3, 5. All transplant ineligible patients received MT consisting of 6 cycles of oral 6-TPG 60 mg/m2 & etoposide (50 mg/m2) days 1 to 20 given 28 days.

Results: The median age was 11 yrs; median WBC was 14.6 X 109/L (range 0.15 to 203 X 109/L); 4 patients had M0, 6 M1, 46 M2, 7 M3, 14 M7 and 5 other, FAB subtypes. Predictors: not done 17.3%; good risk 39.9%; intermediate risk 42.2% & poor risk 3.5%. Of 87, 9 died during induction; 2 had refractory disease; & 4 died during consolidation. Of 70 who reached transplant in the developing world due to either economic constraints or death. Though no standard chemotherapy guidelines are present for JMLL, hydroxyurea had valuable role to improve survival.

PB013

COOPERATIVE GENE EXPRESSION OF FLT3, BAALC, EVI1, FHIT, MN1, ERG IN PEDIATRIC MLL REARRANGED ACUTE MYELOID LEUKEMIA

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Purpose: We measure the mRNA expression levels of FLT3, BAALC, EVI1, FHIT, MN1, ERG genes in patients with MLL rearranged AML and compare the expression levels of these genes with normal controls.

Method: From October 1996 to October 2009, bone marrow samples from 31 newly diagnosed MLL AML were studied. MLL was screened by Southern blot analysis or FISH and identified by RT-PCR assay. KQ-PCR assay with TaqMan probe was performed to measure the expression levels of FLT3, BAALC, EVI1, FHIT, MN1, 3 ERG genes in MLL AML as well as normal controls. The expression of these genes in normal controls was calculated as the copy number of each gene normalized to the copy number of ABL control gene. Statistical assessments: Mann-Whitney test was used to compare the expression levels of target genes and controls. A statistically significant difference was classified with a P value < 0.05.

Results: The most frequent FAB subtype was M5A (in 15 patients) followed by M4 (4), M0 (3), M3 (2), M7 (3), M5b (2), and M6 (1). The MLL gene were t(1;11) (11 cases), t(4;11) (2), t(6;11) (3), t(9;11) (10), t(10;11) (5), t(11;19) (4), MLL-PTD (4), and the other 3 cant be specified. The median expression levels of mRNA for FLT3, BAALC, EVI1, FHIT, MN1, ERG genes in MLL AML patients are 4.7, 0.1, 8.7, 0.2, 0.1, and 0.6 respectively. For normal controls, the median expression levels of target genes are 0.6, 0.2, 199.2, 0.5, 0.1, and 1.2 respectively. MLL AML patients had significantly higher expression level of FLT3 (P < 0.001) and lower levels of EVI1 (P = 0.008) and ERG (P = 0.032) compared to normal controls.

Conclusion: Our study revealed MLL AML was associated with overexpression of FLT3 and lower expression of EVI1 and ERG.
Conclusion: The novel MT used appears to decrease the RR & improve outcome in spite of not transplanting any patient. Our RR of 23.7% compares favorably to our previously reported RR of 43.9% and to that of the AML-BFM08 (RR 33.9%) & MRC-AML12 (RR 35%) trials. Since 66.6% of relapses occurred after completion of MT, increasing the duration of MT to 12 months may help further improve survival.

PB016

HIGH FREQUENCY OF COPY NUMBER VARIATIONS IN MYELOID LEUKEMIA OF DOWN SYNDROME

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Purpose: Myeloid Leukemia of Down syndrome (ML-DS) is a unique disease entity. It is usually characterized by an excess of megakaryoblasts like in acute megakaryocytic Leukemia (AML), and can be preceded by transient myeloproliferative disorder (TMD) in newborns. Both diseases are characterized by mutations in the GATA1-gene.

Method: We studied copy number variations (CNVs) in TMD and ML-DS, with the aim to study whether progression from TMD to ML-DS is associated with clonal evolution, and to detect new abnormalities contributing to pathogenesis. A reference group of non-DS AML, and other pediatric AML-subtypes were used for comparison.

Results: The number of patients with CNVs significantly increased when TMD was compared to ML-DS, and there was a trend for more CNVs per patient, both suggestive of clonal evolution. This mainly concerned (sub) chromosomal amplifications of chromosome 1q and 11, but did not allow the identification of specific oncogenes or tumor suppressors that might be involved in this progression. In addition, we showed that ML-DS had significantly more CNVs than other pediatric AML-subgroups, suggesting that the DS related Leukemias are genetically more unstable. Mutations in telomerase genes were found in 14% of the ML-DS patients, and hence may underlie genomic instability in a minority of ML-DS patients. No mutations were detected in TMD-patients. Moreover, telomere length was not correlated with the frequency of CNVs. Of interest, high frequencies of CNVs were also found in AMKL in non-DS patients, suggesting that genomic instability might be cell lineage dependent rather than just related to trisomy 21.

Conclusion: In conclusion, despite an increase in the frequency of CNVs, suggesting clonal evolution from TMD to ML-DS, other techniques may reveal which genes are involved in the disease progression.

PB017

GENOTYPING AND MINIMAL RESIDUAL DISEASE STUDY IN CHILDREN WITH ACUTE MYELOID LEUKEMIA: PRELIMINARY RESULTS

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Results: From January 2006 to November 2009 genotyping was performed in 105 patients with AML. AML1-ETO fusion gene transcript was found in 18 patients (17.1%). PML-RARA (subtype bcr3) and CBFB-MYH11 gene transcripts were detected in 5 (4.8%) and 4 (3.8%) patients, respectively. Duplication of FLT3 gene was found in 10 (9.5%) cases. Between 91 tested children over expression of WT1 was present in 73 patients (80.2%). Analysis of MRD level in subsequent time points showed significant decrease of number of fusion gene transcript copies and gene WT1 expression.

Conclusion: To establish the rate of molecular marker presence in AML in children and the influence of the presence of MRD on the treatment results as well, the study has to be conducted on a larger group of patients with longer follow-up.

PB018

EXPERIENCE OF A MULTI-INSTITUTIONAL, BFM-BASED PROTOCOL IN BRAZIL FOR ACUTE MYELOID LEUKEMIA

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Purpose: The overall survival of children AML improved favorably reaching 50% to 60% rates in some developing countries. The aim of this abstract is to present preliminary results of the Brazilian Pediatric Oncology Society (SOBOPED) protocol for AML based on the AML-BFM.

Method: All patients diagnosed of AML in different hospitals in Brazil were treated according to this protocol between April 1st 2007 and December 31st 2010.

Results: 73 patients with acute myeloid Leukemia were treated. 34/73 (47%) females and 39/73 (53%) males. Average age, 9 years. M3 15/73 (20%), M2/M3 7/73 (10%) and 27/73 (40%) as low risk. The bone marrow FAB classification was mainly M3 19/73 (26%), M4 15/73 (20%), M7 and M2 9/73 (12%) each. A patient with mainly myeloid biphenotypic Leukemia was treated with this protocol. Polymerase chain reaction (PCR) and caryotype was performed in 66% of the patients. The most common cytogenetic and RT-PCR was t(15;17) (PML/RARα found in 10 patients, t(8;21), AML1/ETO found in 4 patients. The majority (76%) of the patients who did not perform either PCR or caryotype were treated as high risk considering FAB classification. 1/3 (33%) had central nervous system infiltration at diagnosis. 303 chemotherapy cycles were done. The main toxicity was infectious grade II-III. Twenty seven died (36%), being 11 out of sepsis and 9 of disease progression. The early death was 16%, 7 (9.6%) patient relapsed. 44/73 (60%) are still alive and in complete remission. There is a significant difference between children with SR AML (OS 72%) and HR AML (OS 52%).
Conclusion: Due to the risk of complications that AML patients are confronted to, they have to be treated in specialized centers. The clinical support is shown to be extremely important and has helped keeping the mortality rates low. This protocol is feasible to be performed in developing countries like Brazil.

Purpose: A purpose of JAK2 gene has been found in the majority of adult patients with myeloproliferative neoplasms (MPNs). Most of the mutations belong to V617F in the exon 14 or mutations within the exon 12, but few cases with aberrant splicing have been reported. In contrast, mutations of JAK2 have been very rarely reported in pediatric MPNs. We here describe a JAK2 splicing mutational in an infant and a fetus presenting with MPN, cardiac hypertrophy and genitai anomalies.

Method: Cases: The first patient (P1) was born at 36th weeks of pregnancy by a healthy mother, presenting with systemic purpura, hepatosplenomegaly, thrombocytopenia, and a small penis and testes. He was diagnosed as MPN by bone marrow biopsy and cardiac hypertrophy by echocardiogram. He died of liver failure at 7 months. The second patient (P2) was a male fetus carried by the same mother. He suffered cardiac arrest and was stillborn at the 29th weeks of gestation. Autopsy revealed his cardiac hypertrophy, hepatosplenomegaly and hypogonadism. The bone marrow showed hyperplasia of myeloid cells and dysplasia in erythroblasts.

Results: Genetic Analysis: RNA was extracted from the blood cells of P1, as well as from various organs of P2 obtained by autopsy, and subjected to reverse-transcribed polymerase chain reaction (RT-PCR) and direct sequencing. RT-PCR of JAK2 gene revealed a major band (357 bps) and a minor band (270 bps) in all samples. Direct sequencing of the major band showed a normal JAK2 sequence, while the sequencing of the minor band revealed an in-frame deletion of the exons 15 and 16 (total of 267 bps) of the JAK2 gene.

Conclusion: Two siblings with the similar phenotype and the same mutation implication that the splicing mutation of JAK2 might be associated with the abnormalities of hematopoietic, cardiac and genital systems in these patients.

Purpose: Alterations within FLT3, KRAS, NRAS and PTPN11 genes may disrupt Ras/MAPKinase leading to acute Leukemia. Previous studies demonstrated that they occur in a mutually exclusive manner. To address this question we performed a molecular screening to identify FLT3, KRAS, NRAS and PTPN11 mutations in a large cohort of childhood Leukemia.

Method: Between January 2005 and December 2010, samples from 481 children (younger than 18 years) with ALL or AML were available for study. Thirty-six children were younger than 12 months-old (PCR (FLT3 internal tandem duplication), PCR-RFLP (KRAS and FLT3-D835 point mutations) and direct sequencing (KRAS, PTPN11 exons 3 and unexpected results) were performed. The distribution of FLT3, RAS and PTPN11 mutations by Leukemia subtypes, demographics and child profile was evaluated using Pearson’s Chi-square tests.

Results: There were 241 ALL and 240 AML cases, median age of 5 years-old. Overall the FLT3, KRAS, NRAS and PTPN11 found was 7.9%, 16.7%, 22.2% and 4.8% in ALL, respectively; whereas 28%, 7.7%, 32.6% and 14%, in AML, respectively (p < 0.001). The overlapping occurrence of FLT3 and RAS mutations was found in 15.6% of cases. No concomitant alterations in KRAS or NRAS and PTPN11 were found in all cases analyzed. In one AML case the existence of both alterations in FLT3 and PTPN11 was found. Mutations of genes affecting the Ras/MAPKinase pathway were highly prevalent in AML mainly in cases with myelomonocytic differentiation.
PBG02
KRAS, NRAS AND BRAF MUTATIONS IN EARLY CHILDHOOD LEUKEMIA ASSOCIATED WITH PARENTAL SMOKERS
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Purpose: Deregulation of genes KRAS, NRAS and BRAF have been correlated to childhood Leukemia subtypes. In order to explore the association of KRAS, NRAS and BRAF gene mutations with clinical-demographic features and environmental risk factors we tested a series of children aged < 24 months with Leukemia.

Method: Dataset from an infant Leukemia (IL) study were selected to test whether maternal and child exposure to tobacco could be associated with RAS and BRAF mutations. RFLP assay was used to detect KRAS mutations in codons 12 and 13, and direct sequencing to detect NRAS mutations, codons 12 and 13; BRAF mutations, in exons 11 and 15, were screened by target-specific pyrosequencing (PyroMark Q24).

Case-series comparisons were applied in the statistical analyses. Distribution of RAS mutation by Leukemia subtypes, child-parental demographics was evaluated using Pearson’s chi-square tests. Unconditional logistic regression was performed (OR and 95% CI) with adjustments for birth weight, gender, age, subtype of Leukemia and status of MLL gene rearrangements (MLL2).

Results: A total of 210 samples were analyzed. The median age at diagnosis was 11.5 months with 65 pro-B ALL (31.9%) and 65(31.9%) AMLs; 88 cases presented MLLr. Overall, KRAS mutations were detected in 23.5% (48/204) and NRAS mutations in 17.1% (14/82); BRAF mutations found only in AML. KRAS mutations were found [2 fold higher] in children living at home (father or others) OR 2.27, 95% CI (1.13-4.57). Higher rate of KRAS mutations was found in ALL with MLLr (32.3%) compared to AML (21.7%). Maternal smoking before or during pregnancy was not associated with RAS mutations. However, risk association was found between KRAS mutations and children having relatives’ smokers at home (father or others) OR 2.27, 95% CI (1.13-4.57).

Conclusion: RAS mutations were found in both ALL and AML with MLLr and BRAF mutations found only in AML. KRAS mutations were found [fold higher] in children living with smokers at home.

PBG03
RELAPSE-RISK GROUP PARAMETERS OF NEWLY DIAGNOSED PEDIATRIC ACUTE MYELOID LEUKAEMIA PATIENTS TREATED AT CHILDREN CANCER HOSPITAL IN EGYPT
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Purpose: Over the past few years, our understanding of the pathogenesis of AML has shown that different subgroups of AML require different, risk-adapted treatment strategies. In our study, we aimed at identifying relapse-risk group parameters, especially during periods of clinical remission, and illustrating the most common causes of early and late deaths.

Method: Eighty-three (83) previously untreated patients who presented to the Children Cancer Hospital of Egypt with the diagnosis of AML during the period from July 2007 to December 2008, were included in this retrospective study. All biologic and epidemiologic data of the included patients were collected such as; age, gender, clinical presentation, initial white cell count, as well as some biologic markers that may affect response to therapy, reflecting on remission and survival rates. Patients were followed for a period ranging from 2-18.5 months.

Results: 40 patients (58.82%) were still alive in complete remission, 4 patients (5.88%) were alive but relapsed, 23 patients (13.24%) died in complete remission, and 6 patients (8.82%) died in relapse. Only 3 patients underwent hematopoietic stem cell transplantation and all of them were still alive in CR till study date. Early deaths were seen in 15 patients (18.07%), mainly due to bleeding and leukostasis. Late deaths were seen in 23 patients (27.1%), mainly due to progressive disease, sepsis and fungal chest infections.

Conclusion: Analysis of our study data revealed statistically significant association of MLL rearrangements and complex karyotypes with increased risk of relapse(P=0.017 and 0.007 respectively). On the other hand, it didn’t reveal such association of gender, initial TLC < 100X109/L, initial CSF infiltration with blasts, nor FLT3/ITD positivity with increased risk of relapse. The association of t(8;11) and inv.16 with complete remission status was not of statistical significance, yet it approached statistical significance(P = 0.064). Longer follow up period is needed to comment on survival rates.

PBG04
THE INCIDENCE AND OUTCOME OF SOMATIC WT1 MUTATIONS IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA
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Purpose: The Wilms Tumour 1 (WT1) gene is complex, with many physiological roles. WT1 mutations principally in exon 7 have been reported in childhood acute myeloid Leukaemia. We present a series of 70 children diagnosed and treated for acute myeloid Leukaemia (including bipherontopic/trisomy 21) over a ten year period through the Children’s Cancer Centre in Melbourne, in which we have determined the incidence of WT1 mutations and patient outcomes.

Method: Utilised a rapid mutation screening methods by employing high resolution melting to screen diagnostic bone marrow specimens for the presence of somatic mutations of WT1. Samples were then sequenced to confirm the presence of the mutations. These results have been correlated with clinical outcome data.

Results: WT1 mutations found were predominantly frame-shift mutations due to insertions and deletions. Analysis showed the frequency of WT1 mutations was between five to ten percent, and there was a trend towards a poorer outcome in the presence of a WT1 mutation. Overall five year event free survival was 62% with an overall five year survival of 79% Children with WT1 mutations had a shorter event free survival time, with a median duration to event of 13.5 months, compared to children with wild type WT1 who had a median duration to event of 22 months (t-test analysis, p value = 0.026). Of the children with a WT1 mutation, 50% of (15/30) AMLs had died due to their disease within 24 months of diagnosis, compared to a five year overall survival of 80% in children without a WT1 mutation. FLT3 mutation analysis is currently underway, to be correlated with the presence of WT1 mutations.

Conclusion: In summary our preliminary analysis suggests that WT1 mutations are infrequent and confer a poor diagnostic marker in children with acute myeloid Leukaemia, and support the findings of cohort studies overseas.

PC001
PEDIATRIC MATURE B-CELL LYMPHOMA: A RETROSPECTIVE 10-YEAR EXPERIENCE WITH HETEROGENEOUS PROTOCOLS FROM A TERTIARY CARE HOSPITAL IN SERBIA
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Purpose: Intensive chemotherapy protocols in pediatric mature B-cell lymphoma resulted in survival attaining 90%. The results are inferior in less privileged countries. There are no reports of comprehensive data analysis in pediatric mature B-cell lymphoma in Serbia.

Method: A retrospective study was carried out at University Children’s Hospital, Belgrade in children aged less than 18 years diagnosed with mature B-cell lymphoma from 2001 to 2011.

Results: Analysis included 31 children with Burkitt lymphoma (BL), five with diffuse large B-cell lymphoma (DLBCL) and two patients with Burkitt-like lymphoma (BLL). Average age at diagnosis was 9.7 years with male to female ratio 2.35:1. The distribution of stages was 7, 7, 18 and 6 patients with stages I, II, III and IV, respectively. Seven children were stratified to therapy group R1, 17 to R2, 11 to R3 and 13 to R4. One patient had CNS disease and 6 had bone marrow infiltration. Tumor lysis syndrome was successfully managed in all patients by usual procedures. One patient required hemodialization. Children were treated according to NBL, BFM 95 and B-NHL, BFM 04 protocols. 36 children achieved complete remission, one partial remission, and one died of sepsis. A child with biopsy proven residual BL at the primary site was treated with high-dose chemotherapy and autologous bone marrow rescue. This patient is in complete remission 5 years since diagnosis. Two patients had relapsed at primary site two and three months after the end of treatment, respectively. First patient is receiving secondary chemotherapy and another died after relapse. With average follow-up of 61.4 months five-year pEFS was 91.5%. Overall survival was 94.7%.

Conclusion: Further improvement in survival for children with mature B-cell lymphoma in Serbia is needed. There are no reports of comprehensive data analysis in pediatric mature B-cell lymphoma in Serbia. Further improvement in survival for children with mature B-cell lymphoma in Serbia is needed.
T-LBL and their use as potential therapeutic targets warrant further investigation.

**Purpose:** Investigation of Notch 1 and NF-E2 has focused primarily on acute Leukemia and less on lymphoblastic lymphoma (LBL). In this study we investigated the expression of Notch 1 and NF-E2 in LBL and analyzed their relationship to clinical characteristics, treatment results, and survival.

**Methods:** We employed immunohistochemistry to detect expression of Notch 1 and NF-E2 in LBL and analyzed their relationship to clinical characteristics, treatment results, and survival.

**Results:** From October 2000 to August 2008, 34 untreated patients with LBL were enrolled in the study. Median age was 11.8 years (range, 1–25 years). Twenty-six patients were diagnosed with T-LBL and eight patients with B-LBL. Most patients received chemotherapy consisting of modified LBL-BFM-90. Notch 1 was expressed in 73.5% of cases, including 65.4% of T-LBL and 60% of B-LBL (p = 0.015). High expression of Notch 1 was associated with advanced stage but did not relate to the response to chemotherapy in T-LBL. The 5-year overall survival rate was 93.8 ± 6.1% in the high expression group and 80.1 ± 15.8% in the low expression group (p = 0.256). NF-E2 in LBL was expressed in 79.4% of cases, with no difference between T-LBL and B-LBL. NF-E2 expression was higher in T-LBL patients with bulky disease, mediastinal invasion, and high serum lactate dehydrogenase (LDH). NF-E2 expression did not correlate with response to chemotherapy or 5-year overall survival in T-LBL. Expression of Notch 1 and NF-E2 were highly correlated (p = 0.018) in T-LBL but had no significant relationship in B-LBL (p = 0.149).

**Conclusion:** Results showed that Notch 1 was highly expressed in T-LBL and weakly expressed in B-LBL. NF-E2 was highly expressed in LBL with no difference between T-LBL and B-LBL. Notch 1 and NF-E2 may play an important role in the development of T-LBL and their use as potential therapeutic targets warrant further investigation.

**References:**

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**Purpose:** In High income countries, pediatric Hodgkin Lymphoma presents at a median age of 15 years and is rarely seen in children less than 5 years of age. In low income countries there is a sizeable group of patients that present at younger age group. We present the AHOPCA experience with patients younger than 5 years of age.

**Methods:** Low risk (stages IA, IIA, without bulky) were treated with 4 cycles of ABVD with (25 Gy to the involved field if less than a complete remission, or without radiotherapy (CR) after two cycles of ABVD. Intermediate risk (IA and IIA with extranodal extension or bulky mediastinum, IIIA or IB) received 6 cycles of ABVD with early response evaluation after four cycles received 20 Gy if CR and 25 Gys if less than CR. High risk patients were treated with a modified Stanford V and same radiation parameters after 12 week response evaluation. Data was captured prospectively in POND.

**Results:** One hundred biopsy proven patients less than 5 years of age were treated from 8/2004 to 8/2009. Patient characteristics showed male predominance 79%, median age 3 years (range 2–5 years), with nodular sclerosis (45%), mixed cellularity (47%), lymphocyte predominant (7%), and lymphocyte depleted (13%). Most significant toxicities (grade 3) consisted of mild to moderate neutropenia, fever, or mucositis. With a 3 year EFS of 73% (± 4.9%) with abandonment counting as an event and OS of 86% (± 4.3%) these patients did slightly better than older kids with a 3 year EFS of 69% and OS of 85%.

**Conclusion:** Young patients (< 5 years of age), have a very good outcome when treated with a risk adapted response based combined modality approach and tolerable toxicity. These patients appear to be overrepresented in Central America and there histology is shifted towards mixed cellularity.
Purposes: Lymphomas are a late manifestation of Paediatric HIV and usually present in a setting of significant immune depression. There is little literature guidance as to the most optimal therapy in a resource limited setting.

Method: All Non-Hodgkins Lymphomas were reviewed at the Johannesburg Hospital from January 1997 to December 2010. All new patients were routinely tested for HIV. HIV positive patients with NHL diagnosed before 2006 were given palliative treatment only. After 2006 patients were treated with chemotherapy and HAART. These patients were reviewed in detail.

Results: 115 patients with NHL were diagnosed. Of these 58(50%) were diagnosed with Burkitt/Diffuse Large B Cell Lymphoma. 20 of the 58(34.5%) were HIV positive. 11/15 HIV positive patients with NHL were diagnosed. Of these 58(50%) were diagnosed with Burkitt lymphoma. 2006 patients were treated with chemotherapy and HAART. These patients were reviewed in the first line treatment (5F/13M). Clinical stages of disease were II-4, III-10, IV-4 and the risk groups were: low risk-14, intermediate risk-31, high risk-7.

Conclusion: Treatment of HIV positive patients with B cell/Burkitt NHL with a protocol under a lower dose Methotrexate results in good response with acceptable morbidity. HAART may be started as soon as the patient has stabilized without prejudice to outcome.

PC007

RELAPELED ANAPLASTIC LARGE CELL LYMPHOMA (ALCL) IN CHILDREN. A REVIEW OF THE NATIONAL WIDE STUDY.

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Purpose: Risk of relapse and progression of disease in children with anaplastic large cell lymphoma (ALCL) is still very high. We report the clinical characteristics and outcome of patients with relapsed ALCL after use of intensive short-pulse chemotherapy (chth) according to the ALCL99 protocol.

Method: 62/74 patients (pts) with ALCL, staged I-IV were registered in Polish Paediatric Leukaemia/Lymphoma Study Group. 18(29%) developed relapses during or after the first line treatment (5F/35M). Clinical stages of disease were II-4, III-10, IV-4 and the risk groups were standard-7, high-12. Localizations of primary tumour were: lymph nodes/4, lymph nodes and mediastinum/6, others/7. After 1st line of therapy 12 pts achieved CR, 3PR, 3progressed. Relapses were: local/12, multifocal/6. 2 pts relapsed during chth, 12 pts between 1–12 months after the end of the treatment (4are alive in CR, 4died of PD, 4died of toxicity), 6 relapsed after more than 12 months (2 pts had relapse 6 and 7 years after the end of the treatment). Inline chth in relapse were different: ALCL REZ2004; IC+ICI; CVB; ICM+ICI, EINCHL-CC, + VBL. 6 pts relapsed after 2nd CR. 8 pts underwent bone marrow transplantation (BMT) /1x autologous, 8 allo.

Results: 8/18 pts after relapse are alive (44.4%). After 1strelapse 10 pts entered 2ndCR (55.5%), 2 pts in PR (11.1%) and 6 pts suffered from progression (33.3%). After 2nd relapse only 2 pts are alive (both were treated with BVL), 4 pts died. Summarized 8 pts entered 3rd CR. 6 are alive in 2nd CR, 2 in 3rd CR, 5 pts died of progression, 1died of sepsis, and 4 pts died of BVL and other toxicity.

Conclusion: Unfortunately, the total number of relapse for pediatric ALCL is still very high (29%), however around 45% of relapsed patients has chance for next remission of disease. The use of VBL and BMT procedure seems to be promising for relapsed ALCL. The higher survival rates could be achieved by reduction of treatment related toxicity.

PC008

MOBILE PHONE USE IN RURAL CAMEROON FROM 2007 TO 2010: AN INCREASINGLY USEFUL TOOL FOR FOLLOW-UP IN BURKITT LYMPHOMA PATIENTS

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Purpose: To investigate the use of mobile phones (MP) by parents of patients with Burkitt lymphoma (BL) admitted to 2 hospitals in NW Cameroon, as a means of cost-effective follow-up of patients after discharge.

Method: Archived records of 285 patients at Banso and Mbngo Baptist Hospitals were reviewed at the end of December 2010. Ownership of, or access to MPs had been routinely recorded. Guardians of 101 children known to be alive at the last follow-up were called.

Results: Access to MP increased from 33% to 80%, while the number of parents with a personal MP increased annually from 20% in 2007, to 60% in 2010. Successful MP contact was made with 59% of parents, with a similar success rate in MPs owned by other than the parent. Re-charging of MPs proved to be no problem.

Conclusion: MPs are increasingly useful to establish the patient’s status, promote compliance with treatment, and can be expected to minimise abandonment at low cost in rural Cameroon. We plan to issue an MP to parents in future.

PC009

SUBCUTANEOUS PANNICULITIS LIKE T-CELL LYMPHOMA IN A 7-YEAR-OLD GIRL

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Purpose: Subcutaneous panniculitis like T-cell lymphoma (SPTCL) is a rare type of lymphoma of CD3+CD8+ phenotype. The neoplasm is characterized by deep-seated skin nodules or plaques which usually involve the legs and less commonly the trunk. Histopathological investigations revealed the presence of primarily subcutaneous infiltrates of small, medium-sized, or large pleomorphic T cells and macrophages.

Method: We present a case of 7-year-old girl with a three-week history of left buttock tumor, recurrent fever, and weakness. Her physical examination showed the patient’s regular growth and development. Observed infrastructures: hepatomegaly (<5 cm) and splenomegaly (<3 cm) below costal margin and enlargement of left inguinal lymph nodes. In the left buttock muscles a painful and tender tumor was palpable; dimensions: 35 mm ×35 mm ×40 mm. Laboratory test results were as follows: hemoglobin 7.1 g/dl, leucocytes 2.1 g/L, neutrocytes 0.96 G/l, C-protein 77.7 mg/l, lactate dehydrogenase 1436 U/L, D-dimers 346 ng/ml. Moreover, elevated aminotransferases, hypobuminemia and hypomiumoglobinulenia were noted. Blood and urine cultures were negative, cytomegalovirus and Epstein-Barr infections were excluded. CT scans indicated hepatosplenomegaly, peritoneal, pleural, and pericardial exudate. After ineffective antibiotic regimen a tissue biopsy was obtained.

Results: Histopathological diagnosis revealed subcutaneous panniculitis like T-cell lymphoma. Immunophenotypes were as follows CD8 (+), CD 3 (+), Granzyme B (+), CD 56 (+), CD 4 (-), CD 30 (-). The six-week corticosteroid therapy led to temporary improvement, but also resulted in numerous complications such as: hepatotoxic, arterial hypertension, delay of biopsy wound healing, and devastating infections. A specific T-cell lymphomas protocol (EURO-LB 02/ BFM-90) was administrated. It has resulted in further regression of systemic and local symptoms. Currently, the girl is in complete remission during maintenance therapy.
PC010

CLINICAL CHARACTERISTICS AND OUTCOME OF NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA IN CHILDREN - A SINGLE CENTRE EXPERIENCE

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Purpose: Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL) is a distinct subtype of Hodgkin Lymphoma (HL). The optimal treatment strategy in children is unknown. Most studies report excellent event-free survival, with overall survival rates approaching 100%. We provide a retrospective analysis of the clinical characteristics and outcome of 18 pediatric NLPHL patients from our center.

Method: A retrospective analysis was performed on patients 0–15 years of age with NLPHL presenting to Tata Memorial Hospital, Mumbai, between January 2001 to April 2010. The diagnosis was confirmed by expert pathologists based on histology and staining criteria.

Results: Out of 650 HL patients, 21 (3.2%) had NLPHL. 20 were males and 1 female. The median age was 9 years (range 6–14 years). 3/3 patients had early stage disease (3 stage I, 4 stage II), of which one had full disease. All received 4–6 cycles ABVD. 11 patients had advanced stage disease (10 stage III, 1 stage IV), of whom three presented with B symptoms and one had full disease. 10/11 received 4–6 cycles ABVD and 1 received MINE (Mioxantone, Etoposide, IFRT, Prednisone). Two patients in each group also received additional IFRT. CR rates were 71% and 63% respectively in early/advanced stages. Six patients (33.3%) either relapsed/progressed—1 each with stage I and stage II and 4 with stage III. All had received ABVD upfront and one each in stages II and III had received additional IFRT. 4/6 who completed salvage chemotherapy (1 with MINE, 2 with rituximab plus MINE and 1 with GDP (Gemcitabine, Cisplatin, Prednisone)) were in CR (follow up 3–13 months). One patient is currently completing salvage chemotherapy. One patient progressed to T-cell rich B-cell lymphoma and is lost to follow up. With a median of follow up of 22 months (3–128 months), EFS was 66.7% and OS 94.4%.

Conclusion: Pediatric NLPHL treated with ABVD chemotherapy was observed to have a high incidence of relapse/progression. 4/4 of relapsed patients in our cohort achieved remission after salvage chemotherapy. However, a longer follow up is required.

PC011

SPORADIC ORBITAL BURKETT LYMPHOMA IN A NEWBORN: CASE REPORT

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Purpose: Case report

Method: Patients record review

Results: We report the case of a male newborn who presented with right eye swelling at birth. Examination revealed right exophthalmia with compromised eye closure and preserved eye movements. No other systemic manifestations of disease were found. The emergency laboratory workup was as follows: WBC 9.7 x 10^9/l, Hb 10.7 g/dL, PI 153 x 10^3/l, LDH 1032 U/L, normal hepatic and renal function. An MRI revealed a right retroocular solid mass. The child underwent surgery and the tumor had a complete excision but only 5 days later the mass recurred. The histopathology examination was Non Hodgkin Lymphoma immuno positive for CD45, CD10, CD19, CD20, CD22, Lambda +, Kappa -. but only 5 days later the mass recurred. The histopathology examination was Non Hodgkin lymphoma, retro ocular solid mass. The child underwent surgery and the tumor had a complete excision.

Conclusion: Pediatric NLPHL patients did not match any known EBV latency pattern. EBV presence did not alter tumor microenvironment Treg population in our series. Further analysis will be needed to confirm the trend to worse 5y EFS in EBV+ patients.

PC012

EPSTEIN BARR VIRUS (EBV) EXPRESSION AND LATENCY PATTERN IN PEDIATRIC DIFFUSE LARGE B CELL LYMPHOMA (DLBCL). ITS EFFECT ON TREG CELLS MICROENVIRONMENT

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Purpose: EBV incidence in adult DLBCL ranges from 5% to 15%, mostly associated with patients older than 50 years. In 2008 the WHO classification included EBV-positive DLBCL of the elderly, in patients < 50 years which displayed type II or III EBV-latency patterns. Data on pediatric DLBCL patients are quite limited. An increased number of Treg cells were described in EBV+ Hodgkin lymphoma, but this scenario is not described in DLBCL. Aims: To study EBV association and latency pattern in pediatric DLBCL, and to characterize EBV effects on microenvironment Treg population.

Method: We analyzed 25 DLBCL pediatric patients (5 immunocompromised, age 2-16 yrs (median: 7 yrs), male:female ratio 12:13. EBV expression was evaluated by EBERs in situ hybridization, and LMPI, LMP2a, FoxP3 and CD3 expression was assessed by immunohistochemistry in formalin fixed paraffin embedded lymph node biopsies. FoxP3 was expressed in (FoxP3+ cells/field) (n CD3 cells/field) = 100.

Results: Ten out of 25 cases (40%) were EBERs positive, 6/20 (30%) immunocompetent and 4/5 (80%) immunocompromised. Latency pattern was EBV+, LMPI+, LMP2a in 4/5 (80%) cases and EBV+, LMPI+, LMP2a in 6/10 (60%) cases, 4/5 (80%) patients were immunocompromised. EBV expression was not statistically associated with CD3 and FoxP3 markers (p = 0.1107 and p = 0.8492 respectively). In Kaplan Meier survival analysis, 5 yrs event-free survival (5y EFS) in EBV+ cases was 42%, versus 79% in EBV- cases, but this difference was not statistically significant (p = 0.4311).

Conclusion: EBV association in our series was higher than that for adult < 50 years. Most immunocompetent patients displayed EBV latency pattern type I, while immunocompromised patients showed mainly LMPI expression without LMPI2A. These last patients did not match any known EBV latency pattern. EBV presence did not alter tumor microenvironment Treg population in our series. Further analysis will be needed to confirm the trend to worse 5y EFS in EBV+ patients.

PC013

A RISK ADAPTED, RESPONSE- BASED THERAPEUTIC REGIMEN USING OEPAC/COPDAC FOR THE TREATMENT OF CHILDREN WITH HIGH RISK HODGKIN LYMPHOMA; FROM THE CENTRAL AMERICAN Y DOMINICAN REPUBLIC GROUP

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Purpose: Childhood Hodgkin lymphoma (HL) is highly curable in high income countries. Our previous protocol with a modified Stanford V achieved an event- and overall-survival of 50% and 60% respectively. Here we present the follow up study for high risk patients using OE*PA/COPDAC.

Method: Patients received 2 cycles of OE*PA (vincristine, etoposide, prednisone, and doxorubicin) and 4 cycles of COPDAC (cyclophosphamide, vincristine, prednisone, and dacarbazine) followed by involved field radiotherapy (IFRT). IFRT dose depended on the response after 2 cycles of OEPA: 20 Gys if in complete remission or 25 Gys if no complete remission. All stage IIB, IIB, and IV patients with histologically proven HL diagnosed between June 2009 and December 2010 were eligible. All data was entered prospectively into an electronic data base (POND).

Results: All 64 eligible patients were evaluable. Characteristics of the cohort showed male predominance (79%), median age 10 years (2–19 years), nodular sclerosis (60%), mixed cellularity (35%), and lymphocyte predominant (5%) histology. With a median follow up of 7 months we had 3 (5%) abandoned therapies and one relapse. Five (8%) patients have died, four of them from toxicity of therapy at the introduction of the regimen to the group.

Conclusion: The OEPA/COPDAC regimen is well tolerated with acceptable toxicity. Initial elevated mortality improved once the oncologists became better acquainted with the regimen.
We expect a better survival with this regimen compared to our previous trials, however longer follow up is needed.

PC014

LIFE THREATENING CONDITIONS AND EARLY MORTALITY IN PATIENTS WITH NON-HODGKINS LYMPHOMA AND T CELL LEUKAEMIA

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Purpose: To assess the presenting clinical features, the life threatening conditions and early mortality of non-Hodgkins lymphoma (NHL) and T cell Leukaemia (T-ALL).

Method: Retrospective chart review of the presenting clinical features and mortality within the first month of diagnosis.

Results: From 1995 to 2010, there were 52 patients with NHL (n = 33) and T-ALL (n = 19). The median age was 8.73 years of age (1.7 to 17.9). Male to female ratio was 3.7:1. The presenting clinical features were enlarged lymph nodes (n = 21), pain (n = 15), respiratory symptoms (n = 12), gastrointestinal symptoms (n = 7), systemic symptoms (n = 19). On radiological imaging, 12 patients had enlarged mediastinal mass. The pathologies were anaplastic large cell lymphoma (n = 6), Burkitt lymphoma (n = 12), T cell lymphoblastic lymphoma (n = 8), peripheral T cell lymphoma (n = 2), diffuse large B cell lymphoma (n = 2), B cell lymphoma (n = 1), B cell lympho-proliferative disease (n = 1), B cell unclassified NHL (n = 1) and T cell acute lymphoblastic Leukaemia (n = 19). Fifteen patients (28.8%) had life-threatening conditions within the first months of diagnosis. These conditions included airway obstruction and respiratory failure (n = 21), shock (n = 1), renal failure (n = 2), sepsis infection (n = 3), hyperuricemia (n = 2), and multiple causes (n = 5). They required intensive care. Four patients required intubation and mechanical ventilation. Two patients were treated with renal dialysis or renal replacement therapy. The patients were treated with chemotherapy protocol for NHL and T-ALL Leukemia. Three patients died within the first month of diagnosis because of airway obstruction and respiratory failure secondary to mediastinal mass compressing on the airway. Eleven patients died after relapse, with progressive disease or other complications after the first month. Thirty eight patients are alive. The event free and overall survivals at first month of diagnosis were 56.6% and 74.4% respectively (median follow up duration: 8.5 years).

Conclusion: Airway obstruction and respiratory failure is the main cause of early mortality in NHL and T-ALL patients.

PC015

CASE REPORT OF THE 10 YEARS BOY WITH RELAPSED AND REFRACTORY ANAPLASTIC LARGE CELL LYMPHOMA, WHO ENTERED COMPLETE REMISSION DURING PALLIATIVE TREATMENT.

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Purpose: It is retrospective analysis of diagnosis, signs and treatment of the 10 years old boy with anaplastic large cell lymphoma(ALCL) resistant to chemotherapy, who unexpectedly achieved complete remission(CR) during palliative treatment.

Method: 10-years boy was primary diagnosed and treated as Hodgkin Disease(HD) according to HD-97 protocol (with 3 alternate courses: B-DOPA-2,MMVP-1) with initial good response. Four months later after central review, the subtype of lymphoma was reclassified to ALCL and the patient received ALCL-99 regimen for high-risk ALCL. This strategy proved to be efficacious.

Results: One month after the end of the intensive chemotherapy we diagnosed early relapse with high fevers, inquinalis and axillaries lymphadenopathy. The second line treatment with dexamethason,etoposide,trofosfamide. After 1 month of this therapy patient improved. One month later we added vinblastine to therapy (6 mg per 1m2/week i.v.) After 6 months the patient entered partial remission(PR) and after 12 months CR. Now he is still alived over 3 years.

Conclusion: Airway obstruction and respiratory failure is the main cause of early mortality of NHL and T-ALL patients.

PD001

BAYESIAN DESIGN OF A EWING SARCOMA TRIAL

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Purpose: Two induction chemotherapy regimens are widely used for Ewing sarcoma (ES): VIDE in Europe; compressed VDC/IE in USA. It is unclear whether one is better than the other with respect to EFS and/or toxicity, so a randomised trial is planned.

Method: Under conventional sample size considerations (p = 0.05; 80% power), 2500 patients would be needed to detect a 5% absolute difference in 3-year EFS. This number is not considered feasible given the rarity of ES, while a larger treatment effect is unlikely. Hence, a Bayesian design is proposed in which the probabilities that EFS with one treatment is better than the other will be given; e.g. that one treatment is simply better than the other, or that it is > 5% better. If the probability that one treatment is > 5% better than the other is low, toxicity will also be considered when deciding which treatment is preferable.

Results: Given that this is a comparison of two standard regimens (not evaluation of a new drug), clinicians were asked how certain they would need to be that one regimen was better than the other, or that there was little difference between them; a figure of 75–80% was agreed. A range of sample size scenarios has been considered: e.g. with an achievable 600 patients (c.150 events), if the observed difference in EFS was 0%, there would a 13% chance that there was a true benefit for one or other treatment of > 5%; if the observed benefit for EFS for one treatment was 5%, there would a 13% chance that the other treatment was actually better. Both these scenarios fit with the clinical requirement to be at least 80% certain that the correct choice is made.

Conclusion: A Bayesian approach to trial design and analysis should be considered in rare diseases where hypothesis-testing is not feasible under conventional assumptions.

PD002

AMBULATORY HIGH-DOSE METHOTREXATE ADMINISTRATION IN PEDIATRIC OSTEOSARCOMA PATIENTS AT A SINGLE INSTITUTION IN ARGENTINA

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Purpose: To evaluate the feasibility and safety of ambulatory high-dose methotrexate (HDMTX) administration with oral hydration, alkalinization and leucovorin rescue, as well as providing a cost evaluation of outpatient administration.

Method: A retrospective analysis of ambulatory HDMTX administration among selected osseosarcoma patients at our institution was performed. HDMTX (12 g/m²) was given intravenously (IV) over 4 hr after 12 hr of ambulatory oral hydration and urine alkalinization. Families and patients were instructed to continue ambulatory oral hydration and alkalinization so as to monitor urine pH and to adjust the bicarbonate ingestion according to our institution’s treatment algorithm until MTX level <0.2 μmol/L. Patients’ clinical status and MTX levels were checked every 24 hr and oral leucovorin dose was adjusted accordingly. A cost evaluation was performed to assess the difference in costs for outpatients versus inpatient administrations.

Results: From April 2007 to December 2010, 447 courses of HD-MTX were administered at our institution, of which 150 (31.4%) were given ambulatory. Of the 149 evaluable ambulatory HDMTX administrations, 91.2% were successfully completed. Main causes of failure of ambulatory administration were oral tolerance (6 cases) and fever (4 cases). Most patients (81%) had a MTX level of < 10μmol/L at 24 hr post-HDMTX and in only one case was > 50μmol/L (50.96 μmol/L). In only another course more than 72 hr until MTX level <0.2 μmol/L was needed. 18.3% of courses were associated with grade III/IV neutropenia, 2.7% with grade III/IV leukopenia and 4.7% with grade III/IV

PhB and BM (PB-2697/104ABL,BM-693/104ABL). During treatment the number of ALK-positive cells systematically decreased and after 1 year of the palliative treatment the results of PCR tests became negative.

Conclusion: This case supports the idea that ALCL relapsed patients have chance for durable remission and it seems that prolonged treatment with some kind of drugs such as vinblastine is promising.
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thrombocytopenia and anemia. About 39% were associated with grade III/IV hepatic toxicity (asymptomatic hypertransaminasemia), 8% with digestive toxicity and none with renal toxicity. Costs were expected to be half of the in-patient care.

Conclusion: Ambulatory HDMTX administration with oral hydration, alkalization and leucovorin rescue is feasible, safe and with lower cost in selected patients in our setting.

PD003 QUALITY OF LIFE (QoL) IN OSTEOSARCOMA: PRELIMINARY RESULTS OF THE INITIAL TREATMENT PERIOD OF EURAMOS-1 (NCT00143030)

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Purpose: Due to treatment intensity, osteosarcoma patients are particularly vulnerable to late unwanted side-effects. This perspective might also influence QoL during initial therapy. EURAMOS-1 is an international randomized controlled trial to improve outcomes in osteosarcoma through four oncology groups (COG, COSS, EOI, and SSO). Concurrent with treatment, QoL is being assessed as a secondary outcome measure in all participating countries.

Method: QoL is assessed 5–7/11 weeks after start of chemotherapy (TI), 10 weeks post surgery, 72 weeks and 142 weeks after diagnosis, respectively. Depending on group practice and patient’s age, the EORTC QLQ-C30 (self-rating) is used for all patients aged >16 y and the PedQOL or PEDQOL is applied for patients aged <16 y (self- and proxy). TI data was used to assess QoL soon after diagnosis, analyzed by age and gender. Based on a subsample the used instruments were checked for comparability.

Results: 1910 patients joined the trial by October 2010; 1602 patients consented to QoL, and of these, 1162 (73%) already submitted a T1 assessment. Age/sex did not differ between respondents/non-respondents. All questionnaires revealed a markedly reduced subjective well-being at T1 as compared to healthy norms. Independent of age, physical functioning was affected in all patients. The <16 y age group and female patients demonstrated the poorer QoL ratings. Role functioning/social functioning were rated worst by patients >16 y, while the pattern of QoL rating was concordant for patients <16 y and their parents with a tendency for better patients’ ratings.

Conclusion: The comparability of the different instruments is satisfying. Negative ratings were observed for physical functioning, mainly in the <16 y age group. However, in patients >16 y role functioning and social functioning are more important for general QoL than the physical component. Needles biopsy showed Melanotic neuroectodermal tumor. The child’s metastatic work-up was negative (PET scan any max 2.1 local). Patient was given NACT following which interdisciplinary excision with EORTC (Extracorporeal Radiation therapy) with reinplantation was done. Post-operative period was uneventful and immobilisation in POP splint was given for 3 months.

Results: Final histopathology showed no tumor necrosis and adjuvant chemotherapy was not given. Follow-up radiographs at 3 months showed evidence of callus formation at proximal osteotomy site and child has started putting weight on affected limb. Patient is still under follow-up.

Conclusion: Surgery is the only treatment modality widely suggested for the management of MNTL in the literature. Management of such tumors in infants is very challenging with limited reconstruction options. Role of chemotherapy in these lesions is still unproven.

PD005 WALKING ABILITY OF PAEDIATRIC PATIENTS AFTER SURGICAL TREATMENT OF A MALIGNANT BONE TUMOR IN THE LOWER LIMB. EFFECT OF FOLLOW-UP DURATION

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Purpose: With continuously improving survival rates after treatment of malignant bone tumors, functional results gain increasingly more interest. With a tumor location in the lower limb patients’ walking ability can be impaired. The aim of the present pilot study was to investigate walking ability after treatment of a malignant bone tumor and to compare three cohorts of patients with comparable surgical procedures but different follow-up.

Method: The three cohorts were investigated with an accelerometer to determine daily step activities in the course of one week. One cohort was monitored longitudinally at 6, 12 and 18 months after surgery (n = 20, age: 14.5 ± 2.5 y). The other two cohorts were measured once, 7.8 years (n = 22; age 34.5 ± 18.4 y) and 20.1 years (n = 10; age: 35.7 ± 7.7 y) after surgery respectively. All patients received chemotherapy according to the appropriate treatment protocol and endoprosthetic replacement of the affected bone.

Results: Patients in the early follow-up improved their walking ability during the observation period. The amount of steps increased from 4702 ± 3684 steps per day 6 months after surgery to 10214 ± 3200 steps after 18 months. This is comparable to the results of the other two groups with 9107 ± 3831 steps and 9184 ± 1236 steps per day respectively. In all patient groups only a short time was spent on a moderate level of intensity and recommendations for 30 active minutes per day were not reached.

Conclusion: The mean amount of walking reached by all three cohorts classified them as being “active” ( > 10000 steps/day). While great improvements are made during the first 18 months, the step activity level reached at this point in time appears to be at a steady state. Data must be considered as preliminary as greater numbers are needed to improve the representability of the cohorts.

PD006 THE IMPACT OF AN INTERVENTION TO INCREASE PHYSICAL ACTIVITY IN PATIENTS WITH A BONE TUMOR

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Purpose: Physical activity (PA) is generally reduced in patients undergoing cancer treatment. In the present study PA of patients with a malignant bone tumor in the lower extremity was objectively assessed during and after treatment. Furthermore, the effect of interventions encouraging patients to be more active during inpatient stays was evaluated.

Method: The study included 31 patients with a malignant bone tumor in the lower limb. For PA assessment a uniaxial accelerometer was used to monitor patient’s step activity. Patients were measured 6 weeks, 3, 6, 12 and 18 months after surgery. Half of the patients were encouraged to participate in regular PA during inpatient stays. The other half served as a control group.

Results: Patients continuously increased their PA from 1328 ± 10000 steps/day 18 months after surgery to 9868 ± 3145 steps 18 months after surgery (p < 0.003). The greatest improvement could be observed after cessation of treatment. Patients without intervention reached between 45.3% and 97% of the intervention group’s physical activity at the different measurements.

Conclusion: In general, patients with a bone tumor in the lower limb showed a considerably reduced level of activity. Exercise interventions apparently had a positive effect on patients’ daily walking activity at home. All patients improved their level of activity after cessation of treatment and differences between groups were less pronounced after cessation of the intervention. A sufficiently high level of activity could help prevent inactivity-induced sequelea, e.g. osteoporosis. Data must be considered as preliminary as not all patients could be measured at all appointments. Future research and bigger patient samples are needed to address more specific questions.
**PD007**

**SURGERY IN EWING SARCOMA PELVIS - ACCEPTABLE OR “OVERKILL”?”**

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**Purpose:** We analyzed oncological outcome of surgically managed Ewing sarcoma pelvis (ESP) to question if such extensive surgeries were justified. We also compared these to results of surgically treated Ewing sarcomas at appendicular sites.

**Method:** Between January 2001 and October 2009 we operated 25 cases of ESP. All patients were non metastatic at presentation. Age ranged from 4 years to 46 years (mean 18 years). All patients received chemotherapy as per hospital protocols. Twelve cases had type I, 4 had type II, 7 had type III, 4 had type IV, 1 each had type III and type IV. Hemipelvic resections. Reconstruction was done as indicated. Radiotherapy was given postoperatively to all patients with involved margins and/or poor necrosis. 16 cases had necrosis > 90%. 9 cases had necrosis < 90%. One of these had positive margins.

**Results:** 21 cases were available for final review. The follow up ranged from 4 months to 124 months (mean 34.5). There were 2 local recurrences. At time of final review 14 patients were alive with no evidence of disease. Seven had died (1 perioperative mortality, 2 chemotherapy complications, and 4 disease progression). 13 of 14 patients with > 90% necrosis and 7 of < 90% necrosis were survivors. Mean follow up duration for survivors was 51 months. 22 patients were independent ambulators at their last review and the mean MSTS functional score was 23 (range 18–29). The 5 year disease free survival was 65% and overall survival was 71%.

**Conclusion:** Though larger numbers and a longer follow up are mandated, our preliminary results suggest that surgical excision in ESP is justified and offers benefits identical to that of lesions at appendicular sites in terms of local control and oncologic outcome.

**PD008**

**GIANT CELL TUMOR OF BONE IN CHILDREN & ADOLESCENTS - A DIAGNOSTIC CHALLENGE**

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**Purpose:** Giant cell tumor (GCT) of bone rarely occurs in skeletal immature patients. There are very few reports regarding the GCT of bone in children and adolescents. Review of literature revealed that the incidence varies between 1.8% and 10.6%. Here we report a series of GCT of bone in immature skeleton. Since the GCT on a core biopsy can mimic some malignant neoplasms that commonly occur in children, therefore, the purpose of the study is to emphasize the need for correct diagnosis and appropriate treatment to the patients.

**Method:** Retrospective review of the records revealed 100 histologically proven cases of GCT were reported between Jan. 2009 and Dec. 2010, 15 cases were below 18 years, youngest was 8 years old. The clinical and radiological data were analysed. Out of the 15 cases 10 were females and 5 were males. Tumour occurred around the knee joint in 5 cases, small tubular bones in 6 cases and around the ankle 3 cases. Four cases were of recurrent GCT and one had multicentric GCT. Radiological diagnosis did not correlate well with histopathologic diagnosis in 5 cases. One case was signed out as Telangiectatic osteosarcoma and one case as nonossifying fibroma on core biopsy. Patient reported as Telangiectatic osteosarcoma had received chemotherapy before the surgical treatment. The biological behaviour of the disease in children resembled GCT in adults.

**Conclusion:** We report an incidence of 15% of GCT in children in Indian population with female preponderance. Since giant cell tumor of bone is believed to occur after the closure of epiphyseal many radiologists and orthopedician do not entertain the diagnosis of GCT in children. We highlight the need for considering the possibility of GCT in children when confronted with a giant cell lesion on core biopsy to avoid erroneous diagnosis and inaccurate treatment.

**PD009**

**LACK OF CENTRALIZATION AND UNDER-RECRUITING OF YOUNG-ADULTS: LESSONS FROM EUROMAS-1/AOST0331 (NCT00134030)**

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**Purpose:** Investigator initiated clinical trials in rare cancers which affect children, adolescents, and young adults require multinational and interdisciplinary collaboration, yet the challenges associated with such trials remain considerable. We used osteosarcoma as an example to describe the context from which patients with rare cancers are currently recruited.

**Method:** Review of interval recruitment rates in EUROMAS-1, a large randomized multinational trial for patients with resectable osteosarcoma aged 0–40 years jointly performed by COG, COSS, EOL and SSG which is expected to complete recruitment 06/11. Analysis of institutional and age-related variables related to recruitment.

**Results:** Between 04/05 and 02/11, 2,130 patients from 328 institutions in 21 countries were registered (North America: 1,042 patients from 170 institutions; Europe: 1,047/149; Australasia: 41/9). The degree of centralization varied considerably between countries, but an average recruitment Y2 patients/center/year was observed for only five counties (DK, H, NL, and N, UK). The top 10 recruiting centers accounted for only 333/2,130 patients (15.6%), and only 3/328 participating institutions (0.1%) averaged > 5 recruited patients per year. When normalized according to SEER incidence data and compared to younger patients, there was moderate under-recruiting of patients aged 15–19 and considerable under-recruiting above age 19.

**Conclusion:** Despite attempts towards increased centralization, osteosarcoma treatment remains dispersed across multiple institutions. In this context, adolescents and particularly young adults are less likely than younger patients to be included into a pediatric ± trial, even if this is open for their age groups. A very considerable fragmentation of care needs to be taken into account when planning, performing and regulating clinical trials in rare cancers. Supported by the European Science Foundation (ESF) under the EUROCORES Program European Clinical Trials (ECT), through contract No. ERA-CTST-2003-98409 of the European Commission, DG Research, FP6.

**PD010**

**LIMB SALVAGE FOR SKELLETAL SARCOMAS**

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**Purpose:** To determine the efficacy of subamputative/surgery/limb salvage procedures in the management of skeletal sarcomas. To evaluate long term function, complications, local relapse and overall advantage of limb salvage.

**Method:** We evaluated the outcomes of 285 patients under the age of 21 who underwent limb salvage over a 30 year period The primary diagnosis in over 260 were high grade sarcomas. These included osteosarcoma or their variant, Ewing sarcoma or metastatic. The median age was 13.3 years and approximately 40% were skeletally immature (< 12 years of age) The primary site was concentrated around the knee 122 distal femur and 45 proximal tibia. A majority (200) underwent endoprosthetic reconstruction with a mobile joint. In over 60 these involved the use of an expandable prosthesis Major complication included superficial infections treated conservatively Deep or refractory infections (26) were treated by removal of hardware and replacement with antibiotic spacer until cultures were negative. Only two patients had to have an amputation. Loosening or metal fracture was noted in 3%.

**Results:** Only two patients had to have an amputation. Loosening or metal fracture was noted in 3%. The 5 year disease free survival was 65% and overall survival was 71%.

**Conclusion:** Though larger numbers and a longer follow up are mandated, our preliminary results suggest that surgical excision in ESP is justified and offers benefits identical to that of lesions at appendicular sites in terms of local control and oncologic outcome.
Purpose: The survival in non-metastatic Ewing sarcoma in our centre was 46% till 2000 with RCT-II protocol. TMH EFT-2001 study aimed at improving EFS in this group by employing intensified continuous multidrug cohort chemotherapy.

Method: Chemotherapy included 2 courses of VE couplet (vincristine; ifosfamide; and etoposide) followed by 2 courses of VAC couplet (vincristine; cyclophosphamide; and doxorubicin) administered every 3 weeks. Treatment of the primary tumor was with surgery and/or radiotherapy followed by 10 courses of alternating VAC and VE couplets; with Actinomycin D substituted for doxorubicin after a total dose of 360 mg/m2. Vincristine was given weekly throughout the chemotherapy pulses.

Results: We analysed 159 patients recruited from June 2001 to December 2009. The median age was 15.2 years (range, 1.0 to 51 years). Males: Females were 2.1:1, age < 15 years 84(53%) and >15 years 75(47%). Serum LDH was elevated (<500) in 37.6% and Serum Albumin was low (<4 g/dl) in 25%. Local therapy was Radiotherapy alone in 19(12.3%), Surgery alone in 88(55.4%) and Surgery + Radiotherapy in 36(23.1%). A median follow up of 6 months the EFS and OS of the whole group (n=159) are 59.7% and 60.6% respectively. Of the 159 patients, 11(6.9%) relapsed locally only, 4(2.5%) had local and distant relapse and 2(1.3%) had distant metastases only. Patients with age < 15 yrs fared significantly better (EFS 69% vs 48%, p = 0.003) on univariate analysis. No statistical significance was found for male(60% vs 57%; p = 0.611), high serum LDH>48% vs 63% (p = 0.972), low serum albumin<52% vs 60% (p = 0.988),100% necrosis post induction (63% vs 49% p = 0.425), modality of local therapy(post-therapy MTV and TLG) and rMTV and rTLG at SUV cut-offs of 2 and 2.5 g/mL between responders and non-responders and 5% vs 7% showed significant difference. The sensitivity, specificity, positive predictive value, and negative predictive value of post-therapy mSUV (cut-off, 3.2 g/mL), rMTV (cut-off, 0.015), and rTLG (cut-off, 0.015) at SUV cut-off of 2.5 g/mL were 100%, 88.9%, 83.3% and 100% in all, respectively.

Conclusion: The post-therapy rate of 60.6% is significantly improved compared with the 46% survival rate achieved in RCT-II. This is probably caused by use of dose intensified chemotherapy given in a coupled fashion that incorporated high doses of ifosfamide and continuous weekly vincristine between the chemotherapy pulses.

PD013

RETROSPECTIVE ANALYSIS OF TREATMENT-RELATED TOXICITIES IN EWEING SARCOMA PATIENTS RECEIVING RADIOTHERAPY IN COMBINATION WITH OR WITHOUT ACTINOMYCIND

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Purpose: Toxicity of multimodal anticancer therapy in childhood and adolescents has become a focus of interest. In Ewing sarcoma, multimodal treatment consists of chemotherapy and/or surgery. To evaluate the toxicity of actinomycin-D application parallel to radiotherapy in comparison to radiotherapy in the absence of actinomycinD, we analysed German patients registered into the EURO-E.W.I.N.G.99 trial.

Method: 34 Ewing-sarcoma patients who underwent chemotherapy with actinomycinD parallel to radiotherapy were extracted from the EURO99 trial database of the German Society of Pediatric Hematology and Oncology. Additionally, we identified the same number of a suitable control cohort without the use of actinomycinD by means of matched pair analyses, to adjust for risks factors age, tumor origin and total dose of radiation. Toxicity was analyzed according to modified CTC toxicity grade scales of the EE09 protocol.

Results: Among the patients who received actinomycinD (male: 67.7%; female: 32.3%) 20 pts, 58.8% had localized disease, 10 patients pulmonary metastases (R2pulum; 29.4%) and 3 patients had primary mainly skeletal dissemination (R3; 8.8%). 1 pt missing information. The control group was distributed as follows: male: 52.9%; female: 47.1% localized disease (25; 73.5% ; pulmonary metastases 8; 23.5%; disseminated disease: 1; 2.9%). Grade 3 and 4 toxicity was reported in 69 of 693 patients (10.0%) (receiving radiotherapy without actinomycinD), and in 70 of 626 patients (11.2%) receiving radiotherapy with actinomycinD. The majority of toxicities were haematological with no difference amongst groups (123 patients; about 50% patients/group; p = 0.617). Major differences with an increase of 10% in dichotomous scales were observed in the actinomycinD group regarding: granulocytes (77.8% vs. 60.0%; p = 0.168) and platelets (40.6% vs. 31.3%; p = 0.603). 3y-OS was 0.71, SE = 0.09 in both groups.

Conclusion: First results indicate that there are no differences in toxicities in patients with radiotherapy and ActinomycinD. It is of major interest that besides hematologic toxicity no other severe toxicity was reported.

PD014

CHEMOTHERAPY COMPLIANCE AND HISTOLOGICAL RESPONSE IN OSTEOSARCOMA PATIENTS FROM A TERTIARY CARE CENTER IN INDIA

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Purpose: Histological response (HR) to neoadjuvant chemotherapy (NACT) is a robust prognostic marker for survival in osteosarcoma. Chemotherapy compliance can affect dose intensity and density and may affect the final disease outcome. Therefore, undue concern for safety or acceptability should not be allowed to obscure the principal goal of efficacy. We aimed to study chemotherapy compliance and its correlation with HR.

Method: Data were collected, retrospectively, from the medical records of osteosarcoma patients registered from January 2010 to December 2010 in Tata Memorial Cancer Center who received chemotherapy. We use multimagent chemotherapy consisting of ifosfamide, adriamycin, cisplatinum in alternating cycles. Definition of compliance is taken as: if intended number of chemotherapy cycles can be administered in intended time (25% more than ideal time) and in appropriate doses.HR is assessed by Picci’s grading for histological necrosis (HN) and good responders are defined as >90% HN while poor responders as < 90% HN.

Results: Out of a total of 84 patients 57 were males and 27 females. Among them, 62 patients have undergone surgery while 22 patients are yet to complete NACT. Out of these 62 patients, 36 (58%) achieved good histological response, while 26 (42%) were poor histological responders. Among 62 patients who had surgery, 18 (28%) were found noncompliant to NACT. Out of these 18 patients 9 (50%) were poor responders and 9 (50%) were good responders. Among the 44 (71%) compliant patients, 17 (38%) were poor responders and 27 (62%) were good responders.

Conclusion: Our preliminary data suggests that even with resource constraints, we could ensure the chemotherapy compliance in majority of the patients. Further, our HR results which are surrogate measures of final outcome are comparable to international standards. One can hypothesize that optimum chemotherapy compliance may contribute for emeritement in outcome.

PD015

PREDICTION OF TUMOR NECROSIS FRACTION USING VOLUMETRIC AND METABOLIC FDG-PET INDICES IN OSTEOSARCOMA PATIENTS FOLLOWING ONE COURSE OF NEOADJUVANT CHEMOTHERAPY

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EPIDERMAL GROWTH FACTOR RECEPTOR: IS IT A FEASIBLE TARGET FOR THE TREATMENT OF OSTEOSARCOMA?

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Purpose: Epidermal growth factor receptor (EGFR) is recognized as a central regulator of proliferation and progression in many human cancers. We analyzed its expression in osteosarcoma and performed in vitro studies to characterize the downstream pathways of EGFR in osteosarcoma cell lines as well as to test EGFR inhibitors as new therapeutic candidates.

Methods: We retrospectively analyzed 37 biopsy samples of osteosarcoma for EGFR protein expression by immunohistochemistry (IHC). Those cases were diagnosed at the Korea Cancer Center Hospital between 1995 and 2007 and treated with combination chemotherapy and surgery. The relationship between EGFR protein expression and clinicopathologic characteristics and treatment outcome were evaluated. Four osteosarcoma cell lines (HOS, U2OS, MG-63, KHO/SNP) were analyzed for EGFR, p-EGFR expression by western blot analysis. Two EGFR inhibitors, gefitinib and BIBW2992, were tested for their effect on osteosarcoma cells using MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide), colony forming and trypan blue staining assays.

Results: EGFR protein was positive in 33 (89%) biopsy samples (6 low, 16 intermediate, 11 high) and in three cell lines (HOS, MG-63 and KHO/SNP). Intermediate or high staining for EGFR protein was related to peripherally located tumor (P = 0.04) and tumor volume less than 150 ml (P = 0.001). Female gender and osteoblastic subtype tended to be associated with low staining for EGFR protein. EGFR protein expression was not associated with histologic response to preoperative chemotherapy (P = 0.09) or with the survival (P = 0.29). Gefitinib and BIBW2992 were tested at various concentrations (0.01–20 microM), however, did not have any significant inhibitory effect on the viability and proliferation of osteosarcoma cells.

Conclusion: Although our study is retrospective in nature and limited in case numbers, EGFR does not seem to be a feasible target for the treatment of osteosarcoma, contrasting to epithelial carcinomas.

Predictors of Acute Chemotherapy-Associated Toxicity in Patients with Ewing Sarcoma

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Purpose: Ewing sarcoma (ES) is a malignant small round blue cell tumor of bone and soft tissue of childhood. Patients with ES are treated with intensive chemotherapy regimens. We sought to describe predictors of toxicity in this population.

Method: This retrospective cohort study, medical records of patients with pathologically confirmed ES, extraskelatal ES, and primitive neuroectodermal tumor (PNET) treated at the University of California San Francisco and Stanford University between 1980 and 2010 were reviewed. Grade 3 and 4 non-hematologic chemotherapy-associated toxicities during initial frontline therapy were recorded for each patient, along with potential clinical and demographic predictors of toxicity. Univariate analyses were performed using the Fisher exact test. Multivariate analysis was performed using logistic regression methods.

Results: The cohort included 143 patients (89 males; median age 14 years, range 2 months–49 years) with ES/PNET and available toxicity data. The most common grade 3 or 4 non-hematologic toxicities were febrile neutropenia (n = 74 patients), infection (n = 46 patients), and mucositis (n = 11 patients). On univariate analyses, age < 12 years at diagnosis (p = 0.01), Latino ethnicity (p = 0.004), and treatment on a clinical trial (p = 0.005) were associated with higher incidence of toxicity. Tumor size, site, stage, mode of local control, and overall chemotherapy exposure were not associated statistically with the incidence of toxicity. On multivariate analysis, Latino ethnicity (odds ratio 3.8, 95% CI 1.2–12.0, p = 0.02), treatment on a clinical trial (odds ratio 3.1, 95% CI 1.01–9.3, p = 0.04), and age < 12 years (odds ratio 3.1, 95% CI 1.04–9.4, p = 0.04) were independent significant predictors of toxicity.

Conclusion: Patients with ES/PNET who are younger or of Latino ethnicity have higher rates of toxicity that may necessitate increased supportive care measures. Treatment on a clinical trial was associated with higher rates of toxicity, though this finding may represent ascertainment bias.

PROGNOSTIC SIGNIFICANCE OF APN1/CDD1 IN HEPATOBLASTOMA

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Purpose: Hepatoblastoma is a rare malignant tumor of childhood originating from immature hepatic cells. Aminopeptidase-N/CDD1 is an ectopeptidase that plays important roles in the progression of other tumors by promoting tumor invasion and metastasis. Although CDD1 is expressed in fetal stage hepatic progenitor cells, the relationship between hepatoblastoma and CDD1 expression has remained unresolved. We investigated the clinical significance of CDD1 in hepatoblastoma by studying CDD1 protein expression.

Method: The expression pattern of CDD1 was investigated in 30 tissue samples from 27 cases of hepatoblastoma by immunohistochemical staining, including 16 of predominantly embryonal type histology (pE), and 14 samples of predominantly fetal type histology (pF). We also quantified the staining data using the immunoreactive score (IRS) scale, and investigated the relationship between the expression level of CDD1, clinicopathological factors, and clinical outcomes. Furthermore, we studied the biological function of CDD1 in the hepatoblastoma cell lines. Results: CDD1 showed positive staining in all specimens. Hepatoblastoma of the pE type showed higher expression of CDD1 compared to pF hepatoblastoma (median IRS 4 (range: 2–9) versus 2 (range: 1–4)). Strong expression of CDD1 correlated with the presence of vascular invasion. CDD1 low cases showed a significantly 5-year event-free survival higher than CDD1 high cases (100% versus 51.0%; P = 0.026). The 5-year overall survival rate of the CDD1 low cases was also better than those with CDD1 high tumors (100% versus 74.0%; P = 0.114). Both CDD1 neutralizing antibody and the potent CDD1 inhibitor, Ubenimex, significantly suppressed invasive activity in the hepatoblastoma cell line HepG2 in vitro.

Conclusion: Our study suggests that CDD1 may be a novel prognostic marker for hepatoblastoma and that CDD1 is associated with the invasion capacity of hepatoblastoma.

Effect of Phytochemicals on Hepatoma and Metastatic Potential

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Purpose: To explore effect of cisplatin, allisin, resveratrol on the expression of metastasis related genes in hepatoblastoma (NB) cell lines.

Method: Kelly and SHSY5Y cell lines were used. Groups: Gr1 Control, Gr2-Cisplatin, Gr3-Allisin, Gr4-Resveratrol. Agents were administered at pre-optimized doses for 24 hour. After RNA isolation and cDNA converting, expression of 84 custom array genes of tumor metastasis (SABiosciences, PATS028A) was determined by RT-PCR for each condition. Fold changes of gene expressions according to Gr1 of each condition were calculated at manufacturer’s online free data PCR expression analysis page.

Results: KELLY: In Gr2 expression of EPHB2, TIMP3, CDH6, RORB, COL4A2, IL1B, CDH1, MGA5T, CTNNAI1, BHLA, CD44, MTA1, VEGFA decreased. Allisin caused increase in expression of ITGB3, TNFSF10, HGDC, CCLI7, CTSL1, ETVA, KISS1R, HATIP2, IL1B, IL6R, ITGAM, KISS1, MMP10, MMP9, MMP7, MYC, MCL1, SYK, TIMP4, TIP41, TRPM4, CDH1, and FXD50. This high expression wasn’t observed in Gr2 and Gr3. Expression of all genes increased in Gr3 and Gr6. Expression of DDX1, m23-H1 and mm23-H2 increased in Gr1 and Gr2, decreased in Gr6, prominently decreased in Gr4, and not changed in Gr5, and Gr6. SYSHY: Cisplatin caused decrease in expression of KISS1, MET, TRPM1, IGFI, TNFSF10, TSRH, MMP13, MMP7, CDH6, CCLI7, CXCL12 and an increase in expression of PNN, SMA4D, DENR, SFT, NME2. Allisin caused decrease in expression of HGDC, KISS1, TNFSF10, MMP10, IGFI, TRPM1, MMP7, MMP9, CCLI7, CTSL1, FXD50, KISS1R, HATIP2, IL1B, IL6R, ITGAM, and TIMP4. Expression of genes decreased in Gr4, Gr5, and Gr6.

Conclusion: Expression of genes increased in MYCN (+) NB, decreased in MYCN (+) NB cell lines administration of allisin, resveratrol, so additive treatment by these agents should be questioned in MYCN (+) NB. In MYCN (+) NB, expressions of DDX1, mm23-H1, mm23-H2 reduced by using allisin, resveratrol as a single agent, this finding indicates that allisin, resveratrol administration have to be discussed for maintenance treatment in MYCN (+) NB.
IMMUNOHISTOCHEMICAL ANALYSIS OF HEPATOBlastomas REVEALS POTENTIAL BIOMARKERS

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Purpose: Hepatoblastoma is a rare malignant liver tumour found in infants. Many heterogeneous histological tumour subtypes exist. Although survival rates have improved dramatically in recent years with the use of platinum-based chemotherapy, there still exists a subset of HB that does not respond to treatment. There are currently no tumour biomarkers in use and in this study we aim to evaluate potential biomarkers to aid identification of relapse cases that would otherwise be overlooked by current prognostication. This may identify patients that would benefit from more aggressive therapy and could improve overall survival rates.

Method: We used immunohistochemistry to analyse the expression of β-catenin, E-cadherin, CyclinD1, Ki-67 and AFP protein in tumours from 91 patients prospectively enrolled into the SIOPEL 3 clinical trial. The relationship between these biomarkers and clinicopathologic features and patient survival were statistically analysed.

Results: We identified one biomarker, CyclinD1, which has a correlation with mixed epithelial/mesenchymal HB approaching significance (P = 0.07). Survival analysis using these markers has revealed two potential prognostic indicators: Cyclin D1 and Ki-67 (P = 0.01, 0.01).

Conclusion: Immunohistochemical analysis of these biomarkers could aid diagnosis and prognosis in hepatoblastoma.

TRANSCRIPTION FACTOR GATA4 IS ABUNDANTLY EXPRESSED IN CHILDHOOD BUT NOT IN ADULT LIVER TUMORS

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Purpose: Transcription factor GATA-4 is expressed in early fetal liver and essential for organogenesis. It is also implicated in carcinogenesis in several endoderm-derived organs. Hepatoblastoma, the most common malignant pediatric liver tumor, has features of fetal liver including extramedullary hematopoiesis. We now investigated the expression of GATA-4 and its purported target gene erythropoietin (Epo) in liver tumors, and the role of GATA-4 in hepatoblastoma pathogenesis.

Method: The expression of GATA-4 factors and Epo in liver tumors was analyzed using immunohistochemistry, western blotting and RT-PCR. To further investigate the role of GATA-4 in pediatric liver tumors, we used adenoviral transfections of wild type or dominant negative GATA-4 constructs in HUH6 cells.

Results: We found abundant GATA-4 expression in both types of liver tumors in children, whereas it was absent in adult hepatocellular carcinoma. A close family member GATA-6 was expressed in a minority of childhood but not adult liver tumors. Epo, present in the fetal liver, was also expressed in childhood liver tumors. Moreover, a human hepatoblastoma cell line HUH6 was GATA-4 positive and produced Epo. We found that altering the amount of GATA-4 in HUH6 cells did not significantly affect either proliferation or apoptosis.

Conclusion: GATA-4 is abundant in pediatric liver tumors, but unravelling its exact role in these neoplasms awaits further investigation.

CELL CYCLE AND APOPTOSIS REGULATORY PROTEIN (CARP-1) EXPRESSION IN NEUROBLASTOMA

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Purpose: The prognosis for patients with high risk neuroblastoma is still poor. Study of additional prognostic factors will enhance current understanding of the tumor biology and risk stratification. CARP-1 is a recently identified molecule mediating apoptosis signaling by agents like doxorubicin and etoposide. Since these agents are used in the front line treatment of neuroblastoma, we tested whether CARP-1 expression could be another prognostic factor in neuroblastoma.

Method: CARP-1 expression was examined by immunohistochemistry in two neuroblastoma cell lines, SK-N-SH and SK-N-SH Dox. We reviewed medical records of patients with neuroblastoma at CHIM from 2000–2009 and examined CARP-1 expression by immunohistochemistry in the archived, formalin fixed paraffin embedded neuroblastoma tissues.

Results: CARP-1 expression was recorded as positive or negative. Correlation of CARP-1 expression and progression free survival (PFS) was calculated.

Conclusion: CARP-1 expression was detected in SK-N-SH but not SK-N-SH Dox, a doxorubicin-resistant derivative, suggesting that resistance to doxorubicin is associated with decreased CARP-1 expression in NB cells. Of the 22 cases studied, 36% (8/22) tumors expressed CARP-1. There was no significant difference in N-myc amplification status (25% vs. 8%, p = 0.5) among CARP-1 positive vs. negative groups. The proportion of unfavorable Shimada histology was comparable (71% vs. 62%, p = 1) between the two groups. Thirty two percent (7/22) patients progressed or relapsed, including 2/8 (25%) in CARP-1 positive group vs. 5/14 (35%) in CARP-1 negative group. There was no significant difference in the PFS at 1 yr (87% vs. 78%) and 3 yr (66% vs. 71%) between CARP-1 positive vs. negative groups.

Conclusion: In conclusion, CARP-1 expression was decreased in doxorubicin resistant neuroblastoma cell line. Although CARP-1 expression was detected in approximately one third (36%) of neuroblastoma tumors, no significant difference in PFS was identified in CARP-1 positive vs. negative group. Further study with a larger number of patients is warranted to clarify whether CARP-1 expression correlates with patient response and outcome.

TUMOR METASTASIS GENES IN NEUROBLASTOMA STEM CELLS

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Purpose: PET with 18F-FDOPA can serve as a powerful imaging modality in the diagnosis and follow-up of neuroblastoc tumors (NTs). We examined the relationship between tumor uptake of FDOPA and the gene expression level of its main metabolic target, aromatic amino acid decarboxylase (DDC).

Method: Since Aug-06, we began to recruit patients with NTs to receive FDOPA PET at initial diagnosis and/or during follow-ups. FDOPA was given intravenously after premedication with carbipoda. The DDC mRNA expression in relevant tumor tissue was evaluated by quantitative real-time PCR. The uptake of FDOPA was compared with DDC expression level and other clinicopathological factors.

Results: There were 20 patients (male/female, 15/5) eligible for analysis, with a median age at diagnosis of 2.5 (range 0.3-6.9) years. Among them, two (10%) had stage 1, four (20%) had stage 2, and the remaining 14 (70%) had stage 4 disease, including two patients (10%) with MYCN amplification. The histology showed 13 neuroblastomas (NB, 6.5%), 4 ganglioneuroblastomas (GBN, 20%), 1 ganglioneuroma (GN, 5%), and 2 necrotic tissue (10%). Twelve (90%) NTs were FDOPA avid. Real-time PCR revealed the 25th%, 50th%, and 75th% relative DDC expression level to be 3.04, 7.01, and 20.82*10(-3) folds, respectively, as compared with the internal control of GAPDH housekeeping gene. We noted higher DDC expression level in tumors with stronger FDOPA uptake (tumor/normal liver tissue SUV ratio of > 2 vs. < 2, median 14.93 vs. 1.61*10(-3) folds; p = 0.023 by Wilcoxon rank-sum test), and in those with less differentiated histology (NB vs. GBN/GBN necrosis, 8.16 vs. 2.11*10(-3) folds; p = 0.0157). There was no significant correlation between patient age, sex, or staging and their tumor uptake of FDOPA or DDC expression.
Purpose: The discovery of cancer stem cells that have ability of self renewal has changed the aspects of tumorigenesis. Neuroblastoma is an embryonic tumor originating from neural crest. Neuroblastoma tissues and cells lines are shown to include cancer stem cells. The aim of this study is to explore the differences in expression of metastasis related genes between neuroblastoma and cancer stem cells isolated from cell lines.

Method: After culturing cell lines (Kelly- aggressive N-myc positive cell line, SHSY5Y- N-myc negative cell line), CD133 positive cancer stem cells were isolated by magnetic bead isolation method. The metastatic potential and metastasis associated gene expression levels were evaluated in comparison with neuroblastoma cells.

Results: In the metastatic cell culture model which was formed by 8 micron pore, the migration of SHSY5Y cells were more than Kelly cells. In Kelly cells, CD133 positive stem cells showed increased expressions in more than 70 genes compared to Kelly control. ETV4, EWSR1, CD44, TGFBI, MTS1, ITGB3, SSTR2, P2Y1, IL1B, KISS1, SYSK, CD82, TFNFSF10, TSHB are the 100 fold increased genes. In contrast, SHSY5Y cells showed in 52 genes, a 2 fold decrease. MET, TRPM1, TFNFSF10, MMP10, MMP13, KISS1, MMP7, TSHB, MMP3, IGF1, CST7, CLTSL1, IL1B, KISS1R, HSPE1, HATP2, IL1B, ILR2, FLT4, SYK, TIMP4, CDH6, FLT4, MYC are the genes which showed 10 fold decrease in metastasis in comparison with neuroblastoma cells.

Conclusion: In our study a significantly increased expressions of metastasis associated genes were determined in Kelly stem cells; significantly decreased expressions in N-myc negative SHSY5Y stem cells comparing with cells of each group. The presence of differences in metastatic characteristics in stem cells of neuroblastoma cell lines represents two different clinical characteristics. The clinical importance of evaluation the properties of stem cells of each cancer tissue should be searched.

PH008
MICROSATELLITE INSTABILITY IN WILMS TUMOR
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Purpose: The importance of microsatellite instability (MSI) and mismatch repair genes in Wilms tumor (WT) is not well established although it is well defined in colorectal cancer in concept of Lynch syndrome. The aim of this study is to determine the clinicopathologic importance of MSI in WT.

Method: This study included 45 WT cases diagnosed, treated and followed up in Dr Behcet Uç Children Research Hospital. Tumor and normal tissues were obtained from operation materials' paraffin blocks. Real Time PCR melting analysis was performed for MSI assessing BAT25, BAT26, NR21, NR24 genes on the extracted DNA comparing tumor and normal tissues for each case. The melting curve changes between tumor and normal tissue represented instability. Curve change in one gene was scored as low MSI and high MSI in two or more genes. Ki square or Mann Whitney U nonparametric tests were used in statistical analysis on SPSS 16.0.

Results: The mean age of the cases is 3.18 years (0.5-12) and 64% of the cases were male. Tumor and normal tissues were obtained from operation materials' paraffin blocks. Real Time PCR melting analysis was performed for MSI assessing BAT25, BAT26, NR21, NR24 genes on the extracted DNA comparing tumor and normal tissues for each case. The melting curve changes between tumor and normal tissue represented instability. Curve change in one gene was scored as low MSI and high MSI in two or more genes. Ki square or Mann Whitney U nonparametric tests were used in statistical analysis on SPSS 16.0. The results showed a significant increase in proportion to age at diagnosis in subjects with diploid/tetraploid neuroblastomas without MYCN amplification.

PH010
THE NUMBER OF SEGMENTAL CHROMOSOME ABERRATIONS SIGNIFICANTLY INCREASES IN PROPORTION TO THE AGE AT DIAGNOSIS IN SUBJECTS WITH DIPLOID/TETRAPLOID NEUROBLASTOMAS WITHOUT MYCN AMPLIFICATION
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Purpose: In neuroblastoma (NBs) without MYCN amplification, the segmental chromosome aberrations (SGAs) such as 1p loss, 1q loss and 17q gain have been suggested to be associated with the prognosis of the patients. We assessed the correlation between the number of SGAs and other biological factors in primary NBs samples. The number of SGAs per primary NBs sample was analyzed using a SNP array (Human CMV370-Duo, Illumina). The status of MYCN amplification was determined by a SNP array and the FISH method. The DNA ploidy was determined by flow cytometry.

Method: The status of SGA in 54 primary NBs samples was analyzed using a SNP array. The number of SGAs was determined by the number of genotypes differing from the normal diploid genome.

Results: The status of SGA in 54 primary NBs samples was analyzed using a SNP array. The status of MYCN amplification was determined by a SNP array and the FISH method. The DNA ploidy was determined by flow cytometry. The presence of LHRH and its tumoral receptor transcript forms in pediatric neurogenic tumors investigated. The presence of LHRH receptor protein was evaluated by immunohistochemistry. The results support the merit of further investigation of the expression of LHRH receptors and its transcript forms in human pediatric tumors as well as the application of LHRH analogs for receptor-based targeted therapy of such malignancies. The presence of LHRH receptor in pediatric neurogenic tumors suggests the possible existence of an autocrine mitogenic loop. The results support the merit of further investigation of the expression of LHRH receptors and its transcript forms in human pediatric tumors as well as the application of LHRH analogs for receptor-based targeted therapy of such malignancies. The presence of LHRH receptor in pediatric neurogenic tumors suggests the possible existence of an autocrine mitogenic loop.

PH011
AN ADOPTIVE IMMUNO-GENE THERAPY APPROACH TARGETING NEUROBLASTOMA
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Purpose: Although dose intensification of chemotherapy has increased initial response rates in neuroblastoma (NB), this effect has not translated into durable remissions in patients with disseminated disease. Immunotherapy may be an alternative approach following cytoreductive chemotherapy providing a long-term disease control.
ERCC1 expression in neuroblastoma tumor samples and its correlation with patient response potentially be a biomarker of cisplatin resistance in neuroblastoma. Clinical study examining associated with cisplatin resistance in neuroblastoma cell lines and that ERCC1 could potentiate cisplatin-induced cytotoxicity.

Conclusion: These preliminary data in vitro suggest that GL against CD2-positive NB cells may represent a powerful new tool for T-cell therapy in patients with GD2-positive NB or other GD2-positive malignancies.

PI002

HIGH LEVELS OF ERCC1 ARE ASSOCIATED WITH CISPLATIN RESISTANCE IN NEUROBLASTOMA

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Purpose: Excision repair cross-complementation group 1 (ERCC1) is a key enzyme in the nucleotide excision repair pathway, one of the DNA repair pathways. Increased expression of ERCC1 has been shown to correlate with platinum resistance in several adult cancers, by conferring increased ability for the cell to repair itself. Cisplatin is one of the most effective agents in the treatment of pediatric solid tumors, including neuroblastoma, but to date there are no reports investigating ERCC1 in childhood cancers.

Method: To determine the role of ERCC1 expression in cisplatin resistance, we examined the cisplatin sensitivity and ERCC1 expression in three neuroblastoma cell lines, SK-N-SH, SK-N-BE and SH-SY5Y. Cisplatin sensitivity was measured by MTT proliferation assays. quantitative real-time RT-PCR (qPCR), Western blot and immunocytochemistry (ICh) were used to examine the level of ERCC1 expression.

Results: The three neuroblastoma cell lines have variable cisplatin sensitivity, with SK-N-SH being the most sensitive and SK-N-BE the most resistant. In parallel with this, the lowest expression of ERCC1 was seen in SK-N-SH, and highest expression in SH-N-BE cells by qPCR, indicating that the levels of ERCC1 expression were correlated with the degree of cisplatin resistance. Similar results were obtained with ICh and Western blot. In addition, knockdown of ERCC1 by siRNA sensitized the SH-SY5Y cells to cisplatin. On the other hand, treatment with 5-aza-2’-deoxycytidine, a demethylating agent, significantly increased the resistance to cisplatin in SK-N-SH cells, suggesting that hypermethylation of ERCC1 may potentiate cisplatin-induced cytotoxicity.

Conclusion: These results demonstrate that higher levels of ERCC1 expression are associated with cisplatin resistance in neuroblastoma cell lines and that ERCC1 could potentially be a biomarker of cisplatin resistance in neuroblastoma. Clinical study examining ERCC1 expression in neuroblastoma tumor samples and its correlation with patient response to cisplatin-based chemotherapy is underway.

PI003

TREATMENT OUTCOME OF HIGH DOSE 131I-MIBG TREATMENT IN STAGE 4 NEUROBLASTOMA IN HONG KONG

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Purpose: High dose radioactive 131I-MIBG treatment is used as targeted therapy for high risk neuroblatoma patients. In this report, we summarized the outcome of high dose 131I-MIBG treatment in our center.

Method: We performed a retrospective chart review of 131I-MIBG treatment in a tertiary hospital in Hong Kong. Outcome included overall and event free survival, treatment related liver and thyroid impairment were reviewed.

Results: From Aug-2003 to Mar-2011, 15 patients received 131I-MIBG therapy. All patient received one infusion except one patient received two infusions. All patients were having stage 4 disease with 131I-MIBG-avid lesions at initial diagnosis. The median age at first 131I-MIBG therapy was 3.6 years (range 2.1 to 12.2 years). Fourteen 131I-MIBG-therapies were administered as part of conditioning regimen for haematopoietic stem cell transplantation (HSCT) and 2 were given as palliative treatment. Lugols solution was given for thyroid protection. For 131I-MIBG therapy administered as curative treatment (n = 14), the dose ranged from 9 to 12.9 mCi/kg, with median dose of 12 mCi/kg. Carboplatin, etoposide and melphalan was given 7 to 10 days after MIBG treatment as conditioning for thyroid protection. For 131I-MIBG therapy administered as curative treatment (n = 14), the dose ranged from 9 to 12.9 mCi/kg, with median dose of 12 mCi/kg. Carboplatin, etoposide and melphalan was given 7 to 10 days after MIBG treatment as conditioning for
failures were consolidated by thermotherapy, cryotherapy and/or a treatment option, and carried out follow-up on patients for 101 months. Focal tumors were of diagnosis (> the different ICRB groups (International Classification of Retinoblastoma). The age at time of diagnosis (> or < 6 months) was significantly correlated with relapse but not with therapy failure or vision at 6 years of age. Interestingly, there was no significant correlation of ICRB groups with relapse.

Conclusion: Our study supports that chemoreduction with or without focal tumor consolidation is effective for controlling retinoblastoma progression without the need of enucleation or external beam radiation.

RESULTS OF COMBINED CHEMOTHERAPY AND LOCAL OPHTHALMIC THERAPY AND SURGERY FOR RETINOBLASTOMA: A STUDY FROM INDIA

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Purpose: Retinoblastoma until recently chemotherapy was used as adjuvant therapy after enucleation in cases with extrasternal spread. Recent use of chemotherapy for intraocular retinoblastoma “chemoreduction” has allowed not only to decrease number of enucleations and indications for external beam irradiation or limit the extension of local therapy, but also increase chances for vision preservation and decrease the risk of severe complications. There is a lack of data from developing countries.

Method: A study of data from patients diagnosed with retinoblastoma between December 2006 and January 2011 at the Sankara Nethralaya Medical Research Institute. Of the more than 500 new cases of retinoblastoma treated during the study period, 156 children diagnosed between November 2009 and January 2011 were the subject of this study.

Results: Of these 4 patients died (1 neutropenia and rest disease progression) and 9 lost to follow. The median age at diagnosis was 36 months. 115 patients with unilateral and 41 with bilateral tumors. Hundred and one eyes were enucleated, right eye 50 and left eye 51. Among 120 cases who received chemoreduction by vincristine, cyclophosphamide, etoposide and carboplatin as a primary treatment regimen for retinoblastoma. With an incidence of 1:20,000 – 29, Etoposide, Carboplatin & Vincristine Without Cyclosporin (¼ = 20 for each of one, two, three month-old infants for detection of serum NSE levels. Levels according to infants older than one month, and reference levels given by commercial kit should not be used for these age groups.

Conclusion: Although these findings are encouraging, we hope for strategies to improve outcome for retinoblastoma in our center such as proper training, public awareness, team approach and twinning.

SPECTRUM OF UNCOMMON PRIMARY TUMORS OF THE ABDOMEN IN CHILDREN: CAN IMAGING GUIDE CLINICIANS AND PATHOLOGIST FOR EARLY DIAGNOSIS

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Purpose: Wilm's tumor, neuroblastoma, hepatoblastoma, rhabdomyosarcoma and germ cell tumors are the common abdominal tumors in children. They are easy to diagnose based on imaging and pathology. We do come across unusual tumors in clinical practice and the knowledge of their imaging characteristics may help us in guiding clinicians and pathologists. The aim of our study is to document such tumors and describe their imaging features.

Method: We retrospectively analyzed the series of CT studies performed over 26 months (January 2009-February 2011) for diagnosing abdominopelvic masses and looked for imaging incidence of uncommon tumors. Wilm's tumor, neuroblastoma, hepatoblastoma, rhabdomyosarcoma and germ cell tumors were considered as common and any other tumors are the common abdominal tumors in children. They are easy to diagnose based on imaging and pathology. We do come across unusual tumors in clinical practice and the knowledge of their imaging characteristics may help us in guiding clinicians and pathologists. The aim of our study is to document such tumors and describe their imaging features.

Results: Of 115 cases evaluated, 10 cases were considered to be uncommon. Desmoplastic small round cell tumor (1), peritoneal mesothelioma (1), pancreaticoblastoma (1), retroperitoneal teratoma (1), ca colon (1), ca rectum (1), alveolar soft part sarcoma, (1) adrenocortical carcinoma (1), peritoneal GCT (1) and soft tissue PNET in pelvis (1). We could arrive at a correct diagnosis in 7/10 patients while in 3 patients (last three) the radiological diagnosis did not corroborate with the final histological conclusion.

Conclusion: Although the histopathology is essential for appropriate therapy, imaging features can assist in suggesting the diagnosis even in lesser common pediatric abdominal tumors and serve as a guide for treating clinicians and pathologist.


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Purpose: To evaluate chemoreduction by vincristine, cyclophosphamide, etoposide and carboplatin as a primary treatment regimen for retinoblastoma. With an incidence of 1:20,000 live births, approximately 60 children are diagnosed with retinoblastoma in Germany every year. Most retinoblastomas are diagnosed in children under five years of age, with 10% of all retinoblastomas being present at birth. Retinoblastoma is usually a lethal disease without therapy, although spontaneous regression might occur in rare cases. In contrast, current treatment regimens yield an overall survival rate above 95%, although long-term sequelae necessary.

Method: Among 120 cases who received chemoreduction by vincristine, cyclophosphamide, etoposide and carboplatin as a primary treatment regimen for retinoblastoma. With an incidence of 1:20,000 – 29, Etoposide, Carboplatin & Vincristine Without Cyclosporin (¼ = 20 for each of one, two, three month-old infants for detection of serum NSE levels. Levels according to infants older than one month, and reference levels given by commercial kit should not be used for these age groups.

Results: Of these 4 patients died (1 neutropenia and rest disease progression) and 9 lost to follow. The median age at diagnosis was 36 months. 115 patients with unilateral and 41 with bilateral tumors. Hundred and one eyes were enucleated, right eye 50 and left eye 51. Among 120 cases who received chemoreduction by vincristine, cyclophosphamide, etoposide and carboplatin as a primary treatment regimen for retinoblastoma. With an incidence of 1:20,000 – 29, Etoposide, Carboplatin & Vincristine Without Cyclosporin (¼ = 20 for each of one, two, three month-old infants for detection of serum NSE levels. Levels according to infants older than one month, and reference levels given by commercial kit should not be used for these age groups.

Conclusion: Although the histopathology is essential for appropriate therapy, imaging features can assist in suggesting the diagnosis even in lesser common pediatric abdominal tumors and serve as a guide for treating clinicians and pathologist.

SERUM NEURON SPECIFIC ENOLASE LEVELS IN PRETERM, TERM BABIES AND INFANTS LESS THAN THREE MONTHS-OLD

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Purpose: When first described, neuron specific enolase had been thought as a specific marker for neuronal tumors, especially neuroblastoma; but it had been shown that many tumors and clinical conditions other than tumors might have been associated with elevation of neuron-specific enolase, so standardization studies became necessary for healthy individuals. During antenatal follow-up and newborn period, excessive use of ultrasoundography increased possibility of visualization of asymptomatic masses, as well as the most common neoplasm of newborn which is neuroblastoma.

Method: In this study, serum NSE levels were detected according to age in healthy preterm, term babies and infants less than three months-old. Babies with other problems except prematurity and indirect hyperbilirubinemia were excluded. Samples for study of serum NSE levels were obtained at least 72 hours apart from birth for elimination of hypoxia and respiratory distress during labor. Determination of NSE was made by using ECLIA method with Roche Elecsys 2010 equipment. Infants with serum NSE levels higher than 30 ng/mL were clinically evaluated for their health condition and test was repeated when necessary.

Results: A total of 139 specimens were obtained from 39 preterm, 40 term babies and 20 for each of one, two, three month-old infants for detection of serum NSE levels. Levels of mean NSE in these groups were 21.83 ± 15.06; 18.06 ± 12.83; 8.92 ± 4.13; 7.63 ± 3.91; 10.73 ± 4.70; and highest levels were 59.36; 59.80; 16.80 ± 14.05; 21.40 mg/mL respectively. NSE levels of preterm and term babies were significantly higher than infants older than one month (p < 0.001). The highest levels detected in groups were remarkable.

Conclusion: In conclusion, with inability to compare this study with another example in literature, serum NSE levels had been found significantly higher in preterm and term babies according to infants older than one month, and reference levels given by commercial kit should not be used for these age groups.

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82 SIOP ABSTRACTS

PI008
IRINOTECAN AND TEMOZOLOMIDE FOR TREATMENT OF REFRACTORY NEUROBLASTOMA IN A PATIENT WITH RENAL FAILURE ON HEMODIALYSIS: A CASE REPORT
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Purpose: Renal failure is a rare complication of neuroblastoma and its treatment. There have been no reports of treatment of refractory high risk neuroblastoma in the setting of renal failure and chronic hemodialysis. We report a patient who developed anuric renal failure during treatment for neuroblastoma requiring chronic hemodialysis, who was subsequently treated with irinotecan and temozolomide for refractory neuroblastoma.

Method: A 7-year-old girl with high risk stage IV neuroblastoma developed renal failure requiring chronic hemodialysis after undergoing attempted resection of her primary tumor. She only achieved a partial response to induction chemotherapy and surgery and was deemed ineligible for continuation of treatment with high dose chemotherapy and autologous stem cell rescue. Treatment with chemotherapy for refractory neuroblastoma was begun 6 weeks after surgery with irinotecan 20 mg/m2/day IV daily for 4 days and temozolomide (100 mg/m2/day) PO daily for 5 days every 3 weeks. She continued on hemodialysis 3–4 times weekly.

Results: She has tolerated her treatment well except for grade 3–4 hypertension. She has stable disease by CT scan after 9 courses of irinotecan and temozolomide.

Conclusion: Irinotecan and temozolomide can be used for treatment of refractory neuroblastoma in the setting of renal failure and hemodialysis.

PI009
CHORIOCARCINOMA AND GONADOBLASTOMA WITH DYSGERMINOMA IN A 14-YEAR-OLD PHENOTYPIC FEMALE WITH 46, XY KARYOTYPE
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Purpose: Choriocarcinoma is a rare carcinoma characterized by higher risk of developing genital malignancies. Dysgerminoma and gonadoblastoma are the most common germ cell tumors, but the choriocarcinoma is very rare. The diagnosis in choriocarcinoma in children and adolescence is very poor. The early diagnosis of dysgerminoma is necessary in view of the risk of gonadal malignancies.

Method: We present a case of a 14-year-old female with 46, XY karyotype with choriocarcinoma and gonadoblastoma coexisting dysgerminoma.

Results: Our report documents a case of choriocarcinoma in one gonad and gonadoblastoma with a transition into dysgerminoma in the second. Physical examination revealed female normal external genitalia, hirsutism, but the growth of breast and vagina was hypoplastic. The patient had not menarche She presented with hypogonadotropic hypogonadism. Additional laboratory tests revealed huge levels of serum hCG (108 157.66 U/l) and Ca125 (95.5 U/ml), but lactate dehydrogenase and AFP were normal. An ultrasonography and CT showed a large mass (13.9 × 10.7 cm) arising probably from the left ovary. The left gonad resection after surgery with irinotecan 20 mg/m2/day IV daily for 4 days and temozolomide (100 mg/m2/day) PO daily for 5 days every 3 weeks. She continued on hemodialysis 3–4 times weekly.

Conclusion: This is a rare case of choriocarcinoma surgery combined with chemotherapy is the most effective method of treatment.

PI010
RETINOBLASTOMA: CORRELATION BETWEEN HIGH-RESOLUTION MAGNETIC RESONANCE IMAGING AND HISTOLOGY FOR DETECTION OF EARLY STAGE OF OPTIC NERVE INVASION
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Purpose: Neuro-ocular imaging of retinoblastoma patients is required at diagnosis. When primary enucleation is decided, imaging is mandatory to rule out optic nerve invasion. When conservative treatments are used, the pathologic gold standard is not available and local staging is based on both ophthalmic fundus examination and imaging. The purpose of this study was to assess the accuracy of high-resolution magnetic resonance imaging (HR-MRI) using surface coil in depicting early stage of optic nerve invasion.

Method: Thirty-five children (mean age: 31 months) with unilateral retinoblastoma treated by primary enucleation were prospectively included. MRI was performed under general anaesthesia using surface coils to increase signal-to-noise ratio and spatial resolution. Spinal echo T2 and T1 sequences without and with contrast (Gd-DTPA) were performed. High resolution surface coil sequences were obtained with 2 mm slice thickness and 0.3×0.3 mm in-plane pixel size. MR data were reviewed in consensus by two radiologists blinded from pathological results. An abnormal optic nerve enhancement >0.8 mm was chosen as MR criterion of retrolaminar invasion. MR data were secondarily compared to histological findings.

Results: HR-MRI and histology negatively agreed in 32/35 patients, and positively in 2/35 patients. Abnormal optic nerve enhancement in two cases was associated with histological retrolaminar invasion. Five patients had limited (i.e., < 0.8 mm) optic nerve enhancement on MRI without histological retrolaminar invasion, related to either posterior bulging of the lamina cribrosa or pre- or intralaminar invasion. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of HR-MRI in this study were: 100%, 97%, 66%, 100% and 97%, respectively.

Conclusion: HR-MRI is an accurate method to depict or rule out early stage of retrolaminar optic nerve extension of retinoblastoma.

PI011
CLINICAL PROFILE OF RETINOBLASTOMA IN A CHILDREN’S CANCER CENTRE IN SINGAPORE
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Purpose: Retinoblastoma (RB) is the most common primary intracranial tumor of childhood. We review the clinical profile of RB patients in a single centre.

Method: Data were obtained from the Singapore Childhood Cancer Registry, hospital records and Ophthalmology clinic records. Patients below age 15 with diagnosis of retinoblastoma were included. The following data were collected: demographics, presentation, treatment and outcome.

Results: There were 47 RB patients seen in our hospital from 1997–2009, of which 27 were residents and 20 were foreigners. The median duration of follow-up was 37.1 months. The male-to-female ratio was 0.9. The mean age at diagnosis was 26 months (range 1– 96). Majority were Chinese (25/27 – 93%) of local and 9/20 (45%) of foreign patients. The other ethnicities included Malays, Indians, Vietnamese, and Caucasian. Leukocoria was the most common presenting symptom (74%), followed by squint (17%) and poor vision (17%). Mean duration of symptoms was 16 weeks (range 1–120). Majority (32/47, 68%) had unilateral disease. The proportion of bilateral RB among local and foreign patients was 6/27 (22%) and 11/20 (55%) respectively. Two patients had pinealoblastoma. Two had metastatic disease at diagnosis - one had marrow metastasis; the other patient had metastatic involvement of marrow, spine and liver. Only 2/15 (13%) of bilateral RB cases underwent RB gene mutation testing. One patient received radiotherapy. Among local cases, there were 2 deaths (7%) – 1 bilateral RB (died from disease); 1 metastatic bilateral RB (died from sepsis). None of the local patients had developed second malignancies. Follow-up and outcome data were not available for 50% of the foreign patients.

Conclusion: This is a small series of retinoblastoma in Southeast Asia. Good outcomes and follow-up could be achieved for local patients. Most patients did not undergo RB gene mutation analysis due to high cost and lack of availability.

PI012
A CASE OF SOTOS SYNDROME WITH NEUROBLASTOMA
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Purpose: Several genetic syndromes predispose to malignancies. Herein, we report a rare association of neuroblastoma with an overgrowth syndrome.

Method: Retrospective review of the patient records was done.

Results: A 6 month old boy with hypertonia, developmental delay and overgrowth (weight end height > 95th centile) was referred to Pediatric Oncology for evaluation of an abdominal
mass detected incidentally on MRI scan done for evaluation of his hypotonia. He had normal karyotype (46XY), tested negative for Marfan syndrome, Prader-Willi syndrome and myotonic dystrophy. His neurometabolic work-up was normal. He had dolicocephalic skull, down slanting palpebral fissures, large simple hemic, gap between his upper frontal incisors and a high arched palate. Ultrasound and CT scan confirmed the findings of a 5.3 x 4.8 x 4.4 cm supraexternal mass which was metabolobenign/angionduodenal (MBGD) avid. There was no other MBGD uptake in the rest of the body. Urinary catecholamines were normal. Bone marrow was clear. He underwent left adrenalectomy with lymph node (LN) dissection. Pathology showed poorly differentiated neuroblasts with less than 2% ganglion differentiation. 1 parahal LN was infiltrated. Minosis-karyoindex was intermediate. The tumor showed un amplified MYCN, ploidy status 1.434. [LOH but unbalanced 1q translocation was present. Thus, due to the patient age, a diagnosis of a low-risk favourable histology neuroblastoma stage IIB was established. He tested positive for NSD1 gene and a diagnosis of Sotos syndrome was confirmed. The patient was followed clinically by oncology, genetics and neurology as well as supportive care services. He also had MBGD scans every 3 months along with monthly urinary catecholamines. He continues to be well and free of disease recurrence at 1 year follow up.

Conclusion: To the best of our knowledge, this is the youngest patient with Sotos syndrome and neuroblastoma reported in world literature and only second such case. Given the rarity of the condition, further collaborative studies are necessary to evaluate the association and its prognostic significance.

PI013
HIGH DOSES I131*MIBG TREATMENT IN THE PEDIATRIC PATIENT WITH HIGH-RISK NEUROBLASTOMA
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Purpose: High-dose I131*MIBG treatment at our Oncology Center (CIOCC)
Method: The CIOCC Nuclear Medicine Department opened on 2008. Three high risk neuroblastoma (NB) patients have been treated with high-dose I131*MIBG since then. The three cases are discussed: 3yo boy, stage IV NB, N-myc+, del1q. I131*MIBG treatment was administered after chemotherapy induction with COJEC (HR-NBL-1/ESOP) and before surgery of primary tumor attaining CR. Treatment was consolidated with high-dose chemotherapy (BUNEL) and PBSC followed by radiation therapy to tumor bed (21 Gy). He then received high-dose cis-retinoic therapy x 6 months. End of treatment: sep2009. He continues in CR 4 yo stage III abdominal NB, N-myc+, del1q. Progressed on COJEC induction therapy and toptecan/VR/Cex/erucicarbin. Received one high-dose I131*MIBG treatment, attaining VGPR. 95% of the remaining tumor was removed with surgery. Radiation therapy (36 Gyc) was administered post-operatively. Consolidation was completed with high-dose chemotherapy (BUNEL) and PBSCCT and cis-retinoic acid x 6 months. End of treatment: as well as a multidisciplinary cooperation SBST in 2014. Two stage IV NB relapsed 5 years of treatment. Refractory to 2nd-line chemotherapy with CPT-I/TMZ. He received six I131*MIBG doses as palliative care.
Results: The I131*MIBG doses administered were 200mCi in all cases. They were very well tolerated. Side effects noted were mild hypothyroidism and thrombocytopenia. Patient 1 remains in CR 18 months off treatment. Patient 2 remains with stable disease and has finished treatment recently. Patient 3 achieved a good pain control from bone metastases for 21 months after relapse, and finally died of disease.
Conclusion: High-dose I131*MIBG treatment should be considered among the different treatment modalities (surgery, chemotherapy, radiation therapy and immunotherapy) in poor prognosis neuroblastoma patients. It is a well tolerated treatment, with manageable side effects and seems to improve/consolidate tumor response to combination therapy. It is a good treatment for bone pain due to metastatic disease within the context of palliative care in NB patients.

PI014
HISTOPATHOLOGICAL FINDINGS IN CHILDREN WITH MONOCULAR RETINOBlastOMA AFTER INITIAL ENUCLEATION
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Purpose: The aim of this report is to describe histopathological findings in children with monocular retinoblastoma after initial enucleation as indicators for adjuvant chemotherapy.
Method: Forty-three patients have undergone primary enucleation. The median age was 28±17.6 months at the time of enrolment. Specific risk characteristics on histopathology reports were identified.
Results: Seventeen of forty-three patients had standard-risk characteristics as insufficiency or maximum tumor invasion choroid and prelaminar invasion of the optic nerve. Eighteen of forty-three patients had high-risk characteristics as tumor invasion of optic nerve, absent [LOH and extracleral extensions. Conclusion: In conclusion, our histopathologic review of 43 series of retinoblastomas, treated by enucleation, showed that 26 (60, 5%) in 43 had histopathologic risk factors that currently are indicators for adjuvant chemotherapy. The latter include intermediate and high-risk characteristics.

PI015
ANTERIOR SEGMENT INVASION IN RETINOBLASTOMA. IS IT A RISK FACTOR FOR EXTRAOCULAR RELAPSE?
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Purpose: The impact of anterior segment invasion (ASI) as a risk factor for death of metastatic relapse in retinoblastoma is unknown. Our aim was to study the outcome of patients with ASI and it association to other risk factors.
Method: Retrospective review of all patients with non metastatic retinoblastoma treated from January 1989 to September 2010 was analyzed. Patients with postlaminar optic nerve invasion (PLONI) usually received adjuvant chemotherapy and those with tumor at the resection margin also received orbital radiotherapy. Those with choroidal invasion did not receive adjuvant therapy except if concomitant scleral invasion was noted. Anterior segment invasion per se was not an indication of adjuvant therapy.
Results: Of 501 evaluable patients, 67 (13.3%) (20 bilateral) had ASI including anterior chamber in 48 and the remaining ones had iris or ciliary body invasion. 23 had concomitant choroidal invasion (full invasion in 8), 35 had PLONI (13 with cut end invasion) and 7 had scleral invasion, 2 had isolated ASI. Median follow up is 51.4 months (range 6 to 168). Overall 5-year disease-free survival was 0.83 versus 0.97 of patients without ASI (p=0.0001).
There were 7 cases of extracocular relapse despite adjuvant therapy in 6 cases. For patients with isolated choroidal invasion the OS was 0.94 versus 0.96 (P=0.0001) and for PLONI it was 0.90 versus 0.96 (P=0.0001) with and without ASI. For cases that have tumor at the resection margin OS was 0.61 versus 1 (p=0.01) with and without ASI. On multivariate analysis ASI was not associated to death of extracural relapse being scleral invasion the only risk factor identified (p=0.0001).
Conclusion: ASI is usually seen with other pathology risk factors, correlated with advanced disease and does not add a significant risk for extracural relapse in most cases of not metastatic retinoblastoma.

PI016
PLANNIFIED MULTIDISCIPLINARY SURGICAL MANAGEMENT OF DUMBMBELL NEUROBLASTOMA ALLOWS COMPLETE RESECTION AND PRESERVATION OF NEUROLOGIC AND ORTHOPEDIC FUNCTIONS
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Purpose: To report our multidisciplinary surgical management of dumbbell neuroblastoma (NB) after chemotherapy to achieve complete macroscopic resection and preserve neurologic and orthopedic functions.
Method: We conducted a monocentric retrospective study of all patients with dumbbell NB operated on for both intraspinal and extraspinal components between August 2004 and April 2010. Multistage surgery was performed by a multidisciplinary team of 3 pediatric surgeons.
Results: Nine patients were included (age, 15 months to 7 years). Eight tumors were classified L2 and one M. All were MYCN non-amplified. At diagnosis, four patients presented paraplegia, three requiring emergency spinal decompression. For the six thoracic cases, resection was performed through dorsal (lamiotomy) and anterior (posteriorateral thoracotomy) approaches in one to three stages. In two cases, back and front spinal surgery of primary tumor attaining CR. Treatment was consolidated with high-dose I131*MIBG treatment at our Oncology Center (CIOCC)
arthrodesis was needed to stabilize the spine and prevent deformity. For the lumbar case, complete one-stage resection was done in three steps with a single circumferential transverse approach: hemilaminectomy, retropertioneal dissection, spinal arthrodesis. For the two pelvic cases, resection was realized in one or two stages through dorsal and retropertioneal approaches. Resection was macroscopically complete in six patients. Mean surgical duration was 349 minutes. Definitive histology showed seven NB and two ganglioneuroblastomas. Intraoperative hemorrhage complicated three cases. Neurologic morbidity concerned seven patients: one L5 and two crural deficits, one radicular hypoesthesia, one leg monoparesis, one spastic paraparesis and one paraplegia. Orthopedic morbidity was moderate: one minor scoliosis. All patients underwent adjuvant chemotherapy. One patient died of progressive disease, one has an extraspinal residue and seven are in complete remission. Eight patients are alive with a follow-up from 2 months to 6 years.

Conclusion: One-stage complete macroscopic resection of both components of dumbbell NB by a multidisciplinary surgical team is feasible in most patients after appropriate chemotherapy. Primary neurosurgical approach of intraspinal component is recommended to prevent spinal cord compression.

PI017
PROGNOSIS OF NEUROBLASTOMA PATIENTS LESS THAN EIGHTEEN MONTHS OLD USING SERUM-BASED QUANTIFICATION OF MYCN GENE AMPLIFICATION
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Purpose: We previously developed a method for determining MYCN gene amplification status using cell-free DNA fragments in serum that are released into the patient’s blood from cancer cells. Here we analyzed the correlation of the prognosis with serum-based MYCN-amplification status.

Method: We obtained serum samples from 151 neuroblastoma patients and screened them for MYCN amplification (MNA) using real-time quantitative PCR. We then examined whether MYCN status in serum was associated with other prognostic variables and patient survival probability.

Results: Serum-based MNA analysis has good sensitivity and specificity (86% and 95%, respectively), when the cut-off value was set at 5, which was suggested by a ROC curve. The sensitivity and specificity were also high for different International Neuroblastoma Staging System (INSS) stages: 67% and 95%, respectively, in stages 1 and 2, 92% and 86% in stage 3, and 87% and 97% in stage 4. Patients determined to have MNA had significantly worse overall survival than patients without MNA (p < 0.01). Most notably, the serum-based MNA analysis had significant prognostic power for cases diagnosed at less than 18 months of age.

Conclusion: Serum-based MNA analysis predicts tumor MYCN amplification quickly and much less invasively regardless of tumor stage. This assay will be most useful when primary tumor biopsy is not possible and when MYCN status information will influence risk grouping and treatment allocation especially for NB patients at less than 18 months of age.

PI018
DETECTION OF TH, ELAVL4, GD2 AND PHOX2B EXPRESSION IN 331 BONE MARROW SAMPLES OF NEUROBLASTOMA PATIENTS
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Conclusion: Serum-based MNA analysis predicts tumor MYCN amplification quickly and much less invasively regardless of tumor stage. This assay will be most useful when primary tumor biopsy is not possible and when MYCN status information will influence risk grouping and treatment allocation especially for NB patients at less than 18 months of age.

PI019
IMPROVEMENT OF RETINOBLASTOMA OUTCOME THROUGH PUBLIC HEALTH CARE INTERVENTIONS
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Purpose: The aim was to compare the stage and outcome of retinoblastoma during two time periods (1993–2000 and 2001–2008) after the establishment of a paediatric oncology unit (POU) in a resource limited setting in 1993. A secondary aim was to determine whether public health care interventions, introduced during the second time period, had an impact on diagnosis and outcome.

Method: The two time periods were 1993 till 2000 (1st period - establishment of the POU), and 2001 till 2008 (2nd period). All the patients were African. Treatment included local therapy, chemotherapy (Vincristine, Carboplatin and Etoposide), enucleation and external beam irradiation, depending on stage. Public health care interventions introduced in the second period included the introduction of a compulsory year of community service of newly qualified doctors in rural hospitals, improvement of primary health care clinics and advocacy of childhood cancer danger signs nationally (to mention a few to be discussed).

Results: There were 43 patients diagnosed in the first time period versus 62 patients in the second time period. Sixty percent had advanced disease (stages III and IV, as well as bilateral disease with metastasis) in the 1st time period versus only 37% in the 2nd time period. Outcome was improved in the 2nd period with an overall survival of 71% versus only 53% in the 1st period. There was an increase in the number of children with stage I disease limited to the retina only (27%) versus only 16% in the 1st time period. Nutritional status overall was similar in both study periods.

Conclusion: Children were diagnosed with more limited disease in the 2nd time period, which indicated that the public health care interventions did result in early diagnosis with improved outcome. The collaboration with national health programs is important for early diagnosis and improved outcome of childhood cancer.

PI020
RENAL TUMORS WITH EXTENSIVE VASCULAR DISEASE: MANAGEMENT CHALLENGES IN A PEDIATRIC SERIES FROM THE HOSPITAL FOR SICK CHILDREN
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Purpose: Neoplastic vascular invasion in pediatric renal tumors is uncommon but represents significant therapeutic challenges, as the role of chemotherapy alone, anticoagulation and/or caval interruption remains to be clarified. When it occurs, a tumor thrombus extends into renal veins (RV) and inferior vena cava (IVC). Involvement of the right atrium (RA) and pulmonary tumor embolism (PTE) are rare. We report 3 pediatric cases of renal tumors with significant intravascular disease at presentation and discuss their management.

Method: 3 children were diagnosed with renal tumors at our institution (stage III Wilms’ tumor (WT) (1), metastatic renal primitive neuroectodermal tumor (PNET) (1), and metastatic renal cell carcinoma (RCC) (1)).

Results: All 3 children were found to have extension into RV and IVC at diagnosis. Extension into RA and PTE was discovered in 2 patients (RCC, PNET) and in the patient with RCC, there was extensive involvement of both pulmonary arteries and their segmental branches. All patients received multimodal treatment regimen including chemotherapy, immunotherapy (RCC), surgery and radiation, in addition to anticoagulation with low
molecular weight heparin. Anticoagulation was continued for at least 3 months and until resolution of all vascular disease. Two patients went into remission after completing therapy with no evidence of tumor thrombus and remain well and free of disease. The 3rd patient (RCC) did not respond to treatment and eventually died of metastatic disease. Thrombophilia workup was undertaken in all patients revealing heterozygous prothrombin gene mutation (20210 G > A) (PNET) and elevated FXI (1.88 U/L/mL) (WT).

Conclusion: Pediatric renal tumors can rarely present with significant caval/cava-atrial disease and associated PE. Although management of children with such extensive disease can be challenging, multidisciplinary therapeutic approaches can be effective strategy in patients with responsive disease. The role of antithrombotic therapy in these patients requires further exploration.

P002

ANTI-GD2-ANTIBODY CH14.18 OR RETINOIC ACID AS CONSOLIDATION THERAPY IN HIGH-RISK NEUROBLASTOMA

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Purpose: High risk neuroblastoma patients require intensive treatment consisting of induction chemotherapy, high dose chemotherapy (HDCT), autologous stem cell transplant (ASCT), and consolidation therapy. The value of consolidation therapy has been studied in several trials, however information on the efficacy of single agents are limited.

Method: Patients were included in this analysis when they met all of the following criteria: stage 4 neuroblastoma, >1 year at diagnosis, successful induction chemotherapy and HDCT, and at least one cycle of consolidation therapy either with the anti-GD2-antibody ch14.18 or with 13-cis retinoic acid (RA). Between 1997 and 2002, all patients were scheduled for consolidation therapy with antibody ch14.18 (six courses consisting of 20 mg/m2/day ch14.18 for 5 days every 2 months). Between 2002 and 2004, all patients received RA (nine courses RA 160 mg/m2/nd for 14 days every 28 days with a three-month rest between the 6th and the 7th course).

Results: 149 consecutive neuroblastoma patients were included. 74 patients received ch14.18, and 75 patients received RA. The groups were balanced in age (p = 0.706), MYCN amplification (p = 0.718), and remission status prior to ch14.18/RA (p = 0.541). The median observation time was 8.3 years. The 5-year-event free survival rate was 50.5% (+/- 5.8%) in the ch14.18 group and 37% (-/- 6%) in the RA group (p = 0.237). The 5-year overall survival rates were 60% (60% and 50% (-/- 6%) (p = 0.244) for ch14.18 and RA treated patients, respectively. The multivariate analysis also demonstrated no independent impact of consolidation therapy on event free survival and overall survival.

Conclusion: This retrospective analysis of a very homogenous cohort of high-risk neuroblastoma patients demonstrated no difference between 13-cis-RA and ch14.18 as consolidation therapy after high-intensive induction chemotherapy and ASCT.

P002

CO-REGISTRATION OF MRI & SPECT MBG IN THE STAGING OF NEUROBLASTOMA

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Purpose: Co-registration of morphological and functional imaging is well established in paediatric oncology (PET/CT). Conventional staging of neuroblastoma requires the use of both morphological imaging such as CT and/or MRI as well as functional imaging in the form of MBG scanning. It can be difficult on occasion to relate the MBG findings to the morphological findings provided by cross sectional imaging. This study attempted to address these issues by using automated co-registration of MBG with MRI to assess feasibility and clinical utility.

Method: MRI scanning was performed on a 1.5T Philips Intera scanner using abdominal & whole body protocols. MBG imaging was acquired on Siemens & Philips dual head gamma cameras using planar and SPECT imaging. SPECT data was reconstructed into an axial data set and then fused with the MRI data set using the Hermes nuclear medicine software (Nuclear Diagnostics). A clinical assessment of the accuracy (poor, average, good, excellent) was made and any specific points of interest were noted.

Results: 57 scans (21 whole body (WB) and 36 abdomen (A)) in 18 patients were analysed. Co-registration was excellent in 25 (10 WB, 15A), good in 15 (6 WB, 9A), average in 9 (3 WB, 6A) and poor in 8 (2 WB, 6A). On 15 occasions both whole body and abdomen images were acquired during the same examination and co-registration was found to be more accurate with the whole body images in 8 of these cases. Additional clinical information with regards to differential activity within different parts of the primary tumour was noted as well as the presence and absence of nodal and marrow uptake.

Conclusion: Automated co-registration of SPECT MBG with MRI is feasible. Best results were obtained with whole body MRI data sets. Additional information with regards to differential activity within the primary tumour & nodes was identified.

P003

CENTRAL NERVOUS SYSTEM INVOLVEMENT AT DIAGNOSIS AND AT RELAPSE IN CHILDREN WITH NEUROBLASTOMA

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Purpose: Initial central nervous system (CNS) involvement in the course of neuroblastoma is relatively rare. Longer survival obtained by intensified combined therapy in children with disseminated disease could lead to new forms of relapse presentation, such as isolated cerebrorenal metastases. The aim of the study was clinical evaluation of the patients over 1 year of age with stage 4 neuroblastoma with CNS involvement, both at diagnosis and at relapse.

Method: From 1997 to 2007, 117 patients (age 0.2−13.5 years) started NBL treatment, included 58 children over 1 year with stage 4. In 4 (6.9%) cases the CNS involvement was found at diagnosis. In these patients no neurological symptoms were observed. Initially, for 36 children the intensive treatment according to Japanese protocols was used, and for 22 patients HR-NBL-VESIOP program was administered. In 5 children (8.6%) the isolated relapse in brain was diagnosed. The diagnosis of CNS relapse was made from clinical symptoms and CT scanning, and in each case it was confirmed by pathological examination. All 5 children with isolated CNS relapse did not present with infiltration of skull bones, whereas at initial diagnosis the brain lesions were continuous with bone metastases. All but one child with CNS relapse underwent resection of the cerebral tumour followed by local radiotherapy. Second-line chemotherapy was used for 4 children. Observation was terminated in December 2010.

Results: Among 4 children with initial CNS involvement 1 died due to hemorrhage to CNS and 3 are alive without evidence of disease. Among 5 patients with isolated relapse 4 died because of neuroblastoma progression.

Conclusion: Probably brain involvement at initial neuroblastoma diagnosis is not an additional negative prognostic factor. Because of extremely poor prognosis in patients with CNS relapse it should be advised to consider possible implementation of preventive treatment. It is also necessary to invent new more effective treatment methods.

P001

SOFT TISSUE SARCOMA AND NEUROFIBROMATOSIS TYPE 1 IN CHILDREN

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Purpose: Patients with neurofibromatosis type 1 (NF-1) are prone to developed malignancy. The goal of this study was to Determine the frequency of NF-1 in children affected with STS.

Method: We reviewed retrospectively the medical records of thirty-five patients that were diagnosed with STS in the Children Hospital J.M de los Dios de Caracas, Venezuela, between 1995−2005, obtaining data related to age, gender, sites, histology, immunohistochemistry, metastasis, treatment and the diagnosis of NF-1 following these criteria (six or more brown spots (café-au-lait) on the skin measuring more than 5 mm in children and more than 15 mm in adolescents. Two or more neurofibromas (slow-growing tumors of the nervous system) or one plexiform neurofibromas (peripheral nerve tumor).

Results: Between 1995 and 2005, Thirty-five patients were diagnosed with STB. Twenty-one (60%) were male, mean age 8.5 years (range 4-months-16 y). The most common histology was MPNST in 12 patients, followed by fibrosarcoma in 7, schwannoma (neurilemmoma) in 5, synovial sarcoma in 4, leiomyosarcoma in 3, liposarcoma in 2, hemangiopericytoma in 1 malignant fibrohistiocytoma in 1. Immunohistochemical was required for definitive diagnosis in 25 patients (71.42%). 78% of cases. The extremities were the most common site affected (39.47%), followed by chest (26.31%). Twenty-six patients achieved complete remission with surgery and four with surgery and chemotherapy or radiotherapy. There was no
metastatic disease at diagnosis. NF-1 was diagnosed in four of thirty-five patients with STS represented 11.44% of all soft tissue sarcoma. NF-1 was present in 4 patients with MPNST represented 33.33%. Twenty-five (71.42%) survived for more than 15 years. Conclusion: We conclude that there is a strong relationship between soft tissue sarcomas, especially MPNST and NF-1 and recommended monitoring this patients in order to make an early diagnosis and give a greater chance of cure for this disease.

**PJ002**

THE USAGE OF CYTODYNAMIC ANALYSIS FOR THE EARLY DIFFERENTIAL DIAGNOSTICS OF SYNOVIAL SARCOMA AT CHILDREN

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Purpose: To improve the results of the treatment of synovial sarcoma at children by early differential diagnostics of small round-cell sarcomas by cytodynamic analysis.

Method: 19 children and adolescents at the mean age of 10.84 ± 3.28 years (9 males, 10 females) with synovial sarcoma were treated between 1997 and 2008 years. All patients were tested by cytodynamic analysis. Cytodynamic analysis confirmed the diagnosis in 19 cases. The samples were processed in impression smear - 7 cases, fine-needle aspiration biopsy specimens - in 12 cases. Histologically, 5 patients (26.3%) had the biphasic, 12 (63.2%) - the monophasic, and 2 (10.5%) - the poorly differentiated pattern. The most often affected area was the lower extremity - 10 (52.6%) cases. The size > 5 cm was in 13 (68.4%) cases. The amount of patients with metastasis was 8 (42.1%). The treatment of each patient began after applying the cytodynamic analysis. The treatment included: 8 courses of chemotherapy (using ifosfamide or cyclophosphamide, etoposide, carboplatin), PBSC's support, local control consisting of the surgical ablation of the primary lesion and the radiotherapy of the initial tumor and metastasis left after the induction.

Results: The treatment began not later than 48 hours from the tumor puncture with fine needle. The partial effect was registered in 80% of cases. 2-year disease-free survival was 66.1 ± 11.3%, overall 2-year survival -75.6 ± 10.6%.

Conclusion: Cytodynamic analysis is a useful early (during 48 hours) diagnostic aid in difficult cases, which may be chosen for antitumoral treatment.

**PJ003**

RADIOTHERAPY QUALITY CONTROL IN PARAMENINGEAL RMS: A FRENCH RETROSPECTIVE STUDY ON MMT 95-3 PROTOCOL

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Purpose: Retrospective evaluation of the quality of radiotherapy (RT) for patients (pts) included in the MMT 95-3, for parameningeal rhabdomyosarcomas (pmRMS) in France.

Method: Quality of RT for 69 pts (3-18 y) treated in 13 French centers between October 1996 and May 2003 for pmRMS have been retrospectively reviewed by 3 experts. Clinical data (tumor and treatments), and RT data with initial CT or MRI and dosimetry were collected. Evaluation of deviation with the MMT 95-3 protocol was performed, in terms of volume, dose, timing and duration, without knowing the outcome. In a second-time, outcome was correlated with tumor factors, and RT deviations.

Results: 64 pts are evaluable with a median age of 8.8 y. Deviations are observed for 28 pts for PTV1 volume, 7 for PTV2 volume, 16 for PTV dose, and 44 for timing. Main deviations are a smaller PTV1 volume on the skull base, minor dose on PTV1 compensated by greater dose on PTW2, and a delay to start RT (mean delay of 8 weeks, median delay of 3 weeks).

Conclusion: No correlation was observed between global deviations and outcome (relapse rate) in this analysis, but detailed analysis is ongoing and will be presented. Those results could be included for the design of the next RMS IT protocol.

**PJ004**

OUTCOME OF TREATMENT USING A CONSERVATIVE APPROACH TO LOCAL THERAPY FOR LOCALISED EXTREMITY RHABDOMYOSARCOMA: RESULTS FROM SIOP STUDIES MMT 84, 89 AND 95

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Purpose: Extremity sites constitute 10–20% of paediatric RMS. We report results for localised limb RMS treated by MMF 84/08/95 protocols in which strategies were designed to minimize the effects of local therapy.

Method: All patients with localised limb RMS treated from 1984–2003 were included in the analysis. Local therapy was determined by IRS group, pathology, and by response to chemotherapy +/- surgery. All patients received chemotherapy. Endpoints were 5 years overall (OS), event-free (EFS) survival and assessment of total burden of therapy.

Results: 160 patients, median age 5.8 years (1 month-17.4 years) were eligible for analysis. Ninety patients (56%) had alveolar pathology, 106(66.5%) tumours in the lower limb; 97(64%) tumours > 5 cm in size; 22(14%) with regional node involvement. Median follow-up for survivors was 10.3 years (range 2.3–22.9 years). 5 year EFS and OS for the whole group were 46% and 62%. CR was achieved in 154(96%) patients; 79 subsequently relapsed (52 locally). Median time between diagnosis and first relapse was 1.15 years (3.6 months-7.7 years). 82% relapses occurred within 24 months of diagnosis. Five-year survival was 45% after isolated local relapse and 19% after metastatic relapse. Univariate analysis showed older age, higher stage, head/foot site, alveolar pathology and treatment on earlier (MMT84/89) protocols were statistically related to inferior OS, EFS or both. Age (< 5 years) and low clinical stage were independently prognostic for better OS and EFS in multivariate analysis. 87 patients were considered cured (68 in 1st CR and 19 in 2nd CR > 24 months). Including burden of initial and subsequent treatments, 49(56%) avoided significant local therapy, defined as RT or mutilating surgery.

Conclusion: OS > 60% compares favourably with other international experience for RMS at this site. Avoidance of significant local therapy was achieved in 56% of survivors. Results for the youngest children were better than expected (< 3 years OS 78%).

**PJ005**

VASCULAR ENDOTHELIAL GROWTH FACTOR SERUM LEVELS IN CHILDREN WITH NEWLY DIAGNOSED RHABDOMYOSARCOMA

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Purpose: The negative prognostic impact of elevated levels of circulating Vascular Endothelial Growth Factor (VEGF) is described in several malignancies. However, no information is available in childhood rhabdomyosarcoma (RMS). In the present study, serum VEGF-A (sVEGF-A) was measured retrospectively in a series of pts with RMS.

Method: sVEGF-A was assessed in 17 newly diagnosed RMS pts aged 1 to 240 months (median, 54). Three pts were group I, 5 group II, 7 group III, and 2 group IV. sVEGF-A concentrations were determined by quantitative enzyme-linked immunosorbent ELISA kit (R&D Systems). sVEGF-A mean value was investigated in relationship to age, sex, histology, primary site, primary size, and IRS postsurgical group by using two-tailed Student’s T-test.

Results: sVEGF-A mean value was elevated in pts with RMS as compared to controls: 768.6 ± 147.7 pg/ml vs. 198.0 ± 96.9 pg/ml (p < 0.05). In particular, sVEGF-A levels were increased in 13/17 pts. Although not statistically significant because of the limited number of pts, there was a trend for higher sVEGF-A mean levels in embryonal tumors (926.3 vs. 519.1, p = 0.26), advanced groups (882.4 vs. 619.3, p = 0.47), and unfavorable primary sites (819.9 vs. 477.0, p = 0.47).

Conclusion: Circulating VEGF is significantly increased in pediatric pts with newly diagnosed RMS. Further studies in larger series of RMS pts are needed to determine whether measurements of circulating VEGF might have a role in assessing prognosis and modulating treatment.

**PJ006**

TREATMENT OUTCOME OF NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS (NRSTS) IN CHILDREN OF SAUDI ARABIA

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Purpose: To discuss the outcome of therapy for children with NRSTS at KFSH&RC, Riyadh, Saudi Arabia.

Methods: Medical records of children, < 14 years of age diagnosed with NRSTS between 2005 and 2010 were reviewed retrospectively. Data regarding demographics, presentation, pathology, treatment modalities and outcome were collected.

Results: Thirty-eight NRSTS patients were seen at KFSHRC from 2005 to 2010. 19(50%) were boys presenting at younger age (median 7.2 vs 9.9 years; p = 0.05) 12(27.9%) patients presented with metastatic disease. 15(39.5%) underwent upfront surgery. 23(60.5%) received chemotherapy according to our standard institutional protocols. Radiation therapy was given to 5 patients (13.2%). 2 were terminally ill at presentation. 9(23.7%) patients died of their disease. In univariate analysis, death was associated with younger age at presentation (median 0.86 vs 9.22 years, p-value = 0.02). Relapse/Progression rate was 39.5% (4relapse, 11PD).

No significant association was observed regarding death or relapse/Progression with respect to gender, metastatic disease at presentation, or extent of surgical resection for those undergoing surgery. In multivariate analysis, no independent risk factor for death or relapse/Progression was identified when adjusted for metastatic disease at presentation, gender, age at diagnosis and extent of surgical resection. Overall survival at 5 years was 74.3% and was better in females (88.8% vs 58.3%; p = 0.038). Event Free Survival was 46.5% and was significantly better in patients with complete resection (75.5% vs 27.3%; p-value = 0.005). In multivariate analysis, when adjusted for age at presentation, gender, and metastatic disease at presentation, extent of surgical resection was significantly associated with EFS (p-value = 0.029).

Conclusion: Extent of resection played a significant role in the outcome for patients with NRSTS at our institution.

PJ007
NATURAL KILLER CELL PHENOTYPE AND CYTOTOXICITY ARE ALTERED IN PRIMARY DISSEMINATED MULTIFOCAL EWING SARCOMA PATIENTS.

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Purpose: Despite multimodal therapy, most metastatic Ewing sarcoma family of tumours (ESFT) remain incurable. Inactivated cytotoxicity mechanism has reached its limit in efficacy and toxicity. New therapeutic strategies are needed to improve survival in these patients. In vitro studies have shown that ESFT are potentially susceptible to cytokine-activated natural killer (NK) cell cytotoxicity. Preliminary clinical data suggest that donor NK cells may exert anti-tumor activity in children with solid tumours undergoing allogeneic hematopoietic stem cell method.

Method: To provide fundamental insight in the immune NK profile of patients with metastatic ESFT, we examined their NK phenotype and cytotoxicity in details. Natural Killer cell phenotype was performed by multiparametric flow cytometry Natural cytotoxicity of NK cells was assessed by using a conventional 2-hour europium-TDA release assay.

Results: We found that NK cells in ESFT patients had an immature phenotype consisted on high NKbright cell sub-set, low NKp44 receptor and low CD69 marker activation.

Cytotoxicity was decreased, which could be considerably overcome by overnight incubation with IL-15.

Conclusion: These findings underscore the immune escape mechanisms in ESFT, and our results should be useful for future NK cell immunotherapeutic strategies for metastatic ESFT patients.

PJ008
OPPORTUNITY OF SURGICAL TREATMENT FOR RHABDOMIOSARCOMA OF PARAMENINGIVAL REGION IN CHILDREN

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Purpose: To discuss opportunity of surgical treatment for rhabdiosarcoma (RMS) of parameningival region in children.

Method: 24 of 29 patients had embryonal RMS and 5 of 29 had alveolar RMS. 17(60%) patients had IV stage of the disease, 6 (20%) - III stage, 3(10%) - IV stage and 3(10%) had relapses of disease. All 29 patients have received initial 4 courses chemotherapy (CT). 13 of 29 the patients received chemo-radiotherapy and 16 of 29 children were treated by combined therapy in addition surgery for disease stabilization (n = 12) and second-look operations (n = 4). The further treatment (CT and RT) was defined by the histopathologic findings.

Results: Accesses and operation volumes depended on localization and the sizes of a residual tumor. 4 of 16 children have undergone lateral mandibulotomy with tumor removing, 10 of 16 - lateral mandibulectomy with resection vertical branch of mandible and tumor removing including plasty by the big thoracal muscle in 2 of 10 patients and sternocleidomastoid muscle in 5 of 10 patients. One of 16 was treated by gynantonium and one more - by inferior orbitotomy with tumor removing. 9 (75%) of 13 patients did not receive surgery alive with a period of follow-up from 2 months till 4 years. 13 (81, 2%) of 16 patients have undergone surgery alive with a period of follow-up from 1 month till 5 years.

Conclusion: The surgery should be done in patients with RMS of parameningival region for disease stabilization on treatment or as a second-look surgery. This treatment strategy was highly efficacious for patients with unfavorable RMS.

PJ009
SPECTRUM OF PEDIATRIC RHABDOMYOSARCOMA: A SINGLE CENTRE EXPERIENCE

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Purpose: Pediatric Rhabdomyosarcoma (RMS) is a uncommon tumor. We describe the spectrum of RMS seen over a period of 5 years at our centre.

Method: This is a retrospective review of the clinical presentation, staging, grouping, therapy and outcome of children with RMS. Chemotherapy was given according to IRS-V protocol.

Results: Sixteen patients with RMS presented to our centre between March 2005 and January 2010. Complete data was available for 14 patients and is presented. Median age was 4 years (1 month-12 years). M:F ratio was 2.5:1. Sites of presentation were orbit-4, parameningeal-2, head & neck-3, genitourinary-2, others-3. Three patients had metastasis at the time of diagnosis. Clinical groups observed were II in 4, III in 3 and IV in 2 in 3. TNM staging was Stage I-6, II-2, Stage III-3 and Stage IV-3. Histological distribution was spindle-cell variant-2, embryonal-5, alveolar-2 and undifferentiated-5. Prognostic stratification included good risk-4, intermediate risk-7 and poor risk-3. Surgical resection was possible in only 2 patients while others had only biopsy at diagnosis. All patients with good risk had orbital disease, received VAC chemotherapy and local radiotherapy, and are alive and disease-free at a median follow-up of 14 months post-completion. Out of 7 patients with intermediate risk, 1 was lost to follow-up (LFFU), 1 had progressive disease; 2 relapsed and died; 3 received radiotherapy, are alive and disease-free at a median follow-up of 16 months post-completion. Out of 3 high-risk patients, 1 was LFFU, 1 had progressive disease and 1 is alive and disease-free 6 years post completion of chemo-radiotherapy. Estimated 5-year overall and event-free survival are 66.7 ± 12.6% and 57.1 ± 13.2% respectively.

Conclusion: Treating RMS is feasible in the developing world. Results from our centre are encouraging.

PJ101
AGGRESSIVE FIBROMATOSIS IN CHILDREN AND TEENAGER POPULATION

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Purpose: Desmoid tumors or aggressive fibromatoses are an infiltrating fibrosis tumors characterised by local aggressiveness without any metastatic potential and frequent recurrence. They resemble low-grade fibrosarcomas. Most of cases are sporadic but 2% had a genetic origin associated with Gardner’s syndrome, a type of familial adenomatous polyposis (FAP) with extracranial features. They are a rare tumor: < 0.03 of all cancers. We will analysis clinical characteristics, recurrence rate, overall survival and progression free survival in 16 patients.

Method: A retrospective review between January 1990 and December 2007 was performed on 16 patients with a diagnosis of juvenile aggressive fibromatosis.

Results: Mean and median age were respectively 16.4 and 18 years. There was a female predominance with a sex-ratio at 3. Sites involved are as follows: 44% in extremities, 19% in intraabdominal, 12.5% in abdominal wall, 12.5% in chest, 12.5% in breast. Mean time between symptoms and diagnosis was 8.5 months. Treatment is essentially surgical with only 9 complete resection and 7 partial resections. Radiotherapy was performed only in 2 patients having incomplete resection. No patients underwent radiotherapy in case of complete resection or exclusive radiotherapy or chemotherapy. Complete response was obtained in 14 cases and partial response in 1 case. Recurrence was observed in 8 patients with a mean time of 20 months. 4 patients had presented 1 episode of recurrence, 2 with 2 episodes, 1 with 3 episodes and 1 with 8 episodes. Treatment of recurrence was surgery in 4 cases, surgery followed by radiotherapy in 3 cases, and with Tamoxifen in 1 case. Overall survival was 15 years. 80% of patients were alive at 5 years. Progression free survival was 20 months.

Conclusion: Surgery remains the reference treatment of Desmoid tumor. Radiotherapy associated with surgery reduces the risk of local relapse. Others therapies had been described: chemotherapy, hormonetherapy, immunotherapy, anti-inflammatory drug.
DESMOPLASTIC SMALL ROUND CELL TUMOR: ABOUT 6 CASES
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Purpose: Desmoplasic small round cell tumor is an uncommon aggressive malignancy which occurred mainly in young males. They usually present peritoneal involvement at initial presentation.

Method: We reviewed the files of 6 patients treated for desmoplasic small round cell tumor in Salah Azaiz Institute from 2002 to 2010.

Results: Mean age was 16 years. Sex-ratio was 5. Mean interval between the start of signs and the diagnosis was 4.25 months. Initial site was cervical in 1 patient (16.5%), abdominal in 2 patients (33.5%) and pelvic in the remainders (50%). Swelling was the major revealing sign in 83% of patients followed by pain in 50%. Physical examination found peripheric lymph nodes in 5 patients. Tumor size was more than 5 cm in 83% of patients. 5 patients (83%) had metastases at initial presentation. These metastases involved lymph nodes in the 5 cases, liver, lung and ovary in 1 case. 2 patients underwent initial surgery and 1 exclusive surgery. The remainders (3 patients, 50%) received neoadjuvant chemotheraphy. Adjuvant chemotherapy was realised in 2 patients after surgery. The most used chemotheraphy regimen at initial presentation was VIDE (in 4 patients). 1 patient underwent radiotherapy after adjuvant chemotherapy. Complete response (CR) was observed in 50% of cases (3 cases): after surgery and chemotherapy in 2 cases and after exclusive surgery in 1 case. All the patients having CR relapsed. Median time to progression was 3 months. The site of recurrence was locoregional in the 3 cases. These patients underwent surgery (in 2 cases) with CR and salvage chemotherapy without OR. Overall survival was 66% at 2 years and 17% at 5 years.

Conclusion: This experience showed the aggressive behaviour of this entity with low chemosensitivity, high rate of recurrence and short-lasting response to chemotherapy.

HEAD AND NECK EWING TUMOUR/RHABDOMYOSARCOMA: FIVE PAEDIATRIC OR YOUNG ADULT PATIENTS TREATED WITH DEFINITIVE CHEMO-RADIATION USING HELICAL TOMOTHERAPY
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Purpose: Ewing sarcoma and rhabdomyosarcoma of the head and neck region are said to have a worse prognosis. Local disease management is difficult and radiotherapy treatment planning for these patients may be very complex.

Method: We reviewed all children and young adults (less than 30 y-o) treated for Ewing sarcoma or non-rhabdomyosarcoma soft tissue sarcomas.

Results: Five patients (4–19 y-o) were retrieved; pathology was two Ewing sarcoma of the C-spine, one parapharyngeal space Ewing sarcoma, one undifferentiated rhabdomyosarcoma of the temporal bone treated as a Ewing sarcoma, and one nasopharyngeal rhabdomyosarcoma (all biopsy proven). All had intra-cranial and/or intra-snasal extension. Median greatest tumour diameter was 60 mm. Two pts had nodal involvement and 1 had lung metastases. All patients had induction chemotherapy followed by concomitant chemoradiotherapy (mainly ifosfamide/VIP/P16 alternating with cyclophosphamide/adriamycin/vincristine). Radiotherapy dose was 50.4 to 55.8 Gy, 1.8 Gy/ft in 42 to 53 days. Conformity index ranged from 0.9 to 1.38 and homogeneity index from 0.037 to 0.069. Limiting doses were typically spinal cord for spine cases (max D2% accepted: 53.5 Gy) and optic structures (max: 4.7 Gy) for infracranial/ anterior base of skull tumors. Oral mucositis requiring nasogastric feeding was necessary in four cases. With short follow-up (to 24 mo after end of RT), no patient has progressed at the primary site or suffered radiation-related morbidity; one patient died at 19 mo of myocardialdysplasia.

Conclusion: Despite risks associated with radiotherapy for tumours in this location, early results are promising. Dosimetric comparison between IMRT and 3D-conformal treatment will be presented and compromises with respect to conventionally accepted dose constraints will be discussed.

MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR IN NEUROFIBROMATOSIS 1: IS METRONOMIC THERAPY THE WAY TO GO?
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Purpose: Malignant peripheral nerve sheath tumour (MPNST) is a highly aggressive tumour especially in patients with neurofibromatosis 1 (NF1). Without a complete surgical excision, prognosis is guarded given its limited responsiveness to chemotherapy and radiotherapy. We present a case of a 10 year old boy with MPNST with NF1, who achieved complete response following metronomic chemotherapy.

Method: A 10 year old boy, presented with a rapidly progressive painful swelling over the back of 6 months duration. He had features of neurofibromatosis type 1. Magnetic resonance imaging revealed a large paraspinl mass extending from T3 to T11 region. He underwent a
partial surgical excision. The histopathology revealed malignant peripheral nerve sheath tumour arising from a pre-existing plexiform neurofibroma. Five weeks after surgery there was local recurrence measuring 4 x 4 cm. He received external beam radiotherapy and concurrent chemotherapy using Ifosfamide during radiotherapy and Ifosfamide with doxorubicin after completion of radiotherapy. Four weeks after completion of chemoradiotherapy, the lesion was of the same size. In view of poor response to chemoradiotherapy, metronomic chemotherapy, was started using oral etoposide, cyclophosphamide and prednisolone each given for 3 weeks following by 1 week drug holiday. Clinical response was seen after 2 cycles. Computed tomography after 6 cycles did not reveal any residual tumour. Metronomic chemotherapy was continued for a total of 9 months. The patient continues to remain in CR, 5 months after the cessation of therapy.

Results: Metronomic chemotherapy works by a variety of mechanisms including antiangiogenesis, restoration of anticancer immune response, induction of tumour dormancy and activation of hypothetical drug driven dependency/deprivation effect. When conventional treatment fails, these alternate mechanisms may succeed in depriving the tumour of its nutrition or activating immune surveillance.

Conclusion: Metronomic chemotherapy may be effective in certain aggressive tumours where conventional chemotherapy and radiotherapy is unable to achieve remissions.

PJ016
THE RELATIONSHIP OF LYMPHOCYTE SUBSETS IN BONE MARROW AT PRESENTATION IN PEDIATRIC SMALL ROUND CELL TUMORS.
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Purpose: To discuss the role of T-cell, NK and B-cell in immune defense mechanism and to develop the new approaches for immunotherapy.

Method: We analyzed the subsets of lymphocytes in bone marrow in 34 children (male - 19, female - 15) with solid tumors (rhabdomyosarcoma - 18 and Ewing family sarcomas - 16), age 1–16 years. The control group has included 15 patients without cancer. During this study we investigated bone marrow morphology and immunology, including T-cell subsets, NK and B-cell and investigated lymphocytes.

Results: Statistically significant difference in bone marrow lymphocyte subsets was shown between patients with tumors, comparing to control groups, and in the patients with different cancers. Patients with Ewing family sarcomas showed significantly higher proportion of cytotoxic lymphocytes (CD3+ CD8+) comparing to cancer-free children and to patients with rhabdomyosarcoma: 68.5 ± 3.1% (n = 16) vs 50.5 ± 2.4% (n = 14) vs 50.5 ± 3.9% (n = 16), respectively; p = 0.001 and 0.01, respectively. Additionally, the patients with Ewing family sarcomas had lower proportion of CD4+ T-cells and higher proportion of natural killers (CD56+ CD3-) comparing to healthy children: 26.9 ± 3.5% (n = 16) vs 39.3 ± 2.8% (n = 14); 18.0 ± 3.7% (n = 14) vs 9.4 ± 1.7% (n = 12), respectively; p = 0.001 and 0.049, respectively. Children with rhabdomyosarcoma showed characteristic higher TCR6+ T-cells, comparing to healthy individuals: 15.8 ± 1.6% (n = 11) vs 9.2 ± 1.4% (n = 11), p = 0.007.

Conclusion: Thus, our study has found dependence of bone marrow lymphocyte composition on type of cancer in children with small round cell tumors.

PJ017
PAX3-NCNA2 PLAYS A DUAL ROLE IN TUMORIGENESIS OF EMBRYONAL RHABDOMYOSARCOMA
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Purpose: We previously analyzed the complex chromosomal translocation in one case of embryonal RMS by spectral karyotyping (SKY) and identified a translocation involving chromosome band 2q35, which is the locus of the PAX3 gene. The patient is alive and in remission at nine years after treatment. We later identified a PAX3 partner gene as NCOA2 using fluorescence in situ hybridization (FISH) and cDNA sequence analysis. Because the role of PAX3-NCNA2 in rhabdomyosarcoma tumorigenesis is unknown, we investigated its biological function in this study.

Method: C2C12 cell lines expressing wild type PAX3, PAX3-FOXO1, PAX3-NCNA2 and a C-terminal activation domain deletion mutant of PAX3 were established using a murine stem cell virus (MSCV) retrovirus expression system. Anchorage-independent growth was assessed using soft agar colony formation. Myosin Heavy Chain (MHC), a marker of fully differentiated myocytes, was identified immunohistochromically. Myogenic differentiation was induced by switching the medium to DMEM containing 2% horse serum.

Results: Expression of PAX3-NCNA2 protein promoted growth and anchorage-independent growth in C2C12 myoblasts. The number of colonies of the PAX3-NCNA2 stable cell line was half the number of colonies of the PAX3-FOXO1 stable cell line (130.7±9.2 colonies, 230.6±35.9 colonies, respectively). Expression of PAX3-NCNA2, wild-type PAX3 and PAX3-FOXO1 each blocked the fusion of myoblasts to myotubes in differentiation medium. MHC was not detected in any of the PAX3-NCNA2, wild-type PAX3 or PAX3-FOXO1 stable cell lines.

Conclusion: The finding that the PAX3-NCNA2 stable cell line produced fewer colonies than the PAX3-FOXO1 stable cell line may indicate that RMS with PAX3-NCNA2 fusion gene has a less aggressive phenotype and a better prognosis. The PAX3-NCNA2 fusion gene promoted anchorage-independent growth and inhibited myogenic differentiation in mouse myoblasts. These data suggest that PAX3-NCNA2 has a dual role in the tumorigenesis of RMS.

PJ018
WEST OF SCOTLAND EXPERIENCE OF RHABDOMYOSARCOMA IN CHILDREN OVER A DECADE
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Purpose: To report a single institutional experience of children with rhabdomyosarcoma (RMS) from West of Scotland.

Method: Retrospective observational study of RMS patients identified from unit database from 2001 to 2010.

Results: 31 children (18 males) were diagnosed with RMS (6/2% of all solid tumour diagnoses), 56% of patients had alveolar subtype. Median age at presentation was 4 years (IQR 2-8). Anatomical location was varied with 36% involving the genitourinary tract, 18% head and neck, 16% parameningeal, 10% extremities, 10% pelvis and 10% mediastinum or liver. Clinical presentation was highly variable and depended on primary tumour site. Pain, rapidly expanding mass, weight loss, night sweats, bleeding and general malaise were the commonest presenting features. 35% had distant metastases at diagnosis. 72% of these had alveolar disease. Metastatic sites included lungs, bone, bone marrow, pelvis and pancreas. All patients received combination chemotherapy, 68% received radiotherapy and 55% underwent surgery. Chemotherapy regimens used included MMT 95, MMT 98, RMS 2005, bevacintrabum and VAC. Overall survival is 75% with a median follow up time of 47 months (IQR 17-80). 93% (29%) relapsed and only one of them survived. Median time from relapse to death was 2 months (range, 1-15 months). 23% of patients who died received palliative radiotherapy.

Conclusion: The genitourinary tract was the most common site involved followed by the head & neck. All patients were treated with various combination chemotherapy regimens, 68% received radiotherapy and 55% underwent surgery. There was over representation of the alveolar subtype and metastases at presentation compared with other published series. Despite this Event Free Survival is 72%, which compares favourably to the reported literature. Relapse was associated with a very poor outcome.

PJ019
THE PROGNOSTIC ROLE OF PRE-TREATMENT SERUM LEVELS OF INTERLEUKIN-10, INTERLEUKIN-12 AND THEIR RATIO IN CHILDHOOD SOFT TISSUE SARCOMAS, HODGKINS LYMPHOMAS AND ACUTE LYMPHOBlastic LEMiKIAS
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Purpose: Deregulated serum IL-10, IL-12 and their reciprocal balance have been stated in several malignancies of adults. In children with cancer the issue has not been investigated so far.

Method: To determine the diagnostic and prognostic roles of pre-treatment serum levels of IL-10 (Th2 cytokine), IL-12 (Th1) and their ratios in 91 children with soft tissue sarcomas (STS - 30 patients; median age 9.4 years), Hodgkin lymphomas (HL - 30; median age 15.4 years) and acute lymphoblastic leukemias (ALL - 31; median age 6.2 years) treated in the Medical University of Gdańsk, Poland between 1995 and 2004. The control group consisted of...
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of 30 completely healthy children; median age 11.3 years. The serum levels of cytokines were measured pre-treatment by the IL-10 and IL-12p70 ELISA kits: Endogen.

Results: The serum levels of IL-10 and IL-12 levels were the highest in ALL and HL patients, respectively and they exceeded significantly those of STS patients. The presence of general symptoms in HL and high risk group in ALL were associated with significantly higher median IL-10 level. Elevated IL-10 and IL-12p70 levels and decreased IL-12 correlated with poor risk histology in STS (alveolar rhabdomyosarcoma and non-rhabdomyosarcoma STS), poor response to therapy, higher risk of relapse and death from disease progression. Multivariate analysis identified pre-treatment IL-10/IL-12 ratio > 10 and IL-12 < 40 pg/mL as significant predictors for shorter EFS and OS, respectively.

Conclusion: Pre-treatment serum levels of IL-10, IL-12 and IL-10/IL-12 ratios in children with STS, HL and ALL may be of value as additional prognostic tools to predict the response to therapy, risk of relapse and probability of EFS and OS.

P1020

CLINICAL RELEVANCE OF ANAPLASIA IN CHILDHOOD RHABDOMYOSARCOMA

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Purpose: Background: Poor clinical outcome has been correlated to the presence of anaplastic features in various pediatric malignancies such as Wilms tumor and medulloblastoma. Anaplasia in childhood rhabdomyosarcoma has not been included in the International Classification of Rhabdomyosarcoma. A recent report from the Soft Tissue Sarcoma Committee of the Children’s Oncology Group (COG) suggests that anaplasia may impact clinical outcome. Aim: To study the frequency of anaplasia at presentation in childhood rhabdomyosarcoma and its relationship to clinical and pathological characteristics as well as to outcome.

Method: Anaplasia (focal or diffuse) was retrospectively assessed in 91 consecutive pediatric rhabdomyosarcoma patients who were registered at the Children’s Cancer Hospital in Egypt (CCHE) during the period from July 2007 till end of December 2009.

Results: Anaplasia was diagnosed in 16 patients (17.6%), focal in 9 (9.9%) and diffuse in 7 (7.7%). Anaplasia was more likely to occur in older patients having an age > 10 years, in tumors with unfavorable histology (non-embryonal), in the high risk group and stage IV. However, these differences were statistically insignificant (p > 0.05). The 3-year failure free survival rates for patients with and without anaplasia were 27.5% ± 14.7% and 36.9% ± 7.4%, respectively (P = 0.046) and the 3-year overall survival rates were 44% ± 16.1% and 76.5% ± 5.3%, respectively (p = 0.031). Patients with diffuse anaplasia did not have worse clinical outcome than those with focal anaplasia having 57% and 55.6% unfavorable outcomes, respectively.

Conclusion: The frequency of anaplasia in pediatric patients with rhabdomyosarcoma in our study was 17.6%. The presence of anaplasia had statistically significant worse clinical outcome. Multivariate analysis in larger studies is required to confirm whether anaplasia is an independent prognostic factor.

PK002

MULTIDISCIPLINARY APPROACH TO TREATMENT OF WILMS TUMOR - AIIMS EXPERIENCE

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Purpose: To study the clinicopathological features, treatment details and Multidisciplinary treatment of Wilms Tumor treated at Dr B.R.A.-Institute Rotary Cancer Hospital, AIIMS Method: The study included 52 patients, less than 18 years of age, registered in our Paediatric oncology Clinic during June 2006–May 2009. After initial evaluation neoadjuvant chemotherapy was administered from Stage III onwards. In early stages, upfront nephrectomy was offered as a standard therapeutic approach. Radiotherapy was delivered as per NWT–S recommendations.

Results: The mean age was 4.3 years. The study included 35 males and 16 females. Abdominal mass was the commonest presentation (51/65). Favorable histology was seen in 40 patients and unfavourable histology was seen in 13 patients. Forty patients presented with localised disease, 11 presented with metastasis. Fifty patients received surgery, chemotherapy and radiotherapy. All patients received VAC regimen, mean number of cycles was 23.8. Mean RT dose 10.9 Gy/std error 1.96, 95% CI 33.9–41.6. Blank Radiotherapy or abdominal Radiotherapy to a dose of 10.8 Gy/7 fractions was delivered by 2D treatment planning (11patients) and 3D conformal Radiotherapy (40 patients) Mean disease free survival is 37.8 months.

Conclusion: The above regime was well tolerated and detail patient characteristic, clinical profile, treatment outcome will be presented.

PK003

OUTCOME OF HEPATOBLASTOMA: EXPERIENCE FROM A SINGLE CENTRE IN INDIA

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Purpose: Hepatoblastoma (HBL) is the most common primary liver tumor in children. Neoadjuvant chemotherapy with surgical resection has led to increased survival of these patients. This study assesses the outcome of children treated as per guidelines of SIOPEN 3. Method: Fourteen children with HBL treated as per protocol from Jan 2007 to Dec 2009 were analyzed. The diagnosis was established by imaging, alpha-fetoprotein (AFP) and histology/cytology.

Results: Twelve boys & 2 girls with a median age of 11.5 months (1.5–120) were treated. 8 were less than 1 year and 1 child was 10 years old. The involved site was right lobe: 6 (42.9%), left lobe: 4 (24.6%), both lobes in: 1(7.1%); all segments: 3 (21.4%). Multifocal involvement was seen in 3 (21.4%). Median AFP at diagnosis was 2806 ng/ml (3.2–406,918). One patient had AFP < 100 ng/ml. Five (35.7%) were standard risk and nine (64.3%) were high risk disease. Only 1 child had lung metastasis. All received neoadjuvant chemotherapy. 3 treatment related deaths occurred prior to surgery: 1: sepsis; 1: encephalopathy & 1 to viral myocarditis. 10 (71.4%) underwent surgery: complete resection in 8, incomplete resection in 2 children who had incomplete resection received salvage chemotherapy with docetaxel. There was no response to the drug. The 10 year old patient developed progressive disease after the second course of therapy. Median duration of follow up was 28 months (7–48). Four year event free survival was 50%.

Conclusion: 64.3% patients were high risk. Sepsis related mortality is a major setback in developing countries. Liver transplant, not available at our centre, would have helped the children with incomplete resection. Docetaxel as a salvage therapy was not effective in the 2 patients. EFS of 50% achieved within the constraints of a developing country.
Efficacy of Program Treatment in Patients with Neuroblastoma: Results of Single Center Retrospective Study

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Purpose: In order to determine the efficacy of neuroblastoma treatment a retrospective study was conducted in Pediatric Oncology and Hematology Center, Regional Children’s Hospital, Ekaterinburg, Russia.

Method: Since January 1991 till November 2010, 146 children (77 girls and 69 boys) aged from 10 days to 15 years (median 18 months) with primary neuroblastoma were diagnosed. 142 patients were treated according to NB92, NB 97 and NB 2004 protocols (28,6%) 50 (35.2%) and 50 (35.2%) correspondingly. Four children (2.8%) were treated by OPECO/IEC consecutive chemotherapy courses. MYCN status was investigated in 97 (68.3%) patients.

Median of follow up is 37 months.

Results: Patients distribution by stage was as follows: stage I - 31 (21.2%) patients; stage II - 21 (14.4%); stage III - 28 (19.3%); stage IV - 51 (34.9%) and stage IVS - 14 (9.6%). MYCN amplification was detected in 20 out of 97 children (20.6%). Complete remission and very good partial remission have been achieved in 84 (59.2%); partial remission - in 45 (31.7%). Median survival time was 53 months.

Conclusion: Treatment results were observed in patients with stages I, II, III and IVS. Outcome was low for patients with stage IV and stage IVS. Median survival time was 53 months.

PK006

The Turkish Pediatric Oncology Group: Experience from Saudi Arabia

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Purpose: To report on the outcome of therapy for children with low stage neuroblastoma (NBL) seen at KFSH/RCC, Riyadh, Saudi Arabia.

Method: Medical Records of children < 15 years of age diagnosed with stage 1, 2, and 4S NBL between 1982 and 2005 were reviewed. Data regarding demographics, presentation, pathology, treatment and outcome were collected.

Results: There were 240 cases of evaluable NBL, among them 78(32.5%) were low stage disease (Stage 1 = 21 Stage 2A = 14, Stage 2B = 20 and Stage 4S = 23). There were 38 male and 40 female with a median age 11.85 months. Chemotherapy was given in 51 cases (65.4%) with different combinations according to the standard protocols in each era of the study. Surgical resection of the primary tumor was attempted in 62 cases (79.5%). Between 2002 and 2010, 487 patients were eligible. Risk group distribution: LRG (30%), IRG (13%), HRG (37%). MYCN amplified in 22% cases, histopathology was unfavorable in 68% cases. Overall response rate was 96% in LRG and 90% in IRG. Induction response was 85% in HRG. Median follow-up time was 38, 30, and 21 months in LRG, IRG, HRG, respectively. Five-years EFS and OS were 82% and 89% in LRG, 75% and 82% in IRG, 27% and 36% in HRG. Age, stage, histopathology, MYCN amplification, serum levels of LDH, ferritin, and NSE, urine level of VMA, primary tumor site were found significantly related to survival rates.

Conclusion: In LRG 5-years EFS was low due to deaths in stage4S patients and high relapse rate in stage1. In IRG and HRG 5-years OS and EFS were acceptable. Age, stage, histopathology, MYCN amplification, serum levels of LDH, ferritin, and NSE, urine level of VMA, primary tumor site were found significantly related to survival rates.

PK007

TREATMENT OUTCOME OF CHILDREN WITH LOW STAGE NEUROBLASTOMA (NBL): EXPERIENCE FROM SAUDI ARABIA

PK010

THE TURKISH PEDIATRIC ONCOLOGY GROUP NEUROBLASTOMA 2003 (TPOG-NBL-2003) PROTOCOL: FACTORS THAT EFFECT SURVIVAL RATES

PK004

PEDIATRIC HEPATOCELLULAR CARCINOMA IN SINGAPORE - HBV IS NO LONGER THE MAIN CULPRIT

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Purpose: Hepatocellular carcinoma (HCC) is a rare liver cancer in childhood. Outcomes are poor especially in children. Similarity to adult HCC, pediatric HCC is highly associated with Hepatitis B virus (HBV), as well as other causes of liver cirrhosis. Therefore the incidence of pediatric HCC is higher in areas (such as countries in Southeast Asia) where HBV is endemic. We review the pediatric HCC in Singapore from 1997 to 2010 (13 years).

Method: The data were obtained from the Singapore Childhood Cancer Registry, as well as chart records of the 2 main pediatric oncology units in Singapore. Patients aged 0–15 years with diagnosis of HCC were included. The following data were collected: patient demographics, HBV status, staging information, treatment, and survival outcomes.

Results: There were 8 cases of pediatric HCC from 1997 to 2010. Majority (78%, 8/8) were boys, and all (100%) were of Chinese ethnicity. The mean age at diagnosis was 10 years (range 5.2 to 14). HBV was positive in 3 (38%) patients. None were positive for Hepatitis C. Only the 3 HBV-positive patients had evidence of liver cirrhosis on imaging and histology. Four (50%) had metastatic disease at diagnosis. Three (38%) underwent initial surgery for resectable disease; one (HBV+) of these subsequently underwent successful liver transplant. Two patients underwent resection after neoadjuvant chemotherapy. Other treatment for unresectable cases included transarterial chemoembolisation (2 patients) and sorafenib (1 patient). There were only 2 (25%) survivors in this series.

Conclusion: Pediatric HCC is a rare occurrence in Singapore in the recent years since the introduction of HBV vaccine into the National Childhood Immunization Program in 1987. The majority of our pediatric HCC now occur in HBV-negative patients with non-cirrhotic livers. This is similar to the West where HBV is non-endemic. We are in need of better treatment strategies for advanced non-resectable pediatric HCC.

PK008

Conduct: Better treatment results were observed in patients with stages I, II, III and IVS. Other children: 16% vs 57% in stages II, III and IVS patients were 93% vs 8% with complete remission and very good partial remission have been achieved in 84 (59.2%); partial remission - in 45 (31.7%). Median survival time was 53 months.

Conclusion: Outcome was low for patients with stage IV and stage IVS. Median survival time was 53 months.
THE EVALUATION CHILDREN WITH GERM CELL TUMORS IN A PEDIATRIC ONCOLOGY CENTER
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Purpose: The aim of this study was to determine clinical data, treatment methods, survival rates and late sequelae of patients diagnosed with germ cell tumor at Department of Pediatric Oncology, Gazi University Faculty of Medicine.

Method: The socio-demographic characteristics, tumor histopathology, localization, staging, imaging studies, treatment methods, recurrence properties, causes of death and survival rates of 48 patient diagnosed with germ cell tumors were retrospectively evaluated.

Results: There were 48 patients (22 m, 26 f) with mean age at diagnosis was 60 months (0.2-230 months). The patients were followed for 0.2-139 months (mean: 39.12 ± 39.72) months. There were 11 mature teratomas, 4 immature teratomas, 2 mixed malignant germ cell tumors, 2 malignant teratomas, 19 yolk sac tumors, 3 embryonal carcinomas, 6 germinomas, and one choriocarcinoma. The primary tumor localization was sacrococcygeal in 12, abdominal in three, retroperitoneal in five, ovarian in 14, testicul in 12, and CNS in two cases. Twenty-two cases were stage I, six were stage II, eight were stage III, and 12 were stage IV. AFP level was high in 24 (58.5%) of 41 patients with pre-operative AFP assessment. Beta-human chorionic gonadotropin (β-hCG) level was attempted in 34 cases (70.8%), which seven (20.6%) were high. Seventeen (35.4%) cases showed distant metastasis. Initial complete and partial surgical resection was performed in 27 (57.4%) and 12 (25.0%) patients, respectively. Chemotherapy was administered in 28 patients and 6 patients received radiotherapy either for surgical resection or as recommended by the post chemotherapy surgery.

The disease free survival for these patients is 77% (82.9% for stage III and 57.7% for stage IV) for a median of 8.5 years.

PK008

CLINICAL PROFILE, MANAGEMENT AND OUTCOME OF NEUROBLASTOMA: A DEVELOPING COUNTRY EXPERIENCE
Gaurav Khara1, Anand Praakash, Vikas Dua, Ramzan Khan, Veronique Dinand, Satya Prakash Yadav, Annup Sachdeva
1Pediatric Blood Cancer DOI 10.1002/pbc

PK009

RESULTS OF STAGING AFTER SIX WEEKS OF PREOPERATIVE CHEMOTHERAPY IN PATIENTS WITH INOPERABLE WILMS TUMOR AT THE INSTITUTO NACIONAL DE ENFERMEDADES NEOPLASICAS
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Purpose: Evaluate staging results after six weeks preoperative chemotherapy with 3 drugs in children with large inoperable Wilms Tumor (WT).

Method: This is a retrospective study at the IEN between January 1992 and December 2009 for newly diagnosed patients under 15 years of age with WT.

Results: 327 patients were evaluated during this period, 154 (47%) had preoperative chemotherapy and are the group reported here. Of these 13 had bilateral disease, 26 are not evaluable and 7 had other kidney tumors. The evaluable group includes 108 children with WT. 99 with biopsy proven diagnosis and 9 with a clinical and radiological evidence of a renal mass. 52% were females, with an F/M of 1.1, the median age for both sexes was 3 years. 82 had stage III and 26 stage IV pre chemotherapy. After a six week treatment with vincristine, Actinomycin-D and Doxorubicin 50/50 stage III pts were downstaged (28 stage I, 22 stage II, 29/82 remained the same and 3/82 were upstaged. 16/26 stage IV pts were downstaged (7 stage I, 5 stage II, 4 stage III), 10/26 remained the same. The tumor weight and high risk as per COG guidelines.

Conclusion: In our use of preoperative chemotherapy with three drugs has a 60% stage reduction in this group of patients and therapy after nephrectomy needs to be adjusted accordingly to decrease long term side effects. We also recommend that the three drugs regimen be used in patients presenting with large kidney tumors and as recommended by SIOP in Europe, no diagnostic biopsy to be done which can delay diagnosis and complicate the post chemotherapy surgery.

PK010

PEDiatric hepatoCellular CARCinoma - HaT TIME CHANGED ANYTHING?
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Purpose: While literature describes pediatric hepatocellular carcinoma (HCC) in the background of hepatitis B-related liver cirrhosis, our local experience differs. We examined how our hospital’s experience with pediatric HCC had evolved over the last decade.

Method: With IRB approval, clinical charts of patients 18 years and younger treated for pediatric hepatocellular carcinoma in KK Women’s and Children’s Hospital between July 1, 1997 and February 28, 2011 were reviewed. Data pertaining to presentations, investigations, histo-pathology, treatment strategies and outcomes were studied.

Results: We treated 6 boys and 1 girl for HCC during the study period. They were between 6.1–12.7 years old (median 11.3 years). Six patients presented with gastrointestinal complaints. The last patient, a known hepatitis B carrier, had his tumor detected on surveillance biochemical and radiological studies. Only 2 patients were hepatitis-B carriers.

Conclusion: While literature describes pediatric hepatocellular carcinoma (HCC) in the background of hepatitis B-related liver cirrhosis, our local experience differs. We examined how our hospital’s experience with pediatric HCC had evolved over the last decade.

PK011

PEDIATRIC MALIGNANT LIVER TUMORS: RESULTS OF A SINGLE CENTER
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Purpose: Primary malignant tumors of the liver are rare in childhood and hepatoblastomas account for most of them.

Sir Ganga Ram Hospital, Pediatric Hematology Oncology, Delhi, India

Purpose: Neuroblastoma (NB) is the most common extra cranial solid neoplasm in children. There is paucity of data on treatment outcome of NB from the developing world. We describe the clinical profile, treatment and outcome of NB from a single centre in India.

Method: Medical records of previously untreated children, between the ages of 1-month to 18 years, with an established diagnosis of NB from 2002–2010 were retrieved. All the relevant data was recorded on pre-designed proforma. Tumor was staged based on International Neuroblastoma Staging System and classified into low risk, intermediate risk and high risk as per COG guidelines.

Results: There were 33 cases of NB. Eight aged less than 1 year, 11 aged 1–4 years and 11 aged more than 4 years. Male: Female ratio-3:1. 28 were stage III/IV, 4 were stage I/II and 2 were I/IV. Fifteen cases either did not opt for therapy or abandoned after initial therapy. Of the remaining 18 cases, 7 had low risk, 6 had intermediate risk and 5 had high risk NB. Five patients were hepatic resection for a 2-cm well-differentiated HCC. He received no chemotherapy but eventually required a liver transplant. Four patients received platinum-based chemotherapy. Two patients also underwent trans-arterial chemo-embolization and 2 received Sorafend. One child received no therapy. We have 2 current survivors.

Conclusion: Pediatric HCC in our population did not predominantly arise in the background of hepatitis B cirrhosis. Regular surveillance of hepatitis B carriers did however allow early detection potential for cure. Despite evolving treatment strategies, outcomes of pediatric HCC remain dismal.

PK012

PEDIATRIC MALIGNANT LIVER TUMORS: RESULTS OF A SINGLE CENTER
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2Istanbul University, Oncology Institute, Istanbul, Turkey
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Conclusion: Pediatric HCC in our population did not predominantly arise in the background of hepatitis B cirrhosis. Regular surveillance of hepatitis B carriers did however allow early detection potential for cure. Despite evolving treatment strategies, outcomes of pediatric HCC remain dismal.
Method: Characteristics, treatment and outcome of primary malignant hepatic tumors diagnosed and treated in the Istanbul University Oncology Institute, Division of Pediatric Hematology Oncology, between 1996 and 2011 were evaluated retrospectively.

Results: 21 children (13 male, 8 female), were diagnosed and treated with primary malignant tumor of the liver (11 hepatocellular carcinoma [HCC], 9 hepatoblastoma [HB], 1 rhabdomyosarcoma). Another girl with rhabdomyosarcoma was previously reported (Kebzd, 2003). In our series, HCC cases were more than the cases with HB. Regarding the etiology, in cases with HCC, 8 had HBV infection, 1 tiosinen, and 1 Fanconi aplastic anemia. Two infants with HBs had hemophatythropa. According to PRETEXT staging, 12 cases were stage (5) IV, 2 SII, 7 SII. All stage IV patients had either extrahepatic and/or portal/hepatic vein involvement. Patients received cisplatinum/doxorubicin/carboplatinum containing chemotherapy according to SIOPEL-3 protocol or modifications. Six received chemotherapy. Two had liver transplantation from parents, one died with complications, one relapsed after 7 months. Three SII patients with HBs, one SII HCC are alive with no evidence of disease (1, 2 and 8 years, respectively), 1 HCC is alive with disease. Sixteen patients have died with progressive disease at a median of 6 months (1 week–4 years).

Conclusion: The high incidence of HCC in our series is thought to be due to the high incidence of hepatitis B infection in Turkey. It is expected to decrease, due to the routine application of free hepatitis B vaccine to all children in Turkey since 1998. Children with chronic HBV should be followed up for the risk of HCC. Children with hemophathythropa/other predisposing conditions should also be followed up for the risk of liver tumors so that chronic HBV should be followed up for the risk of HCC. Children with hemophathythropa/other predisposing conditions should also be followed up for the risk of liver tumors so that they are diagnosed at early stages.

PK013

INITIATION OF A CLINICAL TRIAL FOR HIGH-RISK NEUROBLASTOMA IN A RESOURCE-POOR COUNTRY (MOROCCO) TO IMPROVE CLINICAL OUTCOME

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Purpose: Germ cell tumor (GCT) is a rare malignancy accounting for 3% of all pediatric tumors. The overall survival rate of children and adolescents with GCT is more than 75% after adopting combined therapy. The aim of this study is to review clinical presentation, management, and outcome in a single-center series with extrachorionic GCT.

Method: Clinical characteristics, pathologic presentations, survival outcomes of 101 children with GCT, treated at our hospital from 1988 to 2010, were analyzed.

Results: Sixty-two out of patients were female and 39 out of them were male. The median age of the patients was 72 months (6–192 months). Abdominal pain and abdominal mass were the most frequent symptoms. Fifty-eight (57%) patients had gynogenic tumor (24 testicular, 34 ovarian), 43% extrachorionic. Histologically, teratomas were found most frequently (mature: 26, immature: 10), followed by yolk sac tumors (n: 33), mixed tumors (n: 13), embryonal carcinoma (n: 10), dysgerminoma (n: 8) and seminoma (n: 1). Twenty-six patients were diagnosed as mature teratoma and we excluded them in the evaluation of staging and survival. 19 out of 75 cases had stage I, 15 had stage II, 38 had stage III and 4 had stage IV disease. Additionally, 3 out of 38 patients with stage III disease and 3 out of 4 patients with stage IV disease were operated at other clinics and they admitted to our clinic with relapse. Chemotherapy was given to 67 patients. Sixteen patients relapsed and the relapse occurred in 10 out of them at admission. 11 patients (14.7%) died. Overall survival (OAS) and event-free survival were 75% (mean follow-up time: 204 ± 15 months) and 65% (mean relapse time: 164 ± 14 months), respectively, after 23 years.

Conclusion: Surgery combined with platinum-containing chemotherapy can improve efficacy and survival of children and adolescents with germ cell tumor.

PK015

HEPATOBLASTOMA AND HEPATOCARCINOMA: 20 YEARS EXPERIENCE IN A PEDIATRIC CENTER

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Purpose: Hepatoblastoma (HB) and hepatocarcinoma (HCC) account for the majority of malignant liver tumors in children. The aim is to review our experience, describe the features, and report overall survival of the population with HB and HCC.

Method: Retrospective analysis on records of 20 children with diagnosis of HB and HCC admitted between January 1990 and December 2009. Patients were treated according to SIOP/SIOPEL protocols.

Results: 16/20 were hepatoblastomas and 4/20 were hepatocarcinomas. Clinical presentation: 14 palpable abdominal mass detected by parents, 3 doctor’s physical routine examination, 3 ultrasound findings and 1 patient had pseudopapathy. Mean time to diagnosis: 1.6 months. Hepatoblastoma: 9/16 were male. Median age: 16 months. All patients had elevated alpha-feto protein (AFP) (mean: 365000 ng/mL, r: 260–200000). Four had elevated BCG (mean 42 mL/mL). Local Staging PRETEXT I: 1 patient, PRETEXT II: 9, PRETEXT III: 2. PRETEXT IV: 4. SIOP staging: 5 high risk (4 PRETEXT IV, 1 lung metastatic disease), 11 low risk. Patients received chemotherapy according to risk and evolution with cisplatin and /or doxorubicin. 14/16 hepatic resections were performed. 10/16 patients are currently alive with no evidence of disease. 6/16: 5 high risk (2 due to disease progression before surgery, 3 relapsed after surgery), 1 sepis after liver transplantation. Overall survival: 62.5%. Mean follow-up: 43.25 months. Hepatocarcinoma: 2/4 patients were male. Ages: 37, 89, 124 and 143 months. Mean AFP was 90 mg/mL (r: 0–350). Two patients were treated with surgery and chemotherapy, currently alive with no evidence of disease. Two patients with non resectable tumors died despite chemotherapy.

Conclusion: Hepatoblastoma is the most common malignant liver tumor of infants less than 2 years old. Patients with localized disease showed good outcomes, while those with extended disease could not be rescued. Hepatocarcinoma is more common in older children and have worse prognosis when complete resection cannot be achieved.

PK016

PROFILE OF GERM CELL TUMOURS IN CHILDHOOD

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Purpose: To study the clinicopathological profile and outcome of pediatric germ cell tumors.

SIOP ABSTRACTS 93

PEDIATRIC BLOOD CANCER DOI 10.1002/pbc

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Purpose: advanced neuroblastoma could be improved in a resource-poor country with implementation of free hepatitis B vaccine to all children in Turkey since 1998. Children with chronic HBV should be followed up for the risk of HCC. Children with hemophathythropa/other predisposing conditions should also be followed up for the risk of liver tumors so that they are diagnosed at early stages.

Clinical and Epidemiological characteristics of Children with GERM CELL TUMORS: A SINGLE INSTITUTIONAL EXPERIENCE OVER A 23 YEAR

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Purpose: To study the clinicopathological profile and outcome of pediatric germ cell tumors.
Method: Retrospective analysis of patients less than 12 years diagnosed as GCT over the last 10 years.

Results: 85 patients were analyzed. The mean age was 4.43 ± 3.9 years. 34 patients had gonadal tumor, 19 (22.4%) ovarian and 15 (17.6%) testicular. 51 had extragonadal tumor, 25 (29.4%) being sacrococcygeal tumors. 63 (70.5%) patients were started on therapy. 48 (76.2%) completed therapy & were analysed. 24 (50%) & 20 (41.7%) and 4 (8.3%) had stage II, III & stage IV disease. Alpha fetoprotein was raised in 32 patients (68%). Histologically, 33(66.7%): teratoma [benign; immature & malignant]; 7 (14.6%): yolk cell tumour; 2 (4.1%): dysgerminoma; 2 (4.2%): mixed GCT; 1 (2.1%): granulosa cell tumour. Three were reported as malignant GCT. Sites involved: sacrococcygeal 16(33.3%); ovarian 14 (29.2%); testicular 8 (16.7%); mediastinal 5 (10.5%); pelvis 3 (6.3%); mesenteric 1 (2.1%); and retroperitoneal in 1 patient (2.1%). Primary surgery was performed in 27 (56.3%). 11 (22.9%) received postoperative chemotherapy. 21 (43.8%) patients received pre-operative chemotherapy followed by surgery. The chemotherapeutic protocol used was BEP [Bleomycin, Etoposide & Cisplatinum]. The number of courses of chemotherapy received was 3.9 ± 1 per patient. There was one sepsis related mortality. All achieved complete remission. Median duration of follow up is 24 months (range: 1–120 months). Two patients with stage III and one with stage IV disease relapsed. The overall survival is 87.5%

Conclusion: Pediatric germ cell tumours have a good prognosis with surgery and chemotherapy. Sacrococcygeal & gonadal tumours are the commonest. Unfortunately 25% refused therapy and 24% defaulted treatment.

PK017
HEPATOBlastoma: A SINGLE INSTITUTE STUDY OF PROGNOSTIC FACTORS
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Purpose: Hepatoblastoma is the most common malignant hepatic tumour of childhood. It has been recognized that histological subtype confers prognostic information in children with hepatoblastoma. In particular, small cell undifferentiated histology (SCUh) has been reported to confer an adverse prognosis. We present a series of 30 children who were diagnosed with hepatoblastoma and treated through the Children’s Cancer Centre, with respect to review of histopathological and radiological risk factors.

Method: We performed a retrospective analysis of all children (n = 30) diagnosed with hepatoblastoma over a ten year period. In addition to review of medical records, a central review of radiology and histopathology was undertaken. Pretreatment classification, histological subtype and response to therapy were correlated with clinical outcome data.

Results: The number of courses of chemotherapy received was 3.9 ± 1 per patient. There was one sepsis related mortality. All achieved complete remission. Median duration of follow up is 24 months (range: 1–120 months). Two patients with stage III and one with stage IV disease relapsed. The overall survival is 87.5%

Conclusion: Pediatric germ cell tumours have a good prognosis with surgery and chemotherapy. Sacrococcygeal & gonadal tumours are the commonest. Unfortunately 25% refused therapy and 24% defaulted treatment.

PK018
OUTCOME OF WILMS TUMOR - SINGLE CENTRE EXPERIENCE
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Purpose: There is a paucity of data on outcome of Wilms tumor (WT) from India. Here we describe the same from a single centre in India.

Method: This is a retrospective review of the clinical presentation, staging, therapy and outcome of children with WT. Chemotherapy was given according to UKCCSG WT-3 protocol.

Results: Twenty-seven patients with WT presented to our centre between February 2005 and January 2010. Median age at diagnosis was 2 years (4 months–9 years). M:F ratio was 4:5. Stage-wise distribution was Stage I (7, 27.8%), Stage II (4, 14.8%), Stage III (3, 11.1%), Stage IV (13, 48.1%). The number of patients with unfavorable histology and 7 had unfavorable histology. Twenty (74%) of 27 patients were treated at our centre and 7 (26%) patients abandoned therapy after diagnosis. Among the 20 treated patients, 18 underwent unilateral nephrectomy and 1 had bilateral partial nephrectomy. Three patients were lost to follow up (10.5%): nephrectomy alone and one with bilateral disease stopped therapy after 3 months. Seventeen children completed therapy as per protocol. Of the 20 patients treated at our centre, 16 are alive and in remission with a median follow up of 2.9 years (range: 1.2 to 6.1 years) and 1 had recurrence in the other kidney. The estimated 5-year overall survival was 77.1±1.38%. The 5-year event free survival (EFS) was 72.9±15.2%. Five-year EFS was 82.4±9.2% for children with favorable histology tumor and 50.0±35.4% for those with unfavorable histology (p value n.s.)

Conclusion: Wilms tumor is highly curable tumor even in the setting of a developing country.
microfolic to 1.4 cm. 2 patients each had AC confined to mucosa, invading muscularis propria or invading transmurally while lymphnode metastases were observed in the patient with FAP. No distant metastases were seen in any patient. The tumor was low grade in all. Six patients underwent appendectomy while only one patient underwent pan-colectomy because of FAP. At a mean follow-up, which was primarily clinical, of 53.42 months, the outcome was excellent with all patients alive and disease free.

Conclusion: Older age (>10 years) at diagnosis, female predominance and small lesions (<1.5 cm) were the salient observations in our study. It can be plausibly concluded that AC commonly present as acute appendicitis or are incidental, are mostly of low grade, and have an excellent prognosis. Surgical resection without adjuvant treatment is adequate. Follow up with serum sediment and chromogranin A may not be recommended in small (<1.5 cm), non-metastatic AC.

PI.002

MESENTERIC MASS MIMICKING A TUMOR IN A CHILD WITH DEFICIENCY OF IGA

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Purpose: Celiac disease is a pathology which can mimic several different diseases. The differential diagnosis that should be considered include tumor and infectious diseases. We report the case of a child who was misdiagnosed as having a mesenteric mass when in fact it was due to IgA deficiency.

Methods: We describe a case of a one year old girl admitted to Service of Pediatric Oncology for an abdominal retroperitoneal mass noted on ultrasound. The patient presented with symptoms of severe abdominal pain and distension, fever, diarrhea, and vomiting. The patient was discharged after 23 days on a gluten free diet. The patient is in good health and thriving at her 3 month follow-up evaluation.

Conclusion: Although IgA deficiency caused a delay in the diagnosis and management of this patient, she was discharged after 23 days on a gluten free diet. The patient is in good health and thriving at her 3 month follow-up evaluation.

PI.003

PEDIATRIC THYROID CANCER. RECENT MANAGEMENT AND OUTCOMES.

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Purpose: Thyroid cancer is rare in the pediatric population. Literature is limited with respect to treatment and outcomes. The disease often presents at an advanced stage but fortunately these children have long survival. We developed a regimen for treating pediatric patients. We report outcomes.

Method: Pediatric patients with thyroid cancer referred to the CCI since 2002 have been systematically treated in a similar manner. Patients received maximal surgery followed by thyroid stimulation. All patients received thyroid ablation (except 2 with radioactive I131 followed by a post therapy scan, placed on a suppression regimen and followed clinically. Patients did not have baseline pre operative thyroglobulin levels but all had post operative thyroid function and thyroglobulin levels. Patients are followed every 6 months with physical examinations, thyroid function testing and thyroglobulin levels. Other clinical investigations are requested as indicated.

Results: Eleven patients presented with thyroid cancer between 2002 and 2010. Four presented with local disease limited to the thyroid gland, six presented with disease in the thyroid gland and metastatic to the regional lymph nodes, and 1 patient presented with disease in the thyroid gland, regional nodes and lung mets. Age range was 5 to 16 years old. Nine cases were papillary, 1 follicular and 1 medullary carcinoma was observed. One case was considered radiation induced as this child had a course of TBI for treatment of his large B cell lymphoma 11 years prior. One patient emigrated from Belarus. One patient had a family history of thyroid cancer. The patient with medullary carcinoma had a family history of MEN II A in his father and both brothers. All patients are alive with no evidence of recurrence. Conclusion: Total thyroidectomy with lymph node dissection followed by I131 thyroid ablation and subsequent thyroid suppression is a highly successful treatment approach for children with thyroid cancer.

PI.004

ACINIC CELL CARCINOMA OF THE PAROTID GLAND IN CHILDREN AND ADOLESCENTS: A POSSIBLE ASSOCIATION WITH THYROIDITIS

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Purpose: Acinic cell carcinoma (AcCC) of the parotid gland is a low-grade malignant salivary gland neoplasm. Previous radiation exposure and familial predisposition are some of the risk factors for AcCC. Our aim was to evaluate the characteristics of children and adolescents diagnosed with AcCC treated at Schneider Children’s Medical Center of Israel.

Method: We retrospectively analyzed the medical records of patients with AcCC of the parotid gland diagnosed between 2004 and 2010.

Results: Four patients were treated with AcCC of the parotid gland: 3 females and 1 male. The age range was 13.5–18 (median 15.7) years at the time of diagnosis. One patient had a family history of a parotid tumor. 2/4 patients had Hashimoto’s thyroiditis treated with levothyrox. The third patient had normal thyroid function, but a family history of hyperthyroidism and hypothyroidism. All patients presented with symptoms of a parotid mass (3 left, 1 right). All had localized disease and negative lymph nodes. None of the patients received any further therapy. All patients underwent partial parotidectomy with no resulting damage to the facial nerve. The tumors were diagnosed as Acinic cell carcinomas, measuring less than < 4 cm. PAS stain was positive in all. Ki67 immunostain demonstrated proliferation of 1–8%. All patients are alive with no evidence of disease with a median follow up time of 25 months (range 4–64 months).

Conclusion: In our experience, the prognosis for pediatric parotid gland acinic cell carcinoma is good and surgery alone should be sufficient in early-stage tumors. We report for the first time an association between acinic cell carcinoma of the parotid gland and thyroiditis in children.

PI.005

LANGERHANS HISTIOCYTOSIS IN CHILDREN OF SAUDI ARABIA

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Purpose: Background: Langerhans histiocytosis (LCH) is a rare disease that affects all age groups, with peak incidence in childhood. The manifestations range from a single bone lesion to a severe multisystem disease with dysfunction of vital organs. The course of the disease is unpredictable, varying from spontaneous regression to rapid progression and death. Little is known about the behavior of this disease in the Middle East, so we describe here our 10 year experience in Riyadh, Saudi Arabia.

Method: Patients and methods: Between January 1998 until December 2008, 35 patients (26 males, and 9 females) were diagnosed at KFSHRC with LCH, median age at presentation was 3.5 years (range, 0.5–13.8 years); 15 patients were classified as single system (SS: one organ/system is involved with the disease) and 20 patients had multisystem disease (MS: more than one organ/system involved). Thirty one patients had bone involvement (88.6%), 12 had skin involvement (34.3%), 9 had bone marrow involvement (25.7%), 7 had liver involvement (20%), and 4 had lung involvement (11.4%). Diabetes insipidus developed in 11 patients (31.4%).

Results: Results: Patients were treated with Vinblastine/steroids, 4 patients also received etoposide (before 2005). Thirteen out of the 15 patients with SS responded to first line therapy in comparison to only 6 of the 20 patients with MS. At 10 years, the overall survival (OS) for all patients was 84.3%, and the event free survival (EFS) was 50%. OS by extent of disease was 100% for patients with SS, and 73.7% for patients with MS (P = 0.053), and the corresponding EFS was 91.7% and 21% (P = 0.004), for the 2 groups respectively.

Conclusion: Conclusions: In Saudi Arabia, children with LCH with SS disease respond well to therapy and have excellent prognosis; those with MS disease however, are more likely to have refractory disease and their prognosis is less favorable.

PI.006

PANCREATIC INFLAMMATORY MYOFIBROBLASTIC TUMOR (IMFT): PRESENTING AS PANCREATIC ABCESS

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MALIGNANT PERIVASCULAR EPITHELIOID CELL TUMOR (PEComA) IN CHILDREN. DESCRIPTION OF A CASE AND REVIEW OF THE LITERATURE

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Purpose: Perivascular epithelioid cell tumor (PEComA) family includes different morphologic entities originating from perivascular epithelioid cells. Their clinical behaviour is not predictable and there are not strict histological criteria of malignancy, although larger tumours with initiatory growth, hypercellularity, cellular atypia, mitotic activity with atypical mitoses and necrosis, generally have a malignant course. Pediatric PEComas are rare, with less than 40 cases reported, mostly in children older than 5 years.

Method: We report a case of a rare form of PEComa of the legamentum teres, in a 2 year old girl, characterized by the occurrence of local relapse, after primary treatment with conventional chemotherapy and surgery, and poor response to imatinib mesilate and finally temsirolimus, utilized after further histopathological analyses confirmed the expression of the p70S6K being the common one in the mTOR pathway. The girl was eventually treated with a debulking surgical procedure and is now alive with disease at 6 years from diagnosis. Data of children affected by this tumor were also obtained from the literature, and analyzed to possibly find pathologic characteristics, that could predict their natural history and therapeutic options.

Results: PEComas in childhood differ from those occurring in adults and, from a histological point of view, may be differentiated in 3 prognostic categories: benign, lacking any unfavourable morphologic marker; intermediate, carrying 2 or more unfavourable prognostic markers, malignant, characterized by unfavourable morphologic features, typical of abdominal-skeletal sarcomas. In literature, 9% of cases occurred as second malignancy, probably due to genonic instability related to previous chemotherapy.

Conclusion: Their different biological characteristics and the potential value of targeted therapies remains to be explored. The indolent evolution and outcome in our patient were similar to those in the group of patients from the literature. In terms of treatment, the present case suggests a minor response to temsirolimus compared to the adult population.
Method: Case report
Results: A ten month old female presented with a single scalp lesion. After initial excision confirming a local recurrence, with additional multiple bony lesions four months later. No other organs were involved. Therapy was initiated using LCH III. New skin LCH lesions developed during therapy, and initiation therapy was repeated. While her bony lesions improved, she developed MS disease five months into maintenance therapy. There was laboratory and bone marrow evidence of hemophagocytic syndrome and biopsy proven disease in the GI tract and liver. The liver biopsy also showed evidence of juvenile xanthogranuloma. An extended cytobine profile at several time points showed markedly increased levels of the pro-inflammatory cytokines IL-6 and IL-8 (20 and 60 times over control, respectively) and a fourfold increase in MCP-1 and IP-10, which mediate powerful chemo attraction and adhesion of inflammatory cells. The child sequentially received cladribine/cytarabine/pulse methylprednisone (MP), etoposide and alemtuzumab. Her condition showed transient improvements followed by deterioration. She suffered a fatal acute intracranial hemorrhage despite platted support and TPO. Autopsy revealed diffuse histiocytic infiltration of the spleen, lymph nodes and bone marrow with focal infiltration of lung, heart, gastrointestinal mucosa and pericardial tissues.
Conclusion: SS LCH is associated with a favorable prognosis. Therapy is aimed at minimizing morbidity while avoiding excess therapy. Rarely these patients progress to a refractory MS disease. We propose that our approach of including the analysis of serum biomarkers will help to better understand the biology of the disease and to identify targeted therapeutics for more efficacious salvage regimens for refractory LCH in the future.

PL011

THE INTERNATIONAL ONLINE REGISTRY OF RARE, CUTANEOUS AND CNS LYMPHOMAS OF CHILDHOOD

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Purpose: Certain types of lymphomas (follicular lymphoma, small cell lymphoma, marginal zone lymphoma, mantle zone lymphoma etc.) are rare in childhood. Also, CNS lymphomas and skin lymphomas are also relatively rare in childhood. The project objective is to study clinico-pathologic correlations and analyse prognostic factors in rare lymphomas, CNS lymphomas and skin lymphomas in children (i.e. in the fragile population), further standardisation of therapy protocols.

Method: Starting international database/registry in Brno (under auspices of I-BFM) is being designed as a virtual site which will collect all diagnostic and clinical information by means of filling the on-line accessible (but secured by codes) forms, placed on the web site of the database/registry. A part of the database/registry will be freely accessible www atlas of microscopic/histologic images (on-line virtual microscope). Data will be acquired interinstitutionally and internationally by means of filling of secured web forms (initial data will be put along with sending a case by cooperating institution, follow-up data will be added progressively). After collection of statistically significant amount of cases from one type of lymphoma, data will be analysed. Information about cases will be supported by web atlas. The atlas will contain free online accessible high resolution diagnostic images of histology of every case with short English description (high resolution virtual microscope) which can help to histopathologists in making the right diagnosis.

Results: After collecting significant amount of cases from cooperating institutions there will be statistical analysis of clinico-pathologic correlations and analysis of prognostic factors.

Conclusion: The project will enable a study of prognostic factors, clinico-pathological correlations and standardisation of therapy protocols in rare lymphomas of childhood, in CNS lymphomas of childhood and in skin lymphomas of childhood (i.e. in fragile population) by means of interinstitutional/international database/registry shared on secured web site (www.rarelymphomas.eu).

PL012

FAMILIAL ADENOMATOUS POLYPOSIS WITH CONCURRENT APPENDICEAL CARCINOID WITH METASTASIS AND OVARIAN CYSTADENOMA

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Purpose: Appendiceal carcinoid (AC) is rare in childhood. We report a previously unreported concordance of AC with familial adenomatous polyposis (FAP) and ovarian cystadenum.

Method: NA

Results: A 17 year old female with FAP underwent subtotal colectomy with ileosigmoid transposition. Interestingly, the appendiceal tumor showed a 1 cm tumor with monomorphic cells, round nuclei, rare nucleoli, and cosinophilic cytoplasm. The diagnosis of AC was confirmed by expression of neuroendocrine markers. It invaded though the muscularis propria into the suberosal adipose tissue. Two out of 30 regional lymph nodes were positive for carcinoid metastasis. The ovary showed a unilocular cyst lined by cubical epithelium without cytological atypia or invasion and the diagnosis of serous cystadenum was made. The patient has been closely followed-up with imaging and surveillance endoscopies since. At 84 months, she remains free of carcinoid recurrence.

Conclusion: Carcinoids with metastasis are extremely rare and right hemicolecotomy has been deemed adequate for these in adult studies. Although follow-up guidelines are unclear, in view of FAP, our patient had regular endoscopic and imaging follow up, which may not be routinely necessary for AC. To the best of our knowledge it is apparent no clear-cut genetic link between carcinoids and FAP. Adenomatous polyposis coli (APC) has a definitive role in FAP, however, these kindred has tested negative for APC gene mutations. K-ras mutations have been identified in serous cystadenum while its role is unclear in appendiceal carcinoids in which p53 has been implicated. Repeat analysis for APC and allied mutations, including K-ras and p53, and further research into the association of carcinoids with polyposis coli and ovarian cystadenum may be warranted.

PL013

LIVER INVOLVEMENT AND PROGNOSTIC EFFECT IN LANGHERHANS CELL HISTIOCYTOSIS

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Purpose: To evaluate liver involvement and its prognostic effect in patients with Langherans Cell Histioctysis (LCH).

Method: Between 1972 and 2005, the patients with LCH were retrospectively evaluated in terms of liver involvement. Hepatomegaly was noted. Elevated liver transaminases, prolonged prothrombin and partial thromboplastin time, hyperproteinemia (total protein < 5.5 g/dl, albumin < 2.5 g/dl), hyperbilirubinemia (total bilirubin > 1.5 mg/dl), ascites, hepatomegaly were accepted as liver involvement. The other organ involvements were also investigated.

Results: 40 patients with liver involvement out of 255 patients diagnosed as Langerhans cell histiocytosis were detected. Male/female ratio was 22/18 (1.2) and median age was 1.5 years. 12 (30%) patients were over 2 years of age. Liver involvement was part of the systemic involvement in all 40 patients. Eleven patients (27.5%) had elevated transaminases, 9 (22.5%) with hepatosplenomegaly, 5 (12.5%) with hepatomegaly, 2 with hyperproteinemia, one patient each with abnormal PT/aPTT and hyperbilirubinemia, respectively. 11 cases had multiple abnormalities. All patients were treated with chemotherapy. Overall (OS) and event-free survival rates were 54% and 25%, respectively. OS was 89% in patients with elevated transaminases, 42% in hepatosplenomegaly, 100% in hepatomegaly, 0% in multiple abnormalities (p = 0.0003). Two patients with hyperproteinemia, and patients with abnormal PT/aPTT and hyperbilirubinemia died with disease. OS was 38% in patients under 2 years of age.

Conclusion: Liver involvement was a poor prognostic factor in patients with LCH. Hepatosplenomegaly, abnormal PT/aPTT, hyperproteinemia, elevated transaminases had worse prognosis than isolated hepatomegaly.

PL014

AURORA KINASE INHIBITION AS A POTENTIAL NEW THERAPEUTIC STRATEGY IN CHILDHOOD ADRENOCORTICAL TUMOR

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Purpose: Adrenocortical tumors (ACT) are rare malignancies, corresponding to only 0.2% of all pediatric cancers, being the majority of the cases diagnosed in Brazil and related to TP53 mutation R337H. Advanced stages of this tumor have been associated with poor prognosis. Recently, our group showed the association between aurora kinases A and B expression and unfavorable event (relapse or death) in 60 childhood adrenocortical tumors (ACT). The aurora kinases have been widely studied in several human cancers as potential therapeutic targets. In this study, we analyzed the effects of different concentrations of ZM447439 (ZM) (a pan-aurora kinases inhibitor) in an adrenocortical carcinoma cell line (Y1) and in a primary culture of pediatric adrenocortical carcinoma (PACC).

Method: Functional studies of cell proliferation, clonogenic survival and apoptosis were performed in triplicate at two different moments. Statistical analysis was made by one or two-way ANOVA and Bonferroni post hoc. To calculate the doses with 50% inhibition of
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proliferation (Dm or IC50 values) were analyzed by the median-effect method (CalcuSyn software; Biosoft, Ferguson, MO).

Results: Both cell lines were sensitive towards ZM showing a concentration-dependent inhibition of proliferation after treatments (P < 0.05). It was observed time effect difference of proliferation between 24h and 48h (P < 0.05), but not between 48 h and 72 h. The IC50 values were of 9.2±2.2 and 15.1±7.1 to Y1 and PACC respectively. ZM caused an inhibition of colony formation of PACC cells, reaching a maximum effect at dose of 0.1μM (P < 0.05).

ZM causes apoptotic death in Y1 cells, where the percentage of apoptotic cells significantly increased after treatment of 10 and 20μM compared to DMSO control (P < 0.05).

Conclusion: These data suggest that aurora kinase inhibition could be a promising candidate for further therapy. ACT-outcome studies should be conducted to confirm this potential, mainly in animal models.

PI015

INCIDENCE, OUTCOMES, AND PROGNOSTIC FACTORS IN CHILDREN WITH ADRENOCORTICAL CARCINOMA (ACC): RESULTS OF A LONG-TERM FOLLOW-UP STUDY ON 271 CASES - A SURVEILLANCE EPIDEMIOLOGY AND END RESULT (SEER) DATABASE STUDY

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Purpose: The primary objective of this study was to describe the clinical and biologic features of recently diagnosed ACC cases in a large, population-based SEER database.

Method: This study was based on the SEER database. All cases of primary ACC diagnosed between 1973 and 2009 in 17 US regions were included. The date of diagnosis, age, race, sex, site of primary tumor and of metastases, histological type, tumor characteristics, treatment modalities, and outcome were recorded. Kaplan-Meier methods and univariate and multivariate Cox proportional hazards models were used to identify factors associated with survival.

Results: Of 271 cases, 161 (60%) were diagnosed between 1995 and 2009. The median age at diagnosis was 4 years (range 0.01-18). ACC was rare in children, with an average annual incidence of 0.03 per 1,000,000. ACC was more common in boys (55%). ACCs were most common in whites (61%). ACCs were described in 9 European and 7 Asian countries. The most common histological types were type A (78%), type AB (12%) and type B (10%). The most common synchronous metastases were in the lungs (28%), liver (23%) and bone (19%). ACCs were more common in males and whites. ACCs in males were younger at diagnosis and had a better survival rate. ACCs were more common in whites. ACCs in whites were younger at diagnosis and had a better survival rate. ACCs were more common in males and whites.

Conclusion: ACC is rare in children. ACCs are more common in males and whites. ACCs are more common in whites and males. ACCs are more common in whites and males.
Cyclophosphamide has a steep dose-response curve making it a good candidate for treatment of hemangioma. 12 patients underwent treatment for more than 3 months, and symptom improvements were observed in 9 patients. Lesions completely disappeared in 20% of patients. 1 patient developed refractory responses to treatment after starting propranolol and hence it was stopped. No other side effects were noted in the 12 patients.

Conclusion: Although larger studies are required to confirm, our study concludes that propranolol is a promising therapeutic option in the treatment of hemangioma.

PL019

PHARMACOKINETICS OF HIGH-DOSE CYCLOPHOSPHAMIDE AND ITS METABOLITES IN PAEDIATRIC PATIENTS

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Purpose: Cyclophosphamide has a steep dose-response curve making it a good candidate for dose intensification. The purpose of this pharmacokinological study performed in children with metastatic soft tissue sarcoma was to better understand the impact of high-dose on the pharmacokinetics and metabolism of cyclophosphamide.

Method: Patients received four courses of chemotherapy including two courses of high-dose cyclophosphamide. Plasma concentrations of cyclophosphamide and the metabolites 4-ketocyclophosphamide (KetoCP), dechloroethylcyclophosphamide (DCCP) and carboxyphosphamide (CXCP) were determined on days 1, 2 and 3 of each course. A population pharmacokinetic model for cyclophosphamide was developed using nonlinear mixed effects modelling and metabolite AUC values compared between days and courses.

Results: Data were available on 21 cyclophosphamide courses from 15 patients. A one compartment model, incorporating a term in surface area for both Clearance (CL) and Volume of distribution(V), best described cyclophosphamide pharmacokinetics. Typical CL and V values were 0.56 L/h and 164 L, respectively. On day 1, CL increased by 14% (95% CI, 5–23%) on days 2 and 3. V tended to be larger for males than similarly sized females but no effect of age was found upon CL or V. Significant increases in metabolite AUCs were observed on days 2 and 3 compared to day 1 and a significant increase in CXCP AUC from course 1 to course 3.

Conclusion: Administration of high-dose cyclophosphamide over several days results in an increase in metabolism, possibly by induction of the activation pathway. This induction is effectively reversed following a four week period between cyclophosphamide doses. The degree of intersubject variation in cyclophosphamide elimination is largely accounted for by body surface area and is less than previously reported.

PL020

A CASE SERIES OF PAEDIATRIC HAEMOPHAGOCYTIC LYMPHOPHISTIOCYTOSIS: A SINGAPORE HOSPITAL’S EXPERIENCE

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Purpose: Haemophagocytic lymphohistiocytosis (HLH) is a rare but rapidly fatal disease affecting children of all ages. Primary and secondary forms of HLH have been well described. This study aimed to review the presentations, epidemiology, causes, morbidity and survival outcomes of paediatric HLH in Singapore.

Method: The study is a retrospective descriptive review of cases of HLH captured in the Children’s Cancer Registry, presenting to KK Women’s and Children’s Hospital from 2006 to 2011.

Results: There were 7 cases of HLH diagnosed from 2006 to 2011. 2 were female and the remaining 5 were male. The ages at presentation ranged from 2 months to 9 years old. 1 case was familial and the remaining 6 cases were secondary HLH. 3 had microbiological evidence of EBV infection, 1 developed EBV associated diffuse large B cell lymphoma whilst on chemotherapy, and 1 child had underlying autoimmune lymphoproliferative syndrome. All were extensively worked up with microbiological, abdominal imaging and autoimmune investigations. 3 children had neurological involvement during treatment presenting with seizures, encephalopathy and/or visual loss. Brain imaging with CT or MRI were done when the children were symptomatic. The time from diagnosis to commencement of treatment ranged from 4 to 22 days (mean 14 days). All but one were treated with HLH 2004 protocol. Outcome with HLH 2004 protocol was excellent 1 mortality occurred in a child who was treated with only immunosuppressive therapy.

Conclusion: HLH often presents as a diagnostic dilemma for fever of unknown origin. A delay in diagnosis often results in significant morbidity and mortality. Diagnosis was made fairly early in our centre, with commencement of treatment within 2 weeks on average. Neurological sequelae is significant in HLH especially familial forms. Neurological sequelae may also appear as a treatment related complication. The survival outcomes with HLH 2004 appear to be excellent in our case series.

PM001

DEHYDROXYMETHYLEPOXYQUINOMICIN EFFICIENTLY SUPPRESSES GROWTH AND INDUCES APOPTOSIS IN PEDIATRIC AND ADULT GLOBLASTOMA CELL LINES

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Purpose: Glioblastoma (GBM) is the most aggressive primary brain tumor accounting for 50% of adult gliomas. In children is much rarer comprising only 5%–10% of childhood intracranial neoplasms. Nonetheless, despite the improvements in neurosurgery, radiation
PM002 METRONOMIC AND TARGETED ANTIANGIOGENESIS THERAPY FOR CHILDREN WITH RECURRENT EMBRYONAL BRAIN TUMORS
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Purpose: Median survival time of recurrent embryonal brain tumors is short regardless of anti-tumor and chemosensitizing properties. The effects of NF-kappaB inhibition by DHMEQ in vitro were evaluated in T98G and LN319 glioblastoma cell lines by means of proliferation (XTT assay), viability (Trypan Blue assay), clonogenic capacity (Escherichia coli, Bacillus subtilis) and apoptosis (Annexin V assay). Cells were treated with different concentrations of DHMEQ for 24, 48, 72 hours and 7 days. All experiments were performed on triplicates and results compared by one-way ANOVA followed by Bonferroni tests.

Results: DHMEQ treatment resulted in cell proliferation arrest in dose and time-dependent manner when compared with control for all GBM cell lines. Cell viability and clonogenicity were also significantly diminished with the consequent increase of apoptotic cells. When combined with TMZ, the drugs showed synergy compared to TMZ treatment alone, except for the two cell lines (T98G and LN319) that express O6-methylguanine-DNA methyltransferase (MGMT). However, pre-treatment with DHMEQ for 6 h showed to efficiently sensitize these cells to TMZ.

Conclusion: Our results show the anti-tumor effect of DHMEQ and its ability to sensitize TMZ-resistant variants suggesting being a good candidate for a new chemotherapeutic agent against GBM.

PM004 LONGITUDINAL MODELS OF COGNITIVE FUNCTION IN CHILDREN WITH CRANIOPHARYNGIOMA DEMONSTRATE THE EFFECT OF RADIATION DOSE
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Purpose: To estimate the association between radiation dose and cognitive function in children with craniopharyngioma treated with conformal and intensity-modulated radiation therapy. Seventy children (median age 8.5 yrs, range 3.2–17.6 yrs) with craniopharyngioma were prospectively evaluated for cognitive effects after receiving conformal or intensity-modulated radiation therapy (54 Gy) between 1998 and 2009. Mean dose was calculated for the entire brain and specific sub-volumes. There were 57 children who were white, 36 females and 25 with CSF shunts. A battery of age-appropriate cognitive tests was administered at baseline, 6 months and annually up to 10 years. Linear mixed effects models were used to model the longitudinal cognitive variables, dose to specific brain regions and various clinical variables.

Results: No association was detected between radiation dose and modeled scores of IQ; however, race (P = 0.0007) and CSF shunting (P = 0.0024) were significant where white race and lack of CSF shunt were associated with higher baseline IQ scores. A quadratic trend was detected in our longitudinal IQ data with negative linear (P = 0.0001) and positive quadratic coefficients (P < 0.007). Older age at radiation was associated with higher longitudinal IQ scores (P = 0.0001). Baseline math scores were associated with race (P = 0.0085) and CSF shunt status (P = 0.0108). Longitudinal math scores were associated with the interaction of mean whole brain dose and time (P = 0.0127). White race was associated with higher (+11.34 points) baseline scores and presence of CSF shunt was associated with lower baseline scores (-8.67 points). The mean whole brain radiation dose and time interaction coefficient was negative with an estimated average loss of 0.00227 points/Gy/year.

Conclusion: Modeling radiation dose and relevant clinical variables with cognitive test scores provides important information about the effect of radiation therapy on cognitive outcomes in children with craniopharyngioma. This information may be used for risk stratification when evaluating treatment options and the effects of newer treatment methods.

PM003 SIX-MONTH MORTALITY IN CNS TUMORS IN CHILDREN: DATA FROM THE ARGENTINEAN PEDIATRIC ONCOLOGY REGISTRY ROHA - NATIONAL RESEARCH IN CANCER
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PM005 LOOKING THROUGH THE PATIENT’S EYES
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Purpose: Magnetic Resonance Imaging (MRI) is currently used to evaluate progression or response to therapy in low grade gliomas involving the optic pathway. Determining what the patient sees is the crux of success for intention to treat. In patients who present with poor vision, the need to save minimal vision becomes even more crucial. Thus, accurate visual
function testing becomes even more important in order to apply the ideal treatment without compromising the disease outcome.

Method: We reviewed the MD Anderson Cancer Center experience over the last 5 years of patients with low grade gliomas involving the optic pathway. Patients with and without Neurofibromatosis 1 were included. Serial ophthalmologic examinations assessing anatomic (optic nerve pallor and cupping, retinal nerve fiber thickness) and functional criteria (relative afferent papillary defect, color vision and visual acuity, confrontation visual field testing, Humphrey visual field testing, 30-2 degree Amsia tests) were plotted for each patient. Comparison was made on a 1:1 basis of MRI findings and ophthalmologic findings between interventions or observation periods.

Results: MRI findings did not always correlate with visual outcome in the majority of our patients. We found that accurate visual function testing in addition to MRI is more predictive of the patient’s functional status. In our analysis, those with poor vision at presentation required a refined ophthalmologic exam to assess response to treatment.

Conclusion: Accurate visual function testing in glioblastoma to MRI is a better measure for intention to treat or determine response. Patients with optic pathway gliomas have a spectrum of visual function. We found that those with poorer vision at presentation required more accurate visual function testing to determine when treatment modifications were necessary.

PM006

ATYPICAL TERATOID/RHABDOID TUMOR AND MALIGNANT SCHWANNOMATOSIS. A FAMILY MATTER: THE CLINICAL PRESENTATION OF INI-1 MUTATION: PRESENTATION OF 3 CASES AND REVIEW OF LITERATURE

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Purpose: Loss of expression of INI-1 has been identified as a distinguishing molecular feature of atypical teratoid/rhabdoid tumors (AT/RT) and other malignant rhabdoid tumors (MRT). Loss of INI-1 expression is associated with both renal and extrarenal malignancies. It is observed most commonly in the pediatric population but is noted in adults. Clinical presentation is unclear and its presence underreported due to overlap with primitive neuroectodermal tumors and rhabdoid tumors.

Method: We report three cases of INI-1 gene mutation and its clinical manifestations within one family. In our series the de-novo INI-1 gene manifested as malignant schwannomatosis in an adult. Inherited INI-1 gene mutations manifested as AT/RT in two children.

Results: In 2004, a seven-month old boy presented with a posterior fossa AT/RT. He received surgical resection, systemic chemotherapy and local radiotherapy but subsequently succumbed to his disease in 2005. In 2010, his mother presented with a malignant peripheral nerve sheath tumor in her leg. Investigations revealed the presence of a de novo INI-1 gene mutation in the mother’s tumor. Subsequent testing of the child’s AT/RT tumor showed the same mutation. Genetic counseling was offered. Since the first child’s death, they had two more children, one in 2007 (female) and one in 2009 (male). Testing identified the mutation in both children. Screening with brain MRI and abdominal ultrasonar was recommended. One week prior to the baseline surveillance scan, the nineteen month-old son presented with neurological symptoms and was diagnosed with a posterior fossa AT/RT. He had complete surgical resection, is currently undergoing systemic chemotherapy and recently completed radiotherapy. The other child is well with negative screening investigations.

Conclusion: In one family we note two pediatric cases of AT/RT and one adult case of malignant peripheral nerve sheath tumor with loss of INI-1 expression. The significance of INI-1 mutation in both the pediatric and adult population needs further investigation.

PM007

CAN ZEBULARINE BE AN ALTERNATIVE DRUG TO TEMOZOLOMIDE RESISTANT GlioBLASTOMA?

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Purpose: Gliomas are one of the most common childhood tumor of central nervous system and they are classified in grades I to IV. Besides attempts with new treatments strategies, patients with gliomas grade IV (glioblastoma) still have poor prognosis. Radiotherapy plus temozolomide increases glioblastoma survival, but patients with high levels of MGMT (O6-methylguanine-DNA methyltransferase) do not respond to temozolomide and needs another chemotherapeutic agent that sensitizes glioblastoma cells to radiotherapy. Zebularine is a novel melanin inhibitor that showed promissory effects in hematological and many solid tumors but little is known about the effects of this drug in glioblastoma. The objectives of this study were to analyze MGMT gene expression in glioblastomas, normal brain, glioblastoma cell lines and verify the effects of zebularine and temozolomide in glioblastoma.

Method: MGMT gene expression was analyzed by real-time PCR in 16 consecutive microdissected glioblastomas, 5 non-neoplastic brain samples, 6 glioblastoma cell lines. Cell lines U251, SF188 and T98G were treated with zebularine (25–300 uM) and temozolomide (5–500 uM). Functional studies of cell proliferation (24–48-72hs), clonogenic survival and apoptosis were performed in triplicate at two different moments. Statistical analysis was made by ANOVA for functional studies and Mann-Whitney for gene expression.

Results: It was observed higher expression of MGMT in normal brain compared with glioblastoma (p = 0.001) and cell lines (p = 0.002). Among cell lines studied, T98G has higher levels of MGMT and presented resistance to temozolomide. Zebularine decreases MGMT expression, cell proliferation, colony formation and increases apoptosis in T98G, SF188 and U251 glioblastoma cell lines.

Conclusion: These data suggest that zebularine may be a potential alternative drug to glioblastoma with high levels of MGMT but others experiments are necessary to confirm the eficacy of zebularine in glioblastoma.

PM008

ENDOCRINE, HYPOPHTHALMIC AND NEURO-DEVELOPMENTAL OUTCOMES FOLLOWING TREATMENT OF CRANIOPHARYNGIOMAS

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Purpose: Craniopharyngiomas (CP) are rare benign pituitary-related tumours whose surgical excision and invasive nature may cause significant neuro-endocrine morbidity and premature mortality. To determine whether an age- and risk-based conservative surgical management approach avoiding further hypothalamic compromise has improved hypothalamic, endocrine and neuro-developmental outcomes at our centre in the last decade.

Method: Retrospective case-note analysis of 33 patients (13 males) of median age 8.13 (2.0–15.8) years with confirmed CP diagnosis between 01/01/1998 and 31/07/2009 and median follow-up of 6 (1.0–12.1) years. Patients had either debulking (open) surgery +/- radiotherapy (DXT = GaP18), debulking (stereotactic) radiosurgery +/- DXT (GpN4), or non-debulking (conservative) cystic aspiration +/- DXT (GpN11) at diagnosis. 20/33 patients had DXT. Endocrine, Hypothalamic (including Obesity) and Neuro-developmental morbidity (MS) was scored out of a maximum of 15, according to DeVile et al 1996 for historical CP comparison, higher scores implicating worse outcomes.

Results: 14 (42.4%) patients recurred, 5-year EFS was 50%. MS score rose [mean +2.76 (95% CI 1.99–3.53); p < 0.05] from diagnosis to last follow-up. Patients were heavier than normal at diagnosis [BMI 1.13 SDS (95% CI 0.54–1.71)], but there was further increase [to 2.08 SDS (95% CI 1.67–2.49) with time with an average gain of 0.953 SDS; (95% CI 0.534–1.39; p < 0.005)], 6 patients were hyperphagic, 5 sleep disorders, 2 had temperature dysregulation and 7 registered blind. All 33 (100%) patients had 1 or more pituitary endocrinopathies most commonly GHD (93.9%) and least commonly D1 (54.5%) and ACTH deficiency (75.8%). 24% needed school support.

Conclusion: Compared with our centre’s previous 1996 series, these outcomes demonstrate a decrease in life-threatening DI (54% vs. 80%) and ACTH deficiency (75% vs. 85%) in survivors from a conservative management, and a similar EFS rate. Obesity however remains a problem which is set at diagnosis.

PM009

PERSONALIZED TARGETED THERAPY FOR REFRATORY PEDIATRIC BRAIN TUMORS

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Purpose: Traditional study designs have proven ineffective to solve many of the problems when trying to cure children with brain tumors.

Method: For pediatric patients with brain tumors that proved to be refractory to standard treatments, individualized protocols were designed based upon the patient’s treatment history and histology specific drug rankings. In addition, each tumor was analyzed with morphoproteomics using a panel of markers to show treatment targets, resulting in novel drugs to be added to the standard chemotherapy cycle.

Results: Eleven (11) treatment protocols were designed using morphoproteomic information and given to eight (8) patients. The histological diagnoses included: medulloblastoma (n = 3), glioblastoma multiforme (GBM, n = 2), atypical teratoid rhabdoid tumor (ATR, n = 1), chordoid plexus carcinoma (n = 1), and supratentorial primitive neuroectodermal tumors. Follow-up was 18 months. All patients achieved tumor control or improvement.
tumors (PNET, n = 1). The markers resulting in the final treatment decision included p-ERK, Topo IIa, Bcl-2, VEGF-A, p-STAT3, ER-beta, m-TOR/C1, and p-NF-kappaBp65. The drugs chosen included Sorafenib, Bevacizumab, Fulvestrant, Rapamycin, Bortezomib, and Curcumin given in combinational fashion with multiple other drugs. The response to the first protocol on the program was CR: 1, PR: 1, SD: 0, PD: 4, and continuous complete remission 2. The median Event Free Survival (mEFS) after the first targeted treatment was 0.35 (± 0.216). For the comparison with the control group, the individual response probability was calculated based upon ordinal regression from the institutional historical data. The histological diagnosis, measurable tumors at treatment start, recent previous treatment and the growth of the tumor prior to treatment turned out to be relevant cofactors in that analysis. Targeted treatment protocols appeared superior in this comparison (p = 0.006 Whitman U test).

Conclusion: We conclude that the concept should continue, be evaluated comparing response to institutional controls in a risk factor adopted computed.

PM010 EVALUATION OF ANTI-NEOPLASTIC EFFECTS OF INHIBITION OF NFkB BY DHMEQ (DEHYDROXYMETHYLEPOXYQUINOMICIN) IN PEDIATRIC MEDULLOBLASTOMA CELL LINES
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Purpose: Medulloblastoma (MB) is the most common malignant central nervous system tumor of childhood representing 15–30% of pediatric brain tumors. DHMEQ is a drug that has shown a low toxicity and high activity in blocking the NF-kappaB, a key transcription factor that control the expression of a large number of genes related to cell proliferation, growth and apoptosis, showing antineoplastic effects in several cancer cell lines. Despite this, there are no reports showing the effects of DHMEQ in MB.

Method: Functional studies of cell proliferation and clonogenic survival were performed on two pediatric MB cell lines: UW402 and UW473. Statistical analysis was made by one or two-way ANOVA and Bonferroni post-hoc. To calculate the IC50 values, data were analyzed by the median-effect method (CalcuSyn software; Biosoft, Ferguson, MO). All assays were performed in triplicate in two different times.

Results: The proliferation assay was performed with different concentrations of DHMEQ (0, 2.5, 5, 7.5, 10 and 20 µg/mL) at different times (24, 48 and 72 hours). IC50 obtained for the cell lines UW402 and UW473 were 9.87 and 8.58 µg/mL, respectively, at the time of 48h. For the two cell lines, it was found dose effect difference (P < 0.05), and time effect difference to UW402. The clonogenic survival assay was conducted with the same drug concentrations at 48 hours. There was significant relevance after the dose 2.5 µg/mL for both cell lines (P < 0.05).

Conclusion: In this study, we demonstrated anti-proliferation effects and inhibition of in vitro colony formation of NF-kappaB targeting by DHMEQ on MB cells, which proves the biological importance of the NF-kappaB targeting in MB cells. Therefore, we suggest DHMEQ as a promising candidate for molecular target therapy of MB. These results need further investigation.

PM011 DIFFUSION TENSOR IMAGING IN COGNITIVE DEFICITS IN CHILDREN TREATED FOR POSTERIOR FOSSA TUMOURS
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Purpose: Cognitive deficits are frequently observed in surviving children treated for posterior-fossa tumours, they are supposed to be due to microstructure brain white matter alterations which are not depicted by conventional MRI. Our purpose is to evaluate brain white matter integrity in these children, using diffusion tensor imaging (DTI).

Method: Seven patients (aged from 7 y – 11 m to 15 y – 3 m) were included in a retrospective study. The design of this study consisted in a neuropsychological evaluation and a 16 directions DTI acquisition. A group of 7 age-matched control subjects was also enrolled. DTI data sources were transferred and post-processed off-line using FMRIB Software Library (FSL) tools. Voxelwise statistical analysis of the FA and diffusivity data was carried out using Tract-Based Spatial Statistics, part of FSL. In order to identify difference between patients and controls, the skeletonised data were fed into a nonparametric permutation two-sample t-tests for both contrasts (controls > patients) and (controls < patients), using Randomise, part of FSL.

The separate analysis of the eigenvalues reflecting respectively axial and radial diffusion showed decreased values in patients in more restricted locations, in axial diffusion: the left corpus callosum, the left parietal white matter and the bilateral temporoparietal junction and in radial diffusion: the bilateral corona radiata, the left fronto-parietal white-matter and the splenium of the corpus callosum.

Conclusion: These results evidenced white matter alterations in patients with normal conventional MRI and could reflect different pathophysiological processes, i.e. remyelination for radial diffusion decrease and reduced axonal diameter for axial diffusion decrease induced by the disease itself and its treatments especially radiotherapy.

PM012 EVALUATING PERSONALIZED MEDICINE: EXPERIENCE IN NEUROONCOLOGY
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Purpose: New ways to analyze data are necessary to evaluate personalized therapy, since prospective randomized trials and the biomathematics developed for them have maxed out the information they can provide.

Method: In clinical practice we use a standardized algorithm to develop personalized targeted therapies for children with brain tumors which are proven to be refractory to conventional treatment protocols. This includes conventional drugs, as well as targeted drugs based on morpho(proteo)mic evaluations of tumor tissue. Here we tested various ways to analyze the outcome.

Results: Eleven treatment protocols were designed using morphoprotemic information. The targeted drugs chosen included Sorafenib, Bevacizumab, Fulvestrant, Rapamycin, Bortezomib, and Curcumin given in combinational fashion with multiple other drugs. The response to was CR: 1, PR: 1, SD: 0, PD: 4 and continuous complete remission 2. The median Event Free Survival (mEFS) after the first targeted treatment was 0.35 years (+/- 0.216). For the comparison with the control group, the individual response probability was calculated based upon ordinal regression from the institutional historical data. The histological diagnosis, measurable tumors at treatment start, recent previous treatment and the growth of the tumor prior to treatment turned out to be relevant cofactors in that analysis. Targeted treatment protocols appeared superior in this comparison (p = 0.006 Whitman U test). In contrast, comparing the progression free survival time after targeted protocols to those given before in the same patients confirmed the tendency but not the significance (p = 0.12 Paired t-test).

Conclusion: We conclude that the concept should continue, be evaluated comparing response to institutional controls in a risk factor adopted computed. The algorithm defining which drug should be used in which marker pattern is the most important aspect to be developed and to be evaluated this way.

PM013 MESENCHYMAL TRANSITION AND PDGFRα AMPLIFICATION/MUTATION ARE KEY DISTINCT ONCOGENIC EVENTS IN PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMAS
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Results: Patients exhibited a diffuse decreased mean diffusion (MD) compared to controls. The separate analysis of the eigenvalues reflecting respectively axial and radial diffusion showed decreased values in patients in more restricted locations, in axial diffusion: the left corpus callosum, the left parietal white matter and the bilateral temporoparietal junction and in radial diffusion: the bilateral corona radiata, the left fronto-parietal white-matter and the splenium of the corpus callosum.

Conclusion: These results evidenced white matter alterations in patients with normal conventional MRI and could reflect different pathophysiological processes, i.e. remyelination for radial diffusion decrease and reduced axonal diameter for axial diffusion decrease induced by the disease itself and its treatments especially radiotherapy.
**PM014**

**METABOLIC SYNDROME AS COMMON ENDOCRINOLOGY LATE EFFECT IN MEXICAN CHILDREN TREATED WITH A CENTRAL NERVOUS SYSTEM TUMOR: REPORT OF A SINGLE MEXICAN INSTITUTION.**

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**Purpose:** General survival in children affected with cancer is nearly 80% of many of them will have late effects during their follow-up. Among survivors, children treated with Central Nervous System Tumors (CNST) have proclivity to endocrinology disturbances mainly hormonal alterations since over 300 genes are detected when analysing correlation between GHG and GE data. Moreover, tumours from this group show proneural profile according to adult glioma classifications and worse prognosis when compared to the first group.

**Conclusion:** Primary glioma xenografts bearing these amplifications/mutations and PDGFRα driven GE profile were sensitized to radiotherapy by treatment with the PDGFRα inhibitor imatinib, showing a spectacular efficacy of this synergetic treatment and providing the rationale for future trials.

**PM015**

**ENDOCRINE AND HYPOTHALAMIC OUTCOMES FOLLOWING TRANSPHENOIDAL AND TRANSCRANIAL SURGERY IN SELECTED PAEDIATRIC PATIENTS WITH CRANIOPHARYNGIOMA AT A SINGLE INSTITUTION ARE COMPARABLE**

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**Purpose:** To address the paucity of understanding of diffuse intrinsic pontine glioma (DIPG).

**Method:** We have carried out integrated medical records analysis of a large series of cases obtained through stereotactic biopsy at diagnosis, comprising CGH and GE profiles.

**Results:** Gene expression profiling revealed clear differences between DIPG and supratentorial high grade gliomas, with brainstem gliomas resembling midline/hyalamic tumours, indicating a closely-related origin and justifying a dedicated study for DIPG. An unsupervised procedure, named K-means, identified two distinct subgroups of DIPG, with distinct survival curves. One displayed mesenchymal and pro-angiogenic characteristics, with stem cell marker enrichment, and 3 genes statistically correlated with CGH and GE data, suggesting that, in this group, oncogenesis is not driven by chromosomal aberrations. The other group displayed oligodendrogial features, and appeared largely driven by PDGFRα, in particular through gain and amplification with corresponding GE signature and/or novel missense mutations in the extracellular domain. This group seems to be driven by chromosomal aberrations since over 300 genes are detected when analysing correlation between CGH and GE data. Moreover, tumours from this group show proneural profile according to adult glioma classifications and worse prognosis when compared to the first group.

**Conclusion:** Metabolic syndrome was the most common endocrinology disturbance on CNST treated patients; we believe that sociocultural aspects could influence this tendency, and this is a very important factor to consider in order to treat them opportunely. We need to revaluate the data to confirm this tendency.

**PM016**

**N-TERMINAL P73 PROTEIN ISOFORMS IN MEDULLOBLASTOMA CELLS AND THEIR INVOLVEMENT IN RETINOIC ACID-INDUCED DIFFERENTIATION**

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**Purpose:** The TP73 gene encodes multiple protein isoforms that have different or even antagonistic roles in proliferation and differentiation both in normal and tumor cells. We have previously shown that DeltaNp73 protein expression is a negative prognostic marker in medulloblastoma [Zitterbart et al., Acta Neuropathol 2007]. Here, we present a detailed morphological study analysing endogenous expression of p53/p63/p73 with special focus on intracellular localization of N-terminal TaP73 and DeltaNp73 protein isoforms in medulloblastoma cell lines. Moreover, the possible role of p73 family signalling in all-trans retinoic acid (ATRA) induced differentiation of medulloblastoma cells was investigated.

**Method:** The reference Daoy and D283 cell lines and four newly established cell lines (MBL-02, MBL-13, MBL-06, MBL-12) were employed in experiments. Immunodetection methods (Western blot analysis, fluorescence and transmission electron microscopy) were used for morphological studies. Expression profiling was performed using Human Cancer Oligo GEArray membranes that cover 440 cancer-related genes.

**Results:** Western immunoblot analysis confirmed constitutive expression of p53 family proteins in medulloblastoma cell lines, which was not affected by use of ATRA at the total protein level. However, both nuclear/ cytoplasmic fractionation and microscopic studies demonstrated heterogeneity in subcellular distribution of TaP73 and DeltaNp73 in different cell lines. DeltaNp73 localization was non-random in cytoplasm of MBL cells. Cluster analyses of the changes in gene expression after ATRA treatment showed GDF15, CDKN1A and HMGA1 up-regulation, whereas CANX, JUND, PRDX4, RBL1, CTNNA1 were down-regulated.

**Conclusion:** These data support the involvement of TP73 family members in medulloblastoma tumorigenesis and have implications for further research in retinoic acid induced differentiation of medulloblastoma cells, with respect to different protein-protein interactions of DeltaNP73.

This study was supported by grant IGA MZCR NS10218-3/2009.

**PM017**

**SILENCING OF CHECKPOINT MITOTIC GENES INHIBITS THE PROLIFERATION AND CLONOGENICITY IN PEDIATRIC GLIOMA CELL LINES**

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**Purpose:** To compare endocrine and hypothalamic outcomes following transphenoidal surgery (TSS) and transcranial surgery (TCS) in paediatric patients with craniopharyngiomas (CP) managed at a single institution.

**Method:** Retrospective case note and neuro-imaging analysis of 22 patients (7 males) of median age 7.92 (0.87–15.87) years with confirmed CP diagnosed between 1995 and 2010, and median follow-up of 6.74 (4.58–12.73) years. Patients either had TSS alone (+/- radiotherapy (DXT) (GpA N8), TCS alone (+/- DXT) (GpB N11) or TCS followed by TSS (at recurrence) (+/- DXT (GpC N3)). Complete tumour resection was achieved in 2 patients; 17/22 had adjuvant DXT. Tumour composition was mainly cystic for patients in GpA (62.5% N8) and mixed (solid & cystic) for GpB (62.5% N8), with a predominant intratumoral cystic location for both groups (100% GpA, 75% GpB). Mean midline tumour heights (GpA 30.38 mm; GpB 38.37 mm; p = 0.416) and volumes (GpA 22.8 mm³; GpB 21.9 mm³; p = 0.928) were similar pre-surgery.

**Results:** 10/22 recurred, and recurrence rates were similar: GpA 37.5%; GpB 36.4%. All patients had at least one pituitary hormone deficiency at last follow-up most commonly GHD and GHRH deficiency (100% for all 3 groups), and least commonly DI (GpA 50%; GpB 55.6%; GpC 100%). Patients developed DI and ACHI deficiency soon after surgery (median 0.5–3.49 years). 12/60% had panhypopituitarism at last follow-up (GpA 55.5%; GpB 50%; GpC 100%), and no post-operative recovery of pituitary function was seen in any patients. Endocrine morbidity scores according to Da Vile et al 1996 were similar (p = 0.44) for all groups. All patients became heavier over time following surgery and patients in GpB were significantly (p = 0.024) heavier (2.61 SDs) than patients in GpA (1.24 SDs) at last follow-up.

**Conclusion:** TSS and TCS have similar endocrine consequences for similar tumour mass and volume, but there is more hypothalamic obesity after TCS.
Glioblastomas are the most common brain tumors in adults and due to their invasive nature they are very difficult to cure. Still, even with all the actual progress in radiotherapy and chemotherapy, glioblastomas have a very poor prognosis with a median survival of 14 months. Several authors have demonstrated differential BUB family genes expression in solid tumors, pointing to a role as putative therapeutic targets. The aim of this study was to analyze the effect of the BUB11 and BUB11B silencing in proliferating glioblastoma cell line on the proliferation and clonogenic capacity.

Method: SF188 glioblastoma cells were transfected with BUB1, BUB1B and negative control siRNA at a concentration of 100nM. The expression of BUB1 and BUB1B were monitored by real-time quantitative PCR. For the experiments combining with temozolomide (TMZ), the drug was added 48 hours after the transfection. Cells were analyzed at 72, 96 and 120 hours after transfection to determine the proliferation rates and 11 days after transfection for the clonogenic assay. The tests were analyzed by oneway ANOVA followed by Bonferroni test. Values of p < 0.05 were considered statistically significant.

Results: BUB1, BUB1B siRNA and BUB1, BUB1B siRNA + TMZ resulted in significantly decreased cell proliferation at 72 and 96 hours compared to the negative control. BUB1 or BUB1B knockdown combined with TMZ was significantly reduced at 120 hours (P < 0.05). In addition, BUB1, BUB1B siRNA and BUB1, BUB1B siRNA + TMZ significantly arrested the clonogenic capacity (P < 0.05).

Conclusion: The results give evidence that BUB1 and BUB1B silencing affects the cellular proliferation and the capacity of cells to form colonies demonstrating the importance of these genes in glioblastoma tumorigenesis. Further studies need to be corroborated our findings.

PM018

EFFECTS OF POLO-LIKE KINESIN 1 INHIBITION ON Glioblastoma CELL LINES

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Purpose: Glioblastoma (GBM) is one of the most frequent and aggressive nervous system tumors and despite treatments with chemotherapy, radiotherapy and surgery, the prognosis remains very poor, with an overall survival of less than one year in most cases. New targets to improve actual treatment are needed, among them the Polo-like kinases have emerged. This family is composed of five members of serine/threonine kinases, PLK1, 2, 3, 4 and 5, that play key roles in several steps during the cell cycle. Polo-like kinase 1 (PLK1) has been shown to be over expressed in different tumors, including GBM, and its expression has been associated with bad prognosis. Polo like kinase 1 (PLK1) inhibitor BI2536 and its combination with Temozolomide (TMZ) has shown to be over expressed in different tumors, including GBM, and its expression has been associated with a bad prognosis.

Method: SF188 and SF188 GBM cell lines were transfected with BUB1, BUB1B and negative control siRNA at a concentration of 100nM. The expression of BUB1 and BUB1B was monitored by real-time quantitative PCR. For the experiments combining with temozolomide (TMZ), the drug was added 48 hours after the transfection. Cells were analyzed at 72, 96 and 120 hours after transfection to determine the proliferation rates and 11 days after transfection for the clonogenic assay. The tests were analyzed by oneway ANOVA followed by Bonferroni test. Values of p < 0.05 were considered statistically significant.

Results: BUB1, BUB1B siRNA and BUB1, BUB1B siRNA + TMZ resulted in significantly decreased cell proliferation at 72 and 96 hours compared to the negative control. BUB1 or BUB1B knockdown combined with TMZ was significantly reduced at 120 hours (P < 0.05). In addition, BUB1, BUB1B siRNA and BUB1, BUB1B siRNA + TMZ significantly arrested the clonogenic capacity (P < 0.05).

Conclusion: The results give evidence that BUB1 and BUB1B silencing affects the cellular proliferation and the capacity of cells to form colonies demonstrating the importance of these genes in glioblastoma tumorigenesis. Further studies need to be corroborated our findings.

PM020

MENINGIOMA AS SECOND MALIGNANT NEOPLASM AFTER ONCOLOGICAL TREATMENT DURING CHILDHOOD AND ADOLESCENCE

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Purpose: Meningioma are rare tumors in childhood and adolescence, representing 1–4% of all intracranial tumors with an incidence of about 0.3 per 100,000. Children and adolescents with meningioma have been recruited prospectively in the German registry HIST-ENDO since 1989. We are reporting on five rare cases of pediatric meningioma that occurred as secondary malignant neoplasia (SMN) after oncological treatment during childhood.

Method: Thirty-eight patients (18/20m) with childhood meningioma were recruited in the German registry HIST-ENDO between 1989 and 2009. In 5 cases meningioma was diagnosed as SMN (2 WHO grade I, 1 WHO grade II, 2 WHO grade III) after treatment of a pediatric oncological disease. Meningioma was diagnosed as a SMN at a median patient age of 12.4 years with median latency of 10.2 years after primary paediatric malignant neoplasm (PMN) (4 brain tumours, 1 ALL, median age at diagnosis: 2.7 years). Meningioma occurred as SMN in the irradiated field of PMN. The outcome after treatment of SMN meningioma (surgery and/or irradiation) was favorable in terms of psychosocial status and functional capacity (FMH score) in 4 of 5 patients of our cohort (1 DOD).

Conclusion: Although the clinical course of meningioma as SMN in childhood was benign in 4 of the reported cases, high doses of radiation at young age should be avoided and other means of therapy should be considered if possible.

PM021

DESCRIPTION OF THE NEUROCOGNITIVE PROFILE OF SCHOOL-AGE PATIENTS AFTER COMPLETING MEDICAL TREATMENT FOR MEDULLOBLASTOMA

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Purpose: To report the neurocognitive profile of school-age children who completed treatment for medulloblastoma focusing on IQ and executive functions.

Method: A prospective, observational, descriptive, cross-sectional study. Measurement instruments: Battery of selected tests from the WISC IV, TOMAL, and CAS, personal interviews. The outcome after treatment of SMN meningioma (surgery and/or irradiation) was favorable in terms of psychosocial status and functional capacity (FMH score) in 4 of 5 patients of our cohort (1 DOD).

Conclusion: Although the clinical course of meningioma as SMN in childhood was benign in 4 of the reported cases, high doses of radiation at young age should be avoided and other means of therapy should be considered if possible.
interviews, medical records, and Graffar scale. Statistical analysis (Stata 9.0). Cognitive variables were correlated with: Hydrocephalus at disease onset, Age at diagnosis, Socio-economic level, Maternal education, Sex, Radiotherapy doses, Cognitive remediation. Cognitive Assessment was made: Median time 59 month (range 11/14) after ending medical treatment.

Results: Study sample (N: 35). Median age: 125 months (range, 70/180) Of all patients, 85% attended normal school; 54% were male. Discrepancies were found between verbal and perceptive reasoning IQ: median (quartile 25–75) 80 (70–85) vs 72 (57–81). A high percentage of the children showed significant deficits (z score > -1.6) in the following executive skills: Processing speed: 97% (median z score; 2.33); Selective visual attention: 86% (median z score; 2); Inhibition: 80% (median z score; 1.66); Planning: 77% (median z score; 2.33); Visual memory: 71% (median Z score; 1.66). Thirty-four percent of the children failed in school (grade retention); and this fail showed significant correlation with: Hydrocephalus at disease onset (p = 0.04); Low socio-economic level (p = 0.018); Deficit in verbal IQ (p = 0.017); Deficit in perceptive reasoning IQ (p = 0.003); Deficit in Processing speed (p = 0.0044); Deficit in visual memory (0.05)

Conclusion: The vulnerability of this population to executive deficits due to the treatment warrants the necessity to include neurocognitive assessments in the follow-up protocol of these patients to allow a better understanding of their cognitive profile for the subsequent design of psycho-educational interventions to facilitate learning processes and improve their quality of life.

QUALITY OF SURVIVAL - QoS OF CHILDREN IN THE RANDOMISED MULTICENTRE PNET4 STUDY OF HYPERFRACTIONATED (HFT) VERSUS STANDARD RADIOTHERAPY (STRT) IN CHILDREN WITH STANDARD RISK MEDULLOBLASTOMA

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Purpose: The purpose of this study was to compare the quality of survival between children in the two treatment arms of the SIOP-E European PNET4 trial.

Method: Participants aged over 4 years with M0 medulloblastoma were enrolled in PNET4 between 2001 and 2006 and allocated to HFT 1.0 Gy twice daily (36 Gy craniospinal, 60 Gy posterior fossa, 68 Gy residual tumour) or STRT 1.8 Gy daily (23.4 craniospinal, 54 posterior fossa). Cisplatin, CCNU and Vincristine were given after radiation therapy in both treatment arms. Event free survival did not differ between treatment arms at a median of 48 months from diagnosis (Lanfering et al, Ped Blood and Cancer 2010 55:806). In late 2010 & early 2011, we applied to PNET4 survivors across Europe the method of assessment of QoS from diagnosis (Lannering et al, Ped Blood and Cancer 2010 55:806). In late 2010 & early 2011, we applied to PNET4 survivors across Europe the method of assessment of QoS previously reported for UK survivors of PNET3 (Bull et al, J Clin Oncol 2007 25:4259-45) in a cross-sectional multi-centre multi-informant questionnaire study. Questionnaires included, as the primary outcome measure, the Health Utilities Index (HUI3) and, in addition, the Behaviour Rating Inventory of Executive Function (BRIEF), the Pediatric Quality of Life Inventory (PediQL), the EORTC QLQ-C30. Data were also collected regarding the patient’s growth and endocrine status, and education.

Results: From an eligible surviving population of 242, QoS data have been provided by 122 (51%) participants in France, Germany, Italy, Netherlands, Spain, Sweden and UK. Intergroup differences in outcome will be tested with Pearson chi squared, t test and Mann-Whitney U test as appropriate.

Conclusion: In the absence of a difference in survival rate, the future choice between STRT & HFT rests on whether their use is associated with a measurable inter-group difference in QoS in this study. This question will be addressed by analysis of these data.

XANTHOGRAVULOMA OF THE SELLAR REGION - RESULTS OF A MULTICENTER PROSPECTIVE STUDY ON DIAGNOSTICS, THERAPY AND PROGNOSIS IN CHILDREN AND ADOLESCENTS

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Purpose: In KRAINOPHARYNGEOM 2001 117 patients with newly diagnosed childhood craniopharyngioma from Germany, Austria and Switzerland were recruited between 2001 and 2007. Additionally, 14 patients with childhood xanthogranulomas were included in our observational study.

Method: All patients were prospectively analyzed for diagnostic features, clinical manifestations, treatment and risk factors for relapses. Histological diagnoses were assessed by reference panel in all cases.
SIOP ABSTRACTS

Results: In 5/14 patients with xanthogranuloma the histological diagnosis was made by
DNA analysis and in 9/14 patients by pathological examination. The median age at diagnosis was 19 months (0–126 months).

Conclusion: The median duration of symptoms before diagnosis was 6 months (1 month–10 years).

PM026

PRIMARY MENINGIOMAS OF CHILDHOOD AND ADOLESCENCE: A SERIES OF 104 CASES

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Purpose: Meningiomas are very rare in children comprising only 0.4–4.6% of all pediatric brain tumors. We analyzed retrospectively the clinical, pathological and management profile of these tumors in a French multicentric series aiming to analyze outcome and prognostic factors.

Method: From 1974 to 2010, 104 children and adolescents with meningiomas were treated in 13 centers. The variables analyzed included age, sex, presentation, associated neurofibromatosis (NF), imaging characteristics, extent of resection and histological study.

Results: There were 58 male (56%) aged 5 months to 17 years (median 11). The distribution of age at diagnosis ranged from 1 month to 17 years. Thirty-nine were male (67%) aged 5 months to 17 years (median 11). The duration of symptoms ranged from 1 month to 5 years. Thirty-three patients had evidence of NF2. The commonest presenting symptoms were focal neurological deficits (48%), raised intracranial tension (38%), and seizures (22%). The location of the operated tumors was as follows: falx (23%), convexity (13%), parasagittal (6%), skull base (2%), intraventricular (2%), and posterior fossa (2%). Gross total, near total or partial resections were performed in 66% of cases. The histological examination showed 56% of meningiomas, 22% of gliomas, 13% of craniopharyngiomas, 6% of ependymomas, 2% of neurofibromas, 2% of meningiomas, 1% of glioblastomas, 1% of gliosarcomas, and 1% of hemangiomas. The median age at diagnosis was 11 years (2 months–17 years). The median duration of symptoms before diagnosis was 6 months (1 month–10 years).

Conclusion: Meningiomas are rarely diagnosed in children and differ from those in adults by their lower prevalence, younger age of presentation, and different clinical and radiological features. The treatment of these tumors is controversial, with surgical resection being the mainstay of treatment. The results of this study emphasize the importance of early diagnosis and prompt treatment to achieve optimal outcomes.

PM027

EVALUATION OF AVAILABLE RESOURCES FOR OPTIMAL MANAGEMENT OF CHILDREN WITH BRAIN TUMORS IN CENTRAL AMERICA

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Purpose: Advances in pediatric cancer in low-income countries have focused on the management of acute Leukemia, for which treatment requires chemotherapy and adequate supportive care. These interventions have not been matched for childhood brain tumors, which require complex multidisciplinary management.

Method: A needs assessment questionnaire to evaluate resources required to deliver multidisciplinary care for pediatric brain tumors was administered to the eight major pediatric oncology programs in Central America; Costa Rica, Dominican Republic, El Salvador, Guatemala, Nicaragua, Panama, and two centers in Honduras.

Results: All 8 centers had access to pediatric oncologists, specialized oncology nurses, and data managers. None had a neurooncologist or a neuropathologist and only one had access to all essential immunohistochemical stains. There was disparity in available neurosurgeons (2 did not have access and 4 lacked adequate equipment), timely radiological tests, and optimal radiation therapy (delays at least some of the time in 7 centers ranging from 2 to 12 weeks and 3 centers with only cobalt machines available). These barriers likely translate into poor outcomes with variance in overall survival; 50% in 3 centers, less than 35% in 3 centers, 70% in 1 center, and unknown in the remaining 1. The majority commented on the lack of multidisciplinary care and delayed diagnosis, the latter of which may contribute to high rates of advanced disease on presentation, 50% stated at least half their patients present with disseminated disease.

Conclusion: Common as well as discrete deficiencies in available resources essential for the management of children with brain tumors have been identified in the major treating facilities in Central America. Potential interventions include regionalized protocols with caveats to accommodate individual barriers, strategies to increase awareness and promote communication among community health care workers, and development of regional training centers for the essential disciplines based on programs with well established services.

PM028

EPIDEMIOLOGY AND SURVIVAL OF CHILDHOOD PRIMARY CENTRAL NERVOUS SYSTEM MALIGNANCIES IN IRAN: RESULTS FROM A SINGLE CENTER

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Purpose: Childhood primary CNS malignancy is one of the most important concerns in pediatric oncology. Therefore, epidemiological and survival data are very helpful for future planning.

Method: In the retrospective cross-sectional analytic study 82 patients whom treated in Ali-Ashgar Children’s Hospital between years 1985 and 1995 was evaluated for age, gender, type of treatment, tumor pathology and survival.

Results: The results of 38 female (46.3%) and 44 male (53.7%) patients were included; mean age was 6.8 ± 3.3 yr (6 mo–14 yr), 45 (58.6%) medulloblastoma, 18 (22%) Astrocytoma, 13 (15.9%) Ependymoma, 3 (3.7%) Glioma. Total resection, radiotherapy and chemotherapy were done for 42.7%, 82.5% and 87.3% of patients, respectively. Mean follow-up time was 51.3 mos (1–106 mos). 5-yrs cumulative survival probability was near 42.4%.

Conclusion: Inferior survival rate in comparison with developed countries may be associated with delay in diagnosis and refer to oncologist and more progressive tumor at diagnosis.

PM029

BRAIN STEM GLIOMA OF CHINESE CHILDREN IN HONG KONG

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Purpose: To assess the outcome of the children with brain stem glioma

Method: The clinical features, pathology, treatment and outcome of patients with brain stem glioma were reviewed.

Results: There were 55 patients from 1995–2009. The median age was 6.9 years of age (1: 2.1–17.8). The male to female ratio was 1:5.1. Twenty-nine patients did not receive any biopsy or surgery. Twelve of them received radiotherapy (RT) and chemotherapy (CT); 8 patients received RT alone; 9 patients were observed without any specific treatment. Eleven patients received debulking surgery. Three of them were then observed, four patients received RT and CT, while four patients only received RT. Fourteen patients had biopsy. Three patients were then observed without any specific treatment; nine patients received RT and CT; two patients received RT only. One patient received total resection without RT or CT. The pathology of the twenty-six patients (biopsy or surgery) with the brain stem glioma were grade I, 4; II, 5; III, 4; IV; 6, not specified: 7 (WHO classification). Nine patients are still alive (complete response: 3, stable disease: 3, partial remission: 3). Forty-six patients died because of progressive disease. The overall survival was 36.3% at 1 year, 15.3% at 2 years and 13.3% at 5 years. Patients who had surgery (n = 12) appeared to perform better than those who did not have surgery (n = 43) (33.3% vs 7.5% at 5 years; p = 0.080). Five patients who received radiotherapy (n = 39) were alive at 5 years while 2 of the patients (n = 16) who did not received radiotherapy was alive (13.7% vs 12.5%; p = 0.184). Chemotherapy, in addition to RT, did not improve the outcome (chemotherapy and RT: 13.4%; RT alone 13.3%; and treated, but the accrual is slow.

Conclusion: The outcome of the brain stem glioma is poor. Innovative therapy is necessary for improvement.

PM030

HIGH-DOSE CHEMOTHERAPY AFTER RADIATION THERAPY IN CHILDREN WITH MEDULLOBLASTOMA AND SPNET OLDER THAN 3 YEARS OF AGE: PILOT EXPERIENCE OF MOSCOW NEURO-ONCOLOGY COOPERATIVE GROUP

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Purpose: Medulloblastoma (MB) is one of the most prevalent malignant brain tumors in childhood. Development of different combination chemotherapy regimens led to improvement of overall and progression free survival in patients with MB. Nevertheless outcomes of high-risk MB yet have to be improved. In the present study we wanted to replicate results obtained by SJMB-96 which consisted of post-operative risk-adapted radiation therapy followed by 4 consecutive cycles of high-dose chemotherapy with PBSC rescue.

Method: From 2007 to 2010 we have enrolled 15 patients at the age of 3 to 17 years old with MB or SPNET. After primary tumor resection and staging PBSC were mobilized and harvested. Risk-adapted radiation therapy followed (24 or 36 Gy CSI, local boost up to 54 Gy). One month after completion of radiation therapy all patients started high-dose chemotherapy that consisted of vincristine (1 mg/m²), cisplatin (75 mg/m²), and cyclophosphamide (4000 mg/m²). On day 5 PBSC transplantsations were performed, the dose of CD34+ cells was lowered relative to the risk in the original SJMB-96, with average of 1.2*10^6/kg. All children received G-CSF until WBC will rise above >2000 in mkl. Bone marrow recovered on day 12–15 after transfusion of PBSC.

Results: 100% of children experienced grade 3–4 hematologic toxicity and 73% (n = 11) encountered febrile neutropenia. Two patients developed grade 3 liver toxicity with elevated hepatic enzymes but without hyperbilirubinemia. No treatment-related mortality was observed. Up to now all patients are alive with median follow up of 19 months.

Conclusion: We conclude that the main toxicity of this regimen is hematological and infections due to prolonged cytopenia. Other toxicity is rare and manageable. SJMB-96 type regimen turned out to be feasible and safe. Efficacy of such treatment and improvement of survival is still to be determined.

PM031

CPT SIOP 2011 REPORT

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Pediatr Blood Cancer DOI 10.1002/pbc
TREATMENT OF RECURRENT DIFFUSE INTRINSIC PONTINE GLIOMA: HOW SHOULD THEY BE ANALYSED?

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Purpose: New ways of analyzing individualized data need to be developed. Examples are recurrent Diffuse Intrinsic Pontine Gliomas (DIPGs), which have been traditionally treated with palliative care. Recently clinical studies are emerging, and individualized treatment attempts are done more frequently. However, an informative way to compare the treatment outcomes has not been established, and historical control data are missing for recurrent disease.

Method: We conducted an IRB approved retrospective chart review of patients with recurrent DIPG treated between 1998 and 2010.

Results: Thirty one patients were identified who were treated with 61 treatment attempts using 31 different regimens. The most frequently used drugs were etoposide (14%), bevacizumab (13%), irinotecan (4%), and valproic acid (13%). Seven patients had repeated radiation to the primary tumor. Response was recorded after 58 treatment attempts and was categorized as 0/7/20/31 for CR/PR/SD/PD, respectively. The median progression free survival after treatment start was 2 months and was found to be correlated to the prior time to progression but not to the number of previous treatment attempts. Repeat radiation resulted in the highest response rates (47%), and longest progression free survival.

Conclusion: Repeat radiation should be tested in a prospective clinical study. The best way to analyze it was to compare to compare EFS to previous EFS. In addition, we suggest adding a quality of life measurement to the endpoint.

SIOPT ABSTRACTS

Purpose: Introduction: Brain tumors (BT) Infants are a special group of patients and a challenge in treatment approach. Long term side effects influence treatment options.

Aims: Determine socio-demographic data, clinical presentation, delay in diagnosis, type of tumor, topography, treatment, survival and patient’s status.

Method: Retrospective review of medical records of BT infants, treated at Hospital S. Joao, between 1993 and 2010. SPPS and Kaplan-Meier survival analysis were used.

Results: Twenty infants; M: F - 4: 1; 0-11 months of age (median 6.2). Type of tumor: Primitive neuro-ectodermal tumor (PNET) (8), choroid plexus tumor (4 papillomas, 2 carcinomas), low-grade glioma (1),ependynoma (1), anaplastic oligodendroglioma (1), teratoid/hemibrain tumor (1), diffuse brain stem glioma (1), non biopsied cerebellum tumor (1). Topography: supratentorial 55% (11), infratentorial 45% (9). Average delay in diagnosis: 24 days (prenatal diagnosis to 90 days). Clinical presentation: increased head circumference (10), irritability (8), vomiting (5), "senset-eyes" (4). Treatment: surgery 85% (17) - (59% partial resection), chemotherapy and surgery 7% (14); one patient underwent local radiotherapy as part of the initial approach. Overall survival at 2 and 5 years were 68% with a median follow-up of 39 months (9-189). Currently 45% of patients are alive without disease (4 PNET, 5 choroid plexus tumors, two of which are carcinomas). Of the nine cases currently without disease, three present developmental delay, especially motor skills.

Conclusion: The sample revealed a wide variety of tumors in this age group, with a preponderance of PNET and choroid plexus tumors. Clinical suspicion is of extreme importance because early diagnosis has prognostic implications. The authors highlight the need of systematic development evaluations on this special group, in order to begin early educational intervention. Due the rarity of these patients, integration in international protocols is crucial in order to improve patient morbidity and survival.

UPFORT HIGH-DOSE CHEMOTHERAPY WITH BUSULFAN-THIOTEPA IN THE TREATMENT OF EARLY CHILDHOOD MEDULLOBLASTOMA WITH CLASSICAL HISTOLOGY OR UNCOMPLETED RESECTION

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Purpose: To evaluate the outcome of young children treated with high-dose busulfan-thiopeta followed by ASCT.

Method: High-dose busulfan-thiopeta with ASCT followed by posterior fossa irradiation strategy.

Results: Of 51 patients treated with ASCT, the median follow-up time was 39 months and 23 patients (45%) were alive without disease. A special group of 17 patients with uncompleted resection or classical medulloblastoma were treated according to this protocol, 6 M, 11 F, median follow-up of 39 months (9-189). Currently 45% of patients are alive without disease (4 PNET, 5 choroid plexus tumors, two of which are carcinomas). Of the nine cases currently without disease, three present developmental delay, especially motor skills.

Conclusion: The sample revealed a wide variety of tumors in this age group, with a preponderance of PNET and choroid plexus tumors. Clinical suspicion is of extreme importance because early diagnosis has prognostic implications. The authors highlight the need of systematic development evaluations on this special group, in order to begin early educational intervention. Due the rarity of these patients, integration in international protocols is crucial in order to improve patient morbidity and survival.

0.06, OS 0.31

0.09. PFS of pts less than 3 yrs old with PT/NPT was 0.10. PFS pts > 3 yrs with PT/NPT was 0.570.21. PFS pts PT/NPT with M0 were 0.550.34, M+ was 0.280. PFS pts PT/NPT with residual tumor (SR+R+B) was 0.380.1, with TR was 0.50.36. In pts who received Philadelphia protocol PFS for PT/NPT was 0.580.29. PFS pts NPT/PHPT who received noncohort control or did not receive any CHPT was 0.50. In pts PT/NPT who received HIT-SKKF2 FFS was 0.10.

Conclusion: Better results were seen in pts with PT without metastases, older 3 y.o., who received Philadelphia protocol.

SURVIVAL IN CHILDREN WITH PINEAL AND NON-PINEAL SUPRATENTORIAL PRIMITIVE NEUROECTODERMAL BRAIN TUMORS

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Purpose: To estimate survival of patients with pineal and nonpineal pNPT.

Method: There were 31 pts with pineal tumors (PT) and 59 pts with non-pineal tumors (NPT). Among pts with PT were 13 girls and 18 boys; median age 8 yrs, 10 pts were less than 3 yrs old. Among pts with NPT were 23 girls and 36 boys; median age 4 yrs, 20 pts were less than 3 yrs old. Among pts were M0, 3-M1; 4-M2; 10-M3; 15-Mx; 10 pts had TR, 26-17, 6-P, 30 pts were treated with Philadelphia protocol, 10 HIT-SKKF2, 2-norcohort CHPT and 6 pts received CHPT. 37 pts received CSI, 4-local RT.

Conclusion: The sample revealed a wide variety of tumors in this age group, with a preponderance of PNET and choroid plexus tumors. Clinical suspicion is of extreme importance because early diagnosis has prognostic implications. The authors highlight the need of systematic development evaluations on this special group, in order to begin early educational intervention. Due the rarity of these patients, integration in international protocols is crucial in order to improve patient morbidity and survival.

CONCLUSION:

The evaluation of the efficacy and the survival of children with high-grade astrocytoma treated with high-dose chemotherapy with busulfan-thiopeta followed by autologous peripheral blood stem cell transplantation (ASCT) showed significant correlations with the dose and time of busulfan chemotherapy. The median progression-free survival (PFS) was 39 months (9-189). Currently, 45% of patients are alive without disease (4 PNET, 5 choroid plexus tumors, two of which are carcinomas). Of the nine cases currently without disease, three present developmental delay, especially motor skills.

Conclusion: The sample revealed a wide variety of tumors in this age group, with a preponderance of PNET and choroid plexus tumors. Clinical suspicion is of extreme importance because early diagnosis has prognostic implications. The authors highlight the need of systematic development evaluations on this special group, in order to begin early educational intervention. Due the rarity of these patients, integration in international protocols is crucial in order to improve patient morbidity and survival.

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PM036

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PM032

PM033

0.21. PFS pts PT/NPT was 0.570.21. PFS pts PT/NPT with M0 were 0.550.34, M+ was 0.280. PFS pts PT/NPT with residual tumor (SR+R+B) was 0.380.1, with TR was 0.50.36. In pts who received Philadelphia protocol PFS for PT/NPT was 0.580.29. PFS pts PT/NPT who received noncohort control or did not receive any CHPT was 0.50. In pts PT/NPT who received HIT-SKKF2 FFS was 0.10.

Conclusion: Better results were seen in pts with PT without metastases, older 3 y.o., who received Philadelphia protocol.
**PM038**

**PHASE 2 STUDY OF SAFETY AND EFFICACY OF NIMOTUZUMAB (THERACIM®) IN PEDIATRIC PATIENTS WITH RECURRENT DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)**

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**Purpose:** Nimotuzumab is an anti-EGFR antibody that has shown promising activity in a previous phase II study in recurrent/refractory DIPG patients. The aim of this multicenter trial was to confirm these preliminary results and to evaluate the safety and efficacy of nimotuzumab in this population.

**Method:** Patients with clinically and radiologically centrally reviewed DIPG who had failed standard first line therapy were eligible. Nimotuzumab (150 mg/m²) was administered intravenously once weekly from week 1 to 7 and once every 2 week from week 8 to 18. Patients with partial response (PR) or stable disease (SD) were continued Nimotuzumab.

**Results:** Of forty-six patients enrolled, 44 (MF = 20/24, median age 6.03-17 years) received at least one dose of nimotuzumab. All had received prior radiotherapy and 25 chemotherapy. Twenty-one patients completed 8 weeks (W8) of treatment, five 18 weeks (W18). Treatment was well tolerated. The majority of adverse events (AEs) were associated with CNS disorders. Eighteen subjects experienced serious AEs, including 3 subjects who experienced grade 5 AEs. Two were assessed as possibly related to study drug: intracranial tumour haemorrhage and tumour necrosis. There was no complete response. At W8, there were 2 PR, 6 SD and 13 progressions (PD). 1 of 2 patients with PR at W8 remained in PR at W18, and 36 subjects (13.6%) with SD at W8 maintained that response at W18. The time to progression following initiation of nimotuzumab treatment for the 3 subjects with SD and the 1 subject with PR at W8 was 119,157,335 and 182 days, respectively. Median survival time was 3.2 months. At the time of the data cut-off, 2 patients were still alive, both with PD 121 and 281 days from the start of nimotuzumab.

**Conclusion:** Nimotuzumab showed modest activity in this confirmatory study. However, it seems that a subset of patients may benefit from anti-EGFR antibody treatment.

**PM039**

**PERIOSTEAL OSTEOSARCOMA - A SINGLE INSTITUTE’S EXPERIENCE**

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Pediatr Blood Cancer DOI 10.1002/pbc

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**Purpose:** Periosteal osteosarcoma is an uncommon variant of osteosarcoma and it is difficult for a single institute to document a large series of these cases. We report our results with this tumor.

**Method:** Between January 2001 and March 2009 810 cases of osteosarcoma were operated at our institute. These included 12 periosteal osteosarcomas. There were 7 males and 5 females. The femur was involved in 5 cases, tibia in 6 and radius in 1. The age ranged from 2 years to 26 years with a mean of 14.5 years. All cases were non metastatic at presentation. Nine cases received multi agent chemotherapy. Ten patients had limb salvage, I had a rotationplasty and 1 had an amputation. Of the 10 limb salvage patients, 6 had conventional wide resection and in 4 hemiepiphysial excision was done. Margins were tumor free in all 12. Response to chemotherapy was evaluable in 3 cases. Four had <90% necrosis. Four patients of limb salvage needed a repeat surgery for reconstruction purposes.

**Results:** 11 patients were available for final follow up. The follow up ranged from 18 months to 107 months with a mean of 59 months. There was one local recurrence which was managed with a subsequent amputation. Two patients succumbed to their disease. One patient died at 20 months and another at 60 months. The mean follow up for survivors was 68 months. One of 9 patients who received chemotherapy and 1 of 3 patients who did not receive chemotherapy died. The 5 year overall survival was 78%.

**Conclusion:** Periosteal osteosarcomas formed 1.5% of the osteosarcomas operated at our institute. These tumors have a better prognosis than conventional osteosarcomas. The role of chemotherapy in their management remains debatable and considering their rarity multi institutional collaborations would be necessary to resolve this question.

**PM040**

**CNS LESIONS IN MALAWI, THE SCOPE OF THE PROBLEM**

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**Purpose:** Malawi is one of the world’s poorest countries but despite this a number of paediatric cancers are treated with modest success. Without a paediatric neuro-oncology infrastructure that is currently not available in Malawi but analysis of children with CNS lesions in Malawi during 2008–2010. These scans were performed on the Malaria research scanner as kind gestures of support by Dr Kampondeni.

**Method:** Children having MRI scans at QECH were identified and the scans copied. Patient data was collected and the scans plus data were reviewed by a neuroradiologist and neuro-oncologist. The scans of 29 patients were analysed and the most likely radiological diagnosis recorded.

**Results:** The median age of patients was 10 years (0.15–18). 17 Males, 12 females. The majority of scans were reviewed due to the presence of neurological signs. 4 children had presumed low grade gliomas, 8 high grade tumours (including medulloblastoma, DIPG, germinoma, ependymoma, and glioma) and 6 had tumours arising outside the CNS (lymphoma, nasopharyngeal carcinoma, Ewing sarcoma). Seven had presumed CNS infections (TB, suppurative bacterial disease) and 4 had other less existing intensive care facilities or radiotherapy brain tumours are unable to be treated with any degree of success. In order to assess the scale of the problem an audit was undertaken of those children who underwent MRI scans of their central nervous system (CNS) during 2008–2010. These scans were performed on the Malaria research scanner as kind gestures of support by Dr Kampondeni.

**Conclusion:** MRI scans reviewed by a neuroradiologist are a useful tool in determining infectious vs non infectious causes of CNS lesions and even in the most resource challenged countries enable effective triage of patients. Infections may be treated effectively in many cases. The treatment of paediatric CNS tumours however requires a complex medical infrastructure that is currently not available in Malawi but analysis of children with CNS lesions can determine the scope of the problem in order to guide development of future paediatric neuro-oncology services.

**PM041**

**CYSTS OF RATHEK CLEFT - RESULTS OF A MULTICENTER CROSS-SECTIONAL STUDY ON DIAGNOSTICS, THERAPY AND PROGNOSIS IN CHILDREN AND ADOLESCENTS**

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Conclusion: We conclude that radical resection is the therapy of choice for low grade gliomas. Histological diagnoses were included in the analysis to confirm the diagnosis. QoS as measured by FMH questionnaire at the time of last evaluation did not reach the level of significance. Obesity had no significant impact on QoS in RCC in contrast to CRA.

Results: RCC was diagnosed at an age of 10.2 years (±1.5). Overall, 11% of RCC (±1.8) had BMI-SDS at last evaluation. RCC patients presented with smaller tumour-masses than CRA patients (p < 0.001) and without hypothalamic involvement (69% in CRA; p < 0.001). Complete surgical resections were achieved in 46% and 59% of CRA. Local external irradiation was performed in 14% of RCC (1 pt after 4 relapses, 3 yrs after diagnosis; 1 pt after 2 relapses, 1.2 yrs after diagnosis) and 27% of CRA. We observed a 3.5% overall survival of 1.09 and 0.97 in RCC and CRA, respectively. 3 yrs-event-free-survival rates were higher in RCC (0.82 ± 0.12) when compared to CRA (0.44 ± 0.06) (p = 0.035).

The follow-up in CRA (3.1 yrs [0.1–7.1]) was influenced by a higher degree of obesity (BMI-SDS at last evaluation: 2.9 [1.8–3.1] compared to tumors in other sites. The most commonly used chemotherapeutic regimen was carboplatin/vincristine (N = 37) followed by vinblastine (N = 17). Six patients received other chemotherapeutic regimen. Causes of switching chemotherapy were progression/poor response (N = 11), and side effects (N = 6). Three-year PFS was 75% ± 12% for those treated with surgery alone versus 44% ± 14% for those who used multimodality treatment (p = 0.022). Partial/complete responses were observed in 72% of patients who received carboplatin/vincristine compared with 40% of those who received other regimens (p = 0.03). During the time period only one patient received radiotherapy secondary to misdiagnosis of high grade glioma.

Conclusion: LGG management in developing countries can be improved through a multidisciplinary approach. The role of telemedicine in this experience was significant in providing suggestions and helping the decisions. The main impact of this approach was the elimination of radiotherapy from the management of most patients with LGG in our center. Carboplatin/Vincristine is an affordable regimen with our results similar to those reported in the literature.

PM044

RANDOMIZED MULTICENTER TRIAL ON PATIENTS WITH CHILDHOOD CRANIOPHYARYNGIOMA (KRANIOPHYARYNGEOM 2007) - UPDATE AFTER 41 MONTHS OF RECRUITMENT

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Purpose: Despite high survival rates (92%) in patients with childhood craniopharyngioma (CP), quality of life (QoL) is frequently impaired due to sequelae such as severe obesity resulting from hypothalamic involvement of CP.

Method: Based on the results of the multicenter prospective study KRANIOPHYARYNGEOM 2000 radical surgery is no appropriate treatment strategy in patients with hypothalamic involvement. Furthermore, tumour progression/relapses are frequent early events in CP patients. The analysis of event-free survival-rates (EFS) in 17 prospectively evaluated patients with CP showed a high rate of early events in terms of tumour progression after incomplete resection (EFS: 0.31 ± 0.07) and relapses after complete resection (EFS: 0.63 ± 0.09) during the first three years of follow-up.

Results: Accordingly, in KRANIOPHYARYNGEOM 2000 QoL, and survival rates in CP pts (> 5 yrs at diagnosis) are analyzed after randomization of the time point of irradiation (XRT) after incomplete resection (immediate XRT versus XRT at progression of residual tumour).

Up to now (03/11/78 pts with CP were recruited (42 pts in the randomization arm, 33 pts in the surveillance arm; 3 pts in the process of review of imaging data, 13 of 42 pts were randomized. 29 pts could not be randomized due to parental decision (11 pts), late schedule (14 pts) and due to decision of the physician (4 pts).

Conclusion: In conclusion, KRANIOPHYARYNGEOM 2007 represents the first randomized trial in CP and the first study in pediatric neurooncology analyzing QoL as an endpoint. Aim

PM043

MULTIMODALITY TREATMENT OF LOW GRADE GLIOMAS IN DEVELOPING COUNTRIES: A SINGLE INSTITUTION EXPERIENCE

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Purpose: to evaluate the development of multidisciplinary approach assisted by a telemedicine and twinning initiative.

Method: We retrospectively reviewed the medical charts of children (< 18 years) with LGG treated at our institution between Jan2004 and December2009.

Results: Sixty five charts were reviewed (36 males, 29 females). Twenty three patients (35%) were less than 5-years of age. Tumor sites were as follows: cerebellum, 14; cerebrum, 11; optic nerve, 4; pineal, 3; suprasellar/basal hypothalamus, 21; thalamus, 3; ventricles, 1; cerebellomedullary, 4; spinal, 3 and brain stem, 1. The most common pathologic diagnosis was pilocytic astrocytoma (N = 43). Twenty seven patients (42%) were treated with surgery alone, while the other 38 received multimodality treatment. Initial surgical interventions were gross total resection (N = 17), subtotal resection (N = 9), and partial resection/biopsy (N = 36). Posterior fossa tumors were more likely to have gross total or subtotal resection (10 out of 14) compared to tumors in other sites. The most commonly used chemotherapeutic regimen was carboplatin/vincristine (N = 37) followed by vinblastine (N = 17). Six patients received other chemotherapeutic regimen. Causes of switching chemotherapy were progression/poor response (N = 11), and side effects (N = 6). Three-year PFS was 75% ± 12% for those treated with surgery alone versus 44% ± 14% for those who used multimodality treatment (p = 0.022). Partial/complete responses were observed in 72% of patients who received carboplatin/vincristine compared with 40% of those who received other regimens (p = 0.03). During the time period only one patient received radiotherapy secondary to misdiagnosis of high grade glioma.

Conclusion: LGG management in developing countries can be improved through a multidisciplinary approach. The role of telemedicine in this experience was significant in providing suggestions and helping the decisions. The main impact of this approach was the elimination of radiotherapy from the management of most patients with LGG in our center. Carboplatin/Vincristine is an affordable regimen with our results similar to those reported in the literature.
of the study is to analyze the appropriate time point of XRT in order to improve QoL in patients with hypothalamic involvement. The recruiting compliance is high. However, the randomization compliance has to be improved in order to reach cohort sizes necessary for reliable statistical analysis and to answer the questions assessed by the randomized trial KRANIOPHARYNGEOM 2007. Supported by Deutsche Kinderkrebsstiftung, Germany

**PM045**

**PRESENTATION, TREATMENT AND OUTCOMES OF CHILDREN WITH CENTRAL NERVOUS SYSTEM GERMINOMAS: A SINGLE INSTITUTION EXPERIENCE**

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**Purpose:** Background: Children with CNS germinomas have an excellent chance of cure, but may have late effects related to chemoradiotherapy. Successful treatment protocols have attempted to reduce the dose or volume of brain radiation while preserving the favourable prognosis. Our aim was to compare the outcomes of patients treated across different regimens at our institution.

**Method:** Methods: A retrospective health record review was conducted for patients with CNS germinomas at the Hospital for Sick Children between 1985 and 2009 inclusive. Results: Results: Among 42 children, 29 (69%) were males and 13 (31%) females. The median age was 13.5 years (range 3.8 to 17.4 years). By site, the germinomas were found in pineal (29%), suprasellar (24%), bifocal (38%) and other (9%) locations. There was a strong association for site by gender, with only 8% of males having an isolated suprasellar tumor, in contrast to 67% of females (p < 0.001). There was a variety of different treatment regimens used. In general, treatment in the older era (before 2001) commonly involved craniospinal (CSI) or whole brain irradiation, whereas treatment in the recent era (after 2001) commonly involved chemotherapy followed by focal and ventricular field irradiation (VFI). Despite the reduction in radiation doses and volume, outcomes across the two periods were not significantly different. The 3-year event-free survival (3-y-EFS) in the older era was 83%, compared to 91% for the recent era (log-rank p-value = 0.32). For the whole group, 3-y-EFS was 87% and overall survival 98%. Median follow-up was 4.7 years. Five children had germinoma recurrences and all were successfully re-treated. One child died soon after initial diagnosis from surgical complications.

**Conclusion:** Conclusions: Children with CNS germinomas continue to have excellent outcomes even as treatment intensity is reduced over successive regimens. Our experience corroborates the hypothesis that CSI can likely be avoided in most children with CNS germinomas.

**PM046**

**A PHASE II TRIAL OF A MULTI-AGENT ORAL ANTIANGIOGENIC (METRONOMIC) REGIMEN IN CHILDREN WITH RECURRENT OR PROGRESSIONAL CANCER**

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**Purpose:** Tumors employ multiple pro-angiogenic mechanisms to promote new blood vessel formation needed for growth. We conducted a prospective, open-label, multi-institutional II study to evaluate the efficacy and tolerability of a multi-agent (“five-drug”) oral antiangiogenic regimen in children and adolescents with treatment-refractory cancer.

**Method:** Patients up to 21 years of age with recurrent or progressive cancer were eligible. Treatment duration was 27 weeks, and included continuous oral administration of fenofibrate, thalidomide, and celecoxib, with alternating 21-day courses of oral etoposide and oral cyclophosphamide.

**Results:** A total of 101 patients were enrolled; 98 began therapy and were evaluable for toxicity. Median age was 10.5 years; 49% were female. Patients were enrolled according to disease strata: Leukemia/lymphoma (4), bone tumors (12), neuroblastoma (3), high-grade glioma (20), low-grade glioma (13), ependymoma (19), medulloblastoma/CNS PNET (9), and miscellaneous (18). Overall, there was well enrollment in this heavily pre-treated population. Best overall response was complete response (CR) in 1%, partial response in 11, stable disease (SD) in 37, progressive disease (PD) in 48, and non-evaluable in 1. Twenty-four patients completed all 27 weeks of planned therapy. Reasons for stopping early included PD (66, including 3 who died while still on study), treatment toxicity (2), and patient/family preference (6). Overall survival and progression free survival (PFS) were 63% [90% confidence interval (CI): 55–71%] and 32% [90% CI 24–40%] at 27 weeks. Best overall response of SD or better was seen in 57% [90% CI 46–67%] of CNS tumors and 35% [90% CI 20–51%] of non-CNS tumors. Sustained responses (PFS > 2 years) were seen in 11 patients, including 4 with ependymoma, 3 with low-grade glioma, and one each with neurocytoma, anaplastic ganglioneurocytoma, lymphangioma, and meningioma.

**Conclusion:** This five-drug oral antiangiogenic regimen showed clinical efficacy in a subset of children with treatment-refractory tumors.

**PM047**

**AGE-RELATED MEDICAL DECISION LIMITS FOR URINARY FREE (UNCONJUGATED) METADRENALINES, CATECHOLAMINES AND METABOLITES IN RANDOM URINE SPECIMENS FROM CHILDREN**

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**Purpose:** Neuroblastoma is the most common extracranial solid tumour in childhood (8% of all childhood cancers), the most frequently diagnosed in infancy, and has one of the highest death rates; whilst chromaffin tumours rarely present in childhood. Both tumour types produce catecholamines and their metabolites. It is difficult to produce reference ranges for tests in children, and currently, no age-related medical decision limits for free metadrenalines in random urine specimens exist in the paediatric literature.

**Method:** Results: Of VMA, HIAA, HVA, NA, AD, DA, INMA, MDA and EMT in 158 random urines obtained from infants, children and young adults were measured by HPLC-ECD. Specimens were excluded from consideration if obtained from the following categories i.e.: (a) harbouring neuroblastotic, chromaffin, carcinoid, or other tumours or malignancies; (b) medical conditions having known association with excess catecholamine excretion; (c) patients administered catecholamine or paracetamol; (d) overly dilute urine; (e) manifesting outlying values following visual inspection.

**Results:** There remained 872 specimens which were grouped into seven age ranges (< 1; 1 to 2; 3 or 4; or 5 to 7; 8 to 10; 11 to 13; 14 to 19 years) for which medical decision limits were determined for each analyte. There was no significant difference between the results for boys or girls. In 55 patients harbouring neuroblastic tumours, HVA (54/55), EMT (14/16), VMA (45/53) and DA (43/53) were the most frequently elevated analytes at a time of diagnosis. In 11 patients presenting in childhood with chromaffin tumours, INMA (11/11) followed by NA (10/11) were the most frequently elevated.

**Conclusion:** Food stuffs containing catecholamines (including flavonoids) and drugs including paracetamol may produce elevated urinary catecholamines. The differences in urinary biochemical excretion patterns between those harbouring either neuroblastotic or chromaffin tumours are both striking and intriguing. We have produced the first validated, age-related, decision limits for free metanephrines in childhood.

**PN001**

**SIGNIFICANT CR NK CELLS EXPANSION, ACTIVATION, AND CYTOTOXICITY AGAINST B-NHL FOLLOWING STIMULATION WITH GENETICALLY REENGINEERED K562MBL1411H (MODK562): POTENTIAL FOR ACI**

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**Purpose:** NK cells may play a significant role in reducing relapse in patients with hematological malignancies following Allot ST (Dunbar et al. Haematologica 2008). Adoptive NK cell therapy is limited by tumor recognition and cell numbers (Shereck/Cairo et al. Hematologica 2008). NK cells may play a significant role in the cure of relapse relapse relapse patients, including 4 with ependymoma, 3 with low-grade glioma, and one each with neurocytoma, anaplastic ganglioneurocytoma, lymphangioma, and meningioma.
SIOP ABSTRACTS

K562 (NK-sensitive) and SDUH-6 (DLBCL) while, in vivo, NOD/SCID mice were xenografted with human BL transfected with mammalian construct luciferase (BLUCZeo- nco) and were subsequently supplied by L. Cooper, MD, PhD. 6 week old NOD.Cg- PkdcrsidcIl2rgtm1Wjl8Rd2 mice received 5x10^6 BL cells, IP, and treated with PBS, BL only, 5x10^6 WTK562E CBMNC, 5x10^6 or 1x10^7 MODK562E CBMNC. BNHL growth monitored by volume, bioluminescent imaging and survival for 10 weeks. Results: MODK562E CBMNC showed increased NK activation (p = 0.05) and granzyme B and perforin expression vs WTK562E (2.2 ± 0.6 and 0.4 ± 0.5 vs 3 ± 0.25 mm/p, p = 0.008, p = 0.001, respectively) and BNHL luminescence (p < 0.01). At 10 xenografts, mice receiving 5x10^7 MODK562E CBMNC demonstrated significantly increased survival vs WTK562E (p < 0.0001).

Conclusion: CBMNC stimuation with MODK562 was associated with significantly increased NK LAMP-1, and perforin and granzyme B expression, enhanced BNHL in-vitro cytotoxicity and in-vivo survival. Future directions include CAR CD20 (MVC-anti-CD20-4IBB-CD3e) transduction into MODK562E CBMNC to enhance B-HCL targeting.

PN002

SURVIVAL IN OVERWEIGHT AND UNDERWEIGHT CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT

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Purpose: There is a growing body of evidence that nutritional status influences the morbidity and mortality of children undergoing treatment for oncological disorders. The aim of this paper is to determine if nutritional status is associated with survival post paediatric hematopoietic stem cell transplant (HSCT).

Method: This was a single centre retrospective study from June 1998 to January 2010. Patients (n = 113) who underwent an autologous or allogeneic transplant at the Royal Children’s Hospital, Brisbane, Australia from June 1998 to January 2007 were included in the study. Data for the study was retrieved by an audit of medical charts. The data included age, sex, height and weight pre HSCT, transplant and donor type, the initial diagnosis of the patient and the type of conditioning used. The outcome measure was overall survival. Survival up to three years post HSCT was defined as the time from the start of conditioning for the transplant until death. Patients were divided into three groups according to their calculated%IBW: underweight, middleweight and overweight. Harada ratios were adjusted for age, sex, transplant type (autologous and allogeneic) and conditioning regime (myeloablative and non-myeloablative).

Results: Fifteen of 113 patients (13%) were underweight and 41 (36%) were classified as overweight. Overweight patients were significantly less likely to survive than middleweight patients (HR, 1.90; 95% CI, 1.09–3.35). There was a non-significantly increase in mortality when underweight patients were compared with middle weight patients (HR, 1.47; 95% CI, 0.58–3.83).

Conclusion: Children who are overweight or obese before HSCT have decreased survival compared to middleweight children. Management of obesity is usually not part of routine clinical nutrition management in pediatric oncology patients this paper builds however on the evidence that a change in clinical practice is required. Future studies should be focused on nutrition and exercise interventions before HSCT and its effect on improving survival.

PN003

OUTCOME OF ALLOGENEIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKAEMIA AFTER CONDITIONING WITH BUSULAN, CYCLOPHOSPHAMIDE, AND ETOPOSIDE

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Purpose: Background: We have previously demonstrated that the addition of etoposide to the conditioning of children with acute myeloid Leukemia (AML) undergoing allogeneic stem cell transplantation (ASCT) (33) (NOD.Cg- PrkdcscidIl2rgtm1Wjl8Rd2) mice received 5x10^6 BL cells, IP, treated and IP with: PBS, BL only, 5x10^6 WTK562E CBMNC, 5x10^6 or 1x10^7 MODK562E CBMNC. BNHL growth monitored by volume, bioluminescent imaging and survival for 10 weeks. Results: MODK562E CBMNC showed increased NK activation (p = 0.05) and granzyme B and perforin expression vs WTK562E (2.2 ± 0.6 and 0.4 ± 0.5 vs 3 ± 0.25 mm/p, p = 0.008, p = 0.001, respectively) and BNHL luminescence (p < 0.01). At 10 xenografts, mice receiving 5x10^7 MODK562E CBMNC demonstrated significantly increased survival vs WTK562E (p < 0.0001).

Conclusion: CBMNC stimuation with MODK562 was associated with significantly increased NK LAMP-1, and perforin and granzyme B expression, enhanced BNHL in-vitro cytotoxicity and in-vivo survival. Future directions include CAR CD20 (MVC-anti-CD20-4IBB-CD3e) transduction into MODK562E CBMNC to enhance B-HCL targeting.

PN004

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A PEDIATRIC PUBLIC HOSPITAL IN ARGENTINA

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Purpose: HSCT has become a curative therapeutic strategy for malignant and non-malignant diseases. We report the comprehensive results of the first 12 year experience in pediatric HSCT.

Method: Methods: retrospective and descriptive study. Period: 9/1998 to 2/2011. 172 patients received HSCT. We report the comprehensive results of the first 12 year experience in pediatric HSCT.

Results: Allogeneic HSCT: there were 89 pts, the 5y OS was 0.612 ± 0.057, the 5y DFS was 0.583 ± 0.059 and transplant related mortality (TRM) was 0.984. The outcomes according to disease: ALL (n = 41), the 5y OS was 0.46 ± 0.087 and the 5y DFS was 0.44 ± 0.086, AML (n = 14), the 5y OS and DFS was 0.44 ± 0.086 respectively and severe aplastic anemia (n = 15), the 5y OS and DFS was 0.73 ± 0.12 respectively. Autologous HSCT there were 85 pts. The 5y OS was 0.54 ± 0.077, the 5y DFS was 0.45 ± 0.074 and TRM was 2.38%. Outcomes by different pathologies: Solid tumors (n = 48), the 5y OS was 0.34 ± 0.11 and the 5y DFS was 0.29 ± 0.10, Hodgkin’s Lymphoma (n = 25), the 5y OS was 0.76 ± 0.13 and the 5y DFS was 0.61 ± 0.13 and AML (n = 10), the 5y OS was 0.67 ± 0.15 and the 5y DFS 0.56 ± 0.16.

Conclusion: Conclusions: Takers: to account the low socioeconomic level of our population, our results seem encouraging; they are similar to the published experiences in other developing countries which can set up a basis for more complex HSCT procedures.

PN005

AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN POOR PROGNOSIS RHABDOMYOSARCOMA IN A DEVELOPING COUNTRY

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Purpose: Ninety four percent of the patients with Rhabdomyosarcoma (RMS) who presented to our Unit (1990–1999) had IRS grade 3 or 4 disease. The DFS of these patients is 38.2%. All patients with metastatic disease have died. The poor outcome led us to search for a new approach to improve outcome.

Method: Since 1999 children with IRS grade 3 RMS with poor histological type and/or large tumour load and/or regional lymph node involvement entered an Autologous Peripheral Blood Stem Cell Transplant (APBSCT) programme. Sequential High Dose Monotherapy (SHDM) with Etoposide and Cyclophosphamide followed by myeloablative doses of Carboplatinum was used. All patients who entered the APBSCT programme received, prior
to entering SHDM phase, six courses of VICE (Vincristine, Ifosfamide, Carboplatinum and Etoposide) or VABO up to week 25 because of large tumour load and they had local treatment with surgery and RT. Patients were required to have no macroscopic disease when entering SHDM.

Results: Twenty six patients with RMS underwent PBSC harvest but 4 never reached transplantation due to progression of disease or complications of treatment. Twelve patients completed the transplant programme (M = 6, F = 6; ages 3.5–15.5 years. To date 10 patients are alive. Eight of them are long term disease-free survivors, 2–12 years post transplantation. One boy developed secondary malignancy -osteosarcoma- five years after transplant and he is on therapy. One patient has just completed the programme. Two patients died due to progression of disease. Complications post transplantation: Mild electrolyte imbalances; one patient developed VOD; two patients developed haemorrhagic cystitis. Engraftment time varied between 9–14 days while platelets recovered 14–42 days post transplantation.

Conclusion: Paediatric patients with poor prognosis grade 3 RMS can be successfully treated in a developing country with APRSCT.

PN006

HEMORRHAGIC CYSTITIS IN A CHILDREN’S CANCER CENTRE IN SINGAPORE
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Purpose: Hemorrhagic cystitis is a known morbidity especially in the hematopoietic stem cell transplant (HSCT) setting. We describe our experience in the last 12 years.

Method: This is a retrospective chart review of patients with hemorrhagic cystitis in our children’s cancer centre from 1998 to 2010. Data on patient characteristics, type of HSCT or chemotherapy, description of hemorrhagic cystitis episodes, their management and outcomes were collected.

Results: There were 9 patients with hemorrhagic cystitis in the 12 years. The age ranged from 3 to 15 years. There were 4 girls and 5 boys. Majority (79%, 78%) occurred during HSCT. The other 2 patients received intensive chemotherapy for metastatic rhabdomyosarcoma and relapsed biphenotypic acute leukemia respectively. The HSCT indications were: chronic myeloid leukemia (1 patient), myelodysplastic syndrome (2 patients), relapsed acute lymphoblastic leukemia (2 patients), acute myeloid leukemia (1 patient) and high-risk neuroblastoma (1 patient, autologous HSCT). Conditioning for all the allogeneic HSCT included cyclophosphamide - BuCy or CyTBI. In HSCT patients, the onset of hemorrhagic cystitis ranged from day +5 to day +68. Duration was 3 to 153 days. Urine BK virus was positive in 4 patients. Two of these received intravenous (IV) with/without intravesical cidofovir, with unsatisfactory results. All patients received blood product support. Five (56.5%) patients, 2 of whom had BK viruria, required bladder catheterization, washout, and cysto-diathermy. One of them needed suprapubic catheterisation. Another one underwent intravesical prostaglandin (PGF2α) with disappointing results. Two patients, both BK positive, had spontaneous resolution. Only one patient (on salvage chemotherapy for relapsed biphenotypic leukemia) had positive urine adenovirus, he eventually succumbed to disseminated adenovirus infection.

Conclusion: Haemorrhagic cystitis caused significant morbidity to immunocompromised (not limited to HSCT) children. Although this is a small series, BK viruria did not seem to correlate with severity. Optimal management of this problem is still unknown.

PN007

IMPROVED SURVIVAL FOLLOWING ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL): A RETROSPECTIVE REVIEW FROM 1984-2009
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Purpose: Over the last 25 years, the complexity of pediatric; transplantation has increased, mainly due to increased use of alternate stem cell sources. We hypothesised that there have been significant improvements in overall survival (OS) and reduced transplant-related mortality (TRM) despite increased transplant complexity.


Results: There have been significant improvements in OS (p < 0.0001) and EFS (p = 0.0168) over time. 5-year OS for Periods 1 and 2 combined was 41.7% and 75.8% for Period 3 (p < 0.0001). Significant improvements in 5-year OS between Periods 1 and 2 combined versus Period 3 were also found when stratified for remission status. (CR alone: 43.1% versus 71.6%, p = 0.0262; CR2: 42% versus 74.4%, p = 0.00683). TRM for Periods 1 and 2 combined was 33%, versus 6% in Period 3 (p = 0.0025). There has been a shift towards use of matched unrelated donors (MUD) and umbilical cord transplants (UCT). UCT is now the commonest source (44.7%) whilst MUD transplants have increased to 21.3%. Matched sibling donor transplants have decreased to 32%.

Conclusion: There has been significant improvement in OS and EFS following HSCT for ALL over the past 25 years, despite increased transplant complexity. This survival improvement is a major reduction in TRM. We hypothesise this has occurred with improved supportive care, including enhanced management of infections (prophylactic and acute), refinements in HLA matching, and greater experience with therapy. In contrast, rates of leukemic relapse post transplant have remained static, indicating that strategies targeting treatment of minimal residual disease post transplant are required.

PN008

EFFECT OF CHANGE IN MANAGEMENT AFTER LUNG BIOPSY IN CHILDREN POST BONE MARROW TRANSPLANTATION
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Purpose: To determine whether the diagnoses provided by lung biopsies change the management of care and review outcomes of children who had lung biopsy post HSCT.

Method: HSCT recipients from January 2000–June 2010 were included. Demographics and outcome data on patients who had lung biopsy post HSCT were collected and analyzed. Results of the lung biopsies were correlated with the clinical management pre, post-biopsy and survival.

Results: 918 patients received HSCT (allog 476, auto 442), 59 biopsies were performed in 48 patients. Biopsy results led to change in management in 34% and 56% in allog and auto recipients, respectively. Management change was mainly escalation of immunosuppression in allog recipients and a palliative route for auto recipients. In a univariate analysis, survival of patients who had their management changed was significantly lower (median survival time 0.04 vs 1.7 yr P = 0.01). There was a trend towards inferior survival for children who had their biopsy in the first 100 days post HSCT and those with any proven infections. Only 31% of allog and 25% of auto recipients survived.

Conclusion: Severe lung injury post HSCT measured by the decision to perform a lung biopsy has a poor outcome. Change in management based on biopsy results, particularly for allog recipients, led to inferior outcome.

PN009

HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN INFANTS
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Purpose: It is rare for an infant to receive HSCT and little is known about indications and outcomes.

Method: Retrospective study. Infants with an underlying immunological disorder were excluded.

Results: April 1992–March 2010, 136 (allogeic 77, autologous 58) children received HSCT in Toronto. Fifty-one (3.7%) were infants. Seventeen infants received allogeneic HSCT for an underlying metabolic disorder (osteoporosis 7, Hunter syndrome 7, GM gangliosidosi 1, Niemann-Pick type A 1 and Krabbes disease 1). Median age of diagnosis was 78 days (antenatal-248 days). Median age at HSCT was 207 days (29–334 days). They all received myeloablative regimens. For a median follow-up of 7.1 yrs (0.9–18.4 yrs) 13 patients are alive with an overall survival in this group of 76%. Causes of death were TRM in 3 and 1 patient (Niemann-Pick type A) died 4 yrs post HSCT from progressive disease. Remaining 34 infants, 10 received autologous HSCT (NBL 3, AML 2, Brain tumor 3, Rhabdomyosarcoma 1, Retinoblastoma 1). Twenty-four infants received allogeneic HSCT (13 related, 11 unrelated)-HLH 8, JMML, 4, WAS 4, ALL 3, AML 2, SAA 1, CGD 1 and Megakaryocytic Thrombocytopenia 1. Median age at diagnosis was 103 days (1-200 days), median age at HSCT was 254 days (142–365 days). All patients received myeloablative regimens. For a median follow-up of 6.7 yrs (0.5–15.6 yrs) 25 infants are alive with an overall survival in this group of 73%. Nine infants (27%) died, 6 due to TRM and 3 because of disease relapse. Eight out of ten infants who received autologous HSCT are long term survivors. Developmental and long term outcomes, the majority were delayed in their development.

Conclusion: Our results for HSCT in infants are very encouraging with excellent functional long term survival.

PN10

ROLE OF GASTROINTESTINAL ENDOSCOPY IN ALTERING THE MANAGEMENT OF GASTROINTESTINAL GVHD IN CHILDREN AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION.

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914 SIOP ABSTRACTS

114 SIOP ABSTRACTS

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Purpose: To review the benefits of GI endoscopies and biopsies in the management of GI aGVHD in children post HSCT.


Results: 450 children underwent allogeneic HSCT at the hospital for Sick Children in Toronto. Seventy-nine (17.5%) patients underwent endoscopy and GI biopsy for suspicion of GI aGVHD. The majority were boys, >10 years of age with hematological malignancies. Donors: Unrelated 50; related 29. Stem cell source were: BM 60%, cord 25% and PBSC 15%. Majority received myeloablative regimens with cyclophosphamine and methotrexate (or methylprednisolone for cords) for GvHD prophylaxis. All the patients engrafted within 8–49 days. Clinical grading of GI aGVHD was, I in 5 patients, II in 39, III in 23 and grade IV in 12 patients. All patients tolerated endoscopy and GI biopsy well except for one patient who developed duodenal hemorahia requiring prolonged GI rest. GI biopsy confirmed aGVHD in 49 (62%) patients and results were negative in 30(38%) patients. Eight patients had positive viral studies from the biopsy (adenos 5, CMV 1, HHV6 1 and EBV 1) and one biopsy was positive for Candida. Thirty- two (40%) patients have started treatment for GI aGVHD before biopsy was done based on clinical criteria, while 24(79%) patients started treatment after the biopsy results. Fifteen (19%) patients required 2nd line therapy for progressive GI GVHD based on clinical non response criteria. 29 (36%) patients died, 20 due to TRM and GVHD complications and 9 children died because of recurrence of their disease.

Conclusion: GI biopsy results after clinical suspicion of aGVHD in children post allogeneic HSCT led to starting or altering therapy in 30% of the patients. Patients who were already on therapy for GI GVHD, biopsy results did not alter their management and escalating therapy was based on clinical progression.

PN011

VERY-LARGE-VOLUME LEUKAPHERESIS IN VERY SMALL CHILDREN

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Purpose: Autologous PBSC collection in very small children below 10 kg body weight (BW) requires specialized proficiency and techniques for harvesting sufficient amounts of CD34+ cells.

Method: We analyzed 108 PBSC phereses after G-CSF mobilisation in 65 children (63 malignancies after chemotherapy, 2 siblings; age 0.45–26.25 yrs; BW 6.5–68.6 kg) between May 1997 and May 2006. Venous access through either double-lumen Hickman-Broviac device (inlet line) plus peripheral (return) line or Sheldon-type dialysis catheter. CS 3000 plus (Baxter/ Fenva) was primed with red cells when BW was below 25 kg. Anticoagulation with heparin bolus before and ACD-A application during the apheresis. Continuous parallel electrolyte-infusion with Ca++ plus K+ and laboratory monitoring during the procedure in order to prevent hypocalcemia and hypopotassemia.

Results: We achieved high flow rates (0.95–3.85 ml/kg/min) and needed an average number of aphereses of 1.67 (decreasing over time) to obtain enough PBSC for transplantation. Up to the 7.6 fold blood volume (BV) was processed, especially in very small children: Group1 (n = 27; BW < 15 kg) median 5 fold BV, group2 (n = 24; 15–30 kg) BV 4.5 BV, group3 (n = 14; > 30 kg BW) 3 BV. Even Collection time was shorter in small children too: Group1 150 min, Group2 160 min, Group3 180 min. CD34+ results: Group1: median 10.87–106, Group2: 10.4–106, Group3: 3.8–106. No severe or life threatening complications, all observed symptoms were slight and self limiting. A strong correlation between CD34+ count in PB before apheresis and the harvesting success could be registered.

Conclusion: Priming of the separator with red cells, permanent high dose electrolyte substitution, and optimized use of venous access catheters provides an option to obtain sufficient PBSC numbers with only one leukapheresis in most cases, even in very small children without any severe complications.

PN012

TREATMENT-RELATED TOXICITIES AND OUTCOME IN EWING SARCOMA PATIENTS RECEIVING PER OS (PO) OR IV BUSULFAN-BASED HIGH-DOSE CHEMOTHERAPY FOLLOWED BY AUTOGLOUS STEM CELL TRANSPLANTATION

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Purpose: Treatment-related toxicities and outcome of BU administered PO or IV were analyzed in patients receiving BU-Melphalan high dose chemotherapy (BU-MEL-HDC) followed by autologous stem cell transplantation according to the EUERO-E.W.I.N.G.99 protocol.

Method: Data from 157 patients (pts) registered from 1999-2009 into the EEG9 trial database of the German Society of Pediatric Hematology and Oncology treated with BU-MEL-HDC were analysed. Amongst 113 pts who received PO BU, 32 were diagnosed for high-risk localized disease (R2loc; 28.3%); 31 for pulmonary metastases (R2pultm; 27.4%); and 50 for other primary dissemination (R3; 44.2%). The 44 pts who received IV BU were distributed as follows: R2loc; 18; 40.9%; R2pultm; 9; 20.5%; R3; 17; 38.6%. Toxicity was analyzed by descriptive statistics according to modified CTC toxicity grade scales. Outcome was analyzed descriptively by event-free-survival (EFS) and overall-survival (OS) controlled for risk factors by multivariate regression analysis.

Results: Grade 3–4 toxicities occurred in 480 of 1759 pts (27.3%) in the PO group, and in 174 of 741 cases (23.5%; p = 0.048) in the IV group. The majority were hematological toxicities observed in 431 pts; >85% of patients per group; p = 0.59. Major differences of more than 10% in single scales were observed in the IV group regarding: general condition (IV: 18.2% vs. PO: 33.3%; p = 0.028; non-dichotomous), stomatitis (51.2% vs. 63.2%; p = 0.032; non-dichotomous); diarrhoea (0% vs. 12.5%; p = 0.033 and elevated bilirubin (2.8% vs. 13.3%; p = 0.104). 5y-EFS (OS) was 0.47 (0.57; SE = 0.08) for IV BU vs. 0.42 (0.49; SE = 0.05) in PO BU. Adjusted for risk group (R2loc; R2pultm; R3) and age (cut-off 15 years), the EFS risk ratio for PO vs. IV BU was 1.35 (95%CI 0.82–2.22), and the OS risk ratio was 1.49 (95%CI 0.85–2.61).

Conclusion: Results from this retrospective analysis indicate a reduction in toxicity and a tendency to favorable survival in IV BU-based HEC.
Purpose: The clinical profile and outcome of EBV-related post-transplant lymphoproliferative disorders in paediatric allogeneic haematopoietic stem cell transplantation were reviewed.

Method: A 6-year retrospective review of EBV-related PTLD in paediatric haematopoietic stem cell transplant setting was performed.

Results: From Jan 2005–Feb 2011, one hundred and three allogeneic HSCT was performed in our centre. Six cases of EBV-PTLD were diagnosed. The incidence was 5.8%. The age ranged from 25 months to 18 years old. The median age was 8 years old. Three patients (7.5%) received unrelated cord blood transplant, two patients (20%) received matched unrelated donor bone marrow or peripheral blood stem cell (PBSC) transplant, one patient (14.3%) received haploidentical transplant. All of them received anti-thymocyte globulin (ATG) as in-vivo T-cell depletion. The median onset time was 3.5 months post-transplant (2 months to 14 months). In five out of six patients, either donor and/or recipients were EBV seropositive and one patient was diagnosed to have primary EBV infection at 8.5 months post-transplant and had EBV reactivation at 10 months post-transplant. The most common presentations were cervical lymphadenopathies (83.3%) and fever (66.7%). Two patients (33.3%) presented with septic-like pictures with hypotension and one of them developed multiple organ failure. One presented with epigastric discomfort. All of them showed EBER positive in biopsy materials. Three out of them (50%) responded to withdrawal of multiple organs failure. One presented with epigastric discomfort. All of them showed EBER positive in biopsy materials. Three out of them (50%) responded to withdrawal of immunosuppressants alone. Two of them (33.3%) responded to addition of rituximab. Majority of them (83.3%) showed remission of PTLD after treatment. One patient died of multiple organs failure before treatment started.

Conclusion: PTLD is not uncommonly seen in paediatric allogeneic HSCT setting especially in matched unrelated donor and haploidentical transplant settings. Early recognition of clinical features of PTLD and timely reduction of immunosuppressants are the keys to manage this condition.

PN015

FEASIBILITY OF ALLOGENEIC TRANSPLANTATION WITH REDUCED-INTENSITY CONDITIONING FOR JUVENILE MYELOMONOCYTIC LEUKAEMIA

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Purpose: Juvenile myelomonocytic Leukemia (JMLL) is a rare hematopoietic malignancy that occurs during early childhood. Allogeneic hematopoietic stem cell transplantation (HSCT) is currently the only curative treatment for JMLL. However, HSCT with conventional myeloablative conditioning (MAC) is closely associated with high transplantation-related mortality (TRM) and high incidence of late effects. In order to reduce acute and late toxicity of MAC, we have employed reduced-intensity conditioning (RIC) for these patients since 9 years ago.

Method: During 1992–2010, ten children were diagnosed with JMLL. After several courses of chemotherapy, all patients received HSCT. Six patients who had been treated during 1992–2002, received MAC consisting of TBI (12 Gy), melphalan (140 mg/m²), and thiotepa (600 mg/m²). Four patients who were treated during 2004–2010, received RIC consisting of melphalan (140 mg/m²), fludarabine (180 mg/m²), and etoposide (200 mg/m²).

Results: Median age at the time of presentation was 17 (range 5–39) months. Five of six patients who received MAC are alive in CR with median follow-up of 13 years (range 12–15). All of them, however, are suffering from late effects of graft reactivation and some of them have other complications. In RIC group, two of four patients received umbilical cord blood transplantation resulting in CR with good QOL over three years. Although the other two patients relapsed after 1st HSCT from matched sibling donor, 2nd remission was achieved after 2nd HSCT, one with RIC at our institute and the other with MAC at the previous institute. All four patients of the RIC group are alive in CR with median follow-up of 3.8 years (range 1–4–5), and with lesser late effects except one who received 2nd HSCT after MAC.

Conclusion: Although the number of patients is small, our findings suggest that the present RIC regimen is comparable and safe. Further studies are needed to confirm the advantage of this alternative.

PN016

OUTCOME OF ALLOGENEIC STEM CELL TRANSPLANTATION IN CHILDREN WITH JUVENILE MYELOMONOCYTIC LEUKAEMIA

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Purpose: The possibility of successful transplantation of cord blood decreases when cellular compatibility are not match, so we have to look for options to improve the chances of successful transplantation.

Method: We performed a pilot study comparing the transplant that were performed with two units of umbilical cord blood of unrelated donor in patients with ALL in second remission and compared with a group of patients who were transplanted with a single unit of umbilical cord blood, we evaluated the cell dose, time of graft and overall survival and event-free survival between both groups.

Results: Was included a total of 5 patients in the transplant group with 2 units and 10 patients in the group with a single unit. Cell dose for the first unit was 5.3 ± 0.06 x 10^6/kg of mononuclear cells.
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cells and the second group 4.5 × 10^6 mononuclear cells per kilogram of body weight
(p = 0.16), in all cases histocompatibility was 4/6 for the first group, second group
compatibility was 4/6 in 5 cases, 5/6 in 4 and 6/6 in 1 case. Graft was achieved in 100%
of patients in group 1, group 2 graft failure was reported in 2 patients with graft
histocompatibility 4/6. The time of the grafting for the first group was 17 days and for group 2
was 32 days (p = 0.02), 4 of 5 patients (50%) who were transplanted with 2 units of umbilical
cord blood were alive and disease free and in the second group only 5 of 10 patients (50%) are
alive and disease free at 12 month follow-up.

Conclusion: The Transplant 2 units of umbilical cord blood in this pilot study demonstrated
to be an appropriate option for improving the performance of recovery time and better survival.

PP001
RHABDOMYOSARCOMA IN CHILDREN AND ADOLESCENTS
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Purpose: The goal of this study was to determine the frequency, epidemiology, clinical features and results of treatment of Rhabdomyosarcoma in a single Institution.
Method: We reviewed the medical records of 14 children with Rhabdomyosarcoma up to 18 years old in our institution from 2001–2010. They were evaluated for their age, gender, histology, stage at diagnosis and treatment.
Results: 14 patients had, their mean age at diagnosis was 7.31 years. Nine patients (64.28%) were male. One (7.14%) was below one year, 2 (14.28%) 1 – 5 y, 4 (28.57%) 6 – 9 y, 3 (21.42%) 10–15 y and 2 (14.28%) 16 – 18 y. The primary tumor site was:
head and neck in 6 (42.85%), GUT 4 (28.57%), extremities 2 (14.28%), Trunk 2 (14.28%).

Conclusion: The incidence of RMS in Venezuela is unknown. This is the first study in our institution in this area. Children with rhabdomyosarcoma of lower stage, embryonal histology, orbital and genitourinary tract primary site had a better survival rate but in this study only 3 (21.42%) patients had stage II, although 70% of RMS may be cured with the current treatment in our institution only 5 (41.66%) survived because of advance disease (stage III-IV in 78.57%). Recommend working in cooperative groups to understand RMS in Venezuela.

PP002
PREVALENCE OF MINOR ANOMALIES IN CHILDREN WITH CANCER
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Purpose: To study the prevalence of minor anomalies in children with malignancies and to compare with age and sex matched normal children. To compare our data with other published literature.
Method: This study was undertaken in Paediatric Hematology/Oncology (PBO) division of Christian Medical College (CMC), Vellore from July 2008-August 2009. 200 cases from PBO clinic and 200 age and sex matched controls from general pediatric clinics were included in this study. Cases were enrolled by simple random sampling. Age and sex matched controls were drawn in by systematic random sampling. A standard proforma used by developmental pediatrics department of our institution was used for screening for dysmorphology.
Results: Among children with cancer, 61 had at least one anomaly compared to 27 in the control group. A total of 86 anomalies were identified among children with various malignancies compared to 34 among controls. Café au lait spots, eye anomalies and benign naevi were the most common isolated anomalies in the study population. Preauricular pit was the single most common isolated anomaly in this study. There was no difference in the number or spectrum of anomalies between embryonal tumours vs non-embryonal tumours or lymphoproliferative malignancies vs solid tumours. Prevalence of minor anomalies reported in other studies ranged from 60–69% in children with cancer and 25–56% in controls compared to 31% and 14% respectively in our study.
Conclusion: 31% of children with cancer had at least one minor anomaly compared to 14% among controls in our study. Higher prevalence of anomalies in children with cancer supports the role of genetic factors in the etiology of childhood malignancies.

PP003
CANCER SURVIVAL FOR INDIGENOUS COMPARED TO NON-INDIGENOUS AUSTRALIAN CHILDREN
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Purpose: To explore the roles of place of residence, economic disadvantage, and stage at diagnosis in the survival rates of Indigenous compared to non-Indigenous children.
Method: All children residing in Australia and diagnosed with cancer between 1997 and 2005 were identified through the Australian Paediatric Cancer Registry. Validation of cancer records and Indigenous status were achieved through medical chart review. Place of residence was coded according to categories of the accessibility/remoteness index for Australia. The area-level socio-economic disadvantage index compiled by the Australian Bureau of Statistics was used to classify place of residence at diagnosis. Date and cause of death were also obtained from the Registry, which routinely updates its records via linkage with the Australian National Death Index. Multivariate Cox regression analysis was used to assess the differences in survival between Indigenous and non-Indigenous cases. Undated 5-year survival probabilities by ethnicity were calculated using the Kaplan-Meier method. Cases were followed-up until death or Dec 31, 2006, whichever came sooner.
Results: Over the 9-year period, 166 Indigenous children and 5200 non-Indigenous children were identified. The overall 5-year survival was 72.7% for Indigenous children and 81.1% for non-Indigenous children (p = 0.004). Indigenous children with cancer were 1.55 times more likely (95% CI 1.15–2.09, p = 0.004) to die within 5 years of diagnosis than their counterparts. The hazard ratio remained statistically significant after adjustment for place of residence and socio-economic disadvantage (HR = 1.44, 95% CI 1.05–1.97, p = 0.022) and for cancer diagnostic groups (adjusted HR = 1.50, 95% CI 1.11–2.02, p = 0.008). Overall, Indigenous cases were similar to non-Indigenous children with regards to cancer stage at diagnosis.
Conclusion: The disparities in place of residence, economic disadvantage, and cancer diagnostic groups only partially explain the survival disadvantage of Indigenous children. The reasons underlying the disparities in cancer outcomes between these two groups are likely to be multifactorial.

PP004
GEOGRAPHICAL ANALYSES OF THYROID CANCER IN GREAT BRITAIN, 1976–2005
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Purpose: Previous studies have suggested that recent increases in the incidence of thyroid cancer may be due to exposure to radiation from the Chernobyl disaster. We studied geographical variation in the incidence of primary thyroid cancers diagnosed in 0–49 year olds in parts of Great Britain (GB) during 1976–2005. We specifically aimed to compare incidence between the pre- and post-Chernobyl periods (1976–1986 and 1987–2005, respectively) and analyse putative associations with area-based measures of deprivation and population density.
Method: Case data on thyroid cancer were obtained from four regional cancer registries in GB (Northern and Yorkshire, North West, Wales and Scotland). Relative risks (RRs) and 95% confidence intervals (CIs) were calculated for each geographical area. Negative binomial regression was used to examine the effects of area-based measures of deprivation and population density.
Results: 4327 cases of thyroid cancer were analysed. The most marked statistically significant increases were seen in the areas of North Yorkshire (RR = 2.55; 95% CI 1.49–4.36), Hartlepool (RR = 5.53; 95% CI 1.28–23.98), North East Lincolnshire (RR = 2.55; 95% CI 1.05–6.19), North Lincolnshire (RR = 3.46; 95% CI 1.02–11.77), York (RR = 4.28; 95% CI 2.92–6.14), Cumbria (RR = 2.89; 95% CI 1.47–5.67), Carefully (RR = 2.67; 95% CI 1.00–7.14), Rhondda (RR = 14.41; 95% CI 1.96–106.07), the Scottish Borders (RR = 3.64; 95% CI 1.42–9.33), North Ayrshire (RR = 2.76; 95% CI 1.06–7.21) and North Lanarkshire (RR = 2.82; 95% CI 1.51–5.30). There were statistically significant associations with population density (RR for an increase of one person per hectare = 1.016, P < 0.001) and deprivation (RR for an increase of one unit in the deprivation score = 1.071, P < 0.001).
Conclusion: Higher incidence of thyroid cancer was observed in a number of geographical regions, including some which experienced high levels of fallout from the Chernobyl
explosion. Higher rates were also associated with urban living and greater deprivation, indicating that other environmental or lifestyle factors may play a role in aetiology.

PP005

SURVIVAL FROM CHILDHOOD CANCER IN NORTHERN ENGLAND, 1968–2005

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Purpose: Cancer is the second most common cause of death in children in the developed world. The study aimed to investigate patterns and trends in survival from childhood cancer (aged 0–14 years) in patients diagnosed in northern England during the period 1968–2005.

Method: Data on cases of childhood cancer were extracted from the Northern Region Young Persons’ Malignant Disease Registry (NRYPMDR), which is fully population-based. All cases of childhood cancer diagnosed in the region are notified to the NRYPMDR, leading to a high level of overall completeness and ascertainment, which is estimated to be more than 98%. Five year survival rates were calculated using Kaplan-Meier estimation for four successive time periods (1968–1977, 1978–1987, 1988–1997 and 1998–2005). Cox regression analysis was used to analyse associations with age and demographic factors.

Results: The study included 2,958 cases (1,659 males, 1,299 females). The five year survival rates for all cancers improved significantly from 39% in 1968–1977 to 79% in 1998–2005 (P < 0.001). The five year survival rates increased from 24% to 81% for Leukaemia (P < 0.001), from 46% to 87% for lymphoma (P < 0.001), from 43% to 73% for central nervous system tumours (P < 0.001), from 21% to 75% for bone tumours (P < 0.001), from 36% to 58% for soft tissue sarcoma (P < 0.001) and from 59% to 97% for germ cell tumours (P < 0.001). Survival was worse for cases of acute lymphoblastic Leukaemia (P < 0.001) and astrocytoma (P < 0.001) aged 10–14 years compared with 0–4 year olds.

Conclusion: There were marked improvements in survival from childhood cancer over the last four decades. Future work should examine geographical and demographic patterning in cancer survival and other factors that may lead to delays in diagnosis.

PP006

SOCIOECONOMIC DIVERSITY AND THE INCIDENCE OF CHILDHOOD LEUKAEMIA IN NORTHERN ENGLAND

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Purpose: Previous studies have investigated the putative association between the incidence of childhood acute lymphoblastic Leukaemia (ALL) and area-based measures of socio-economic level and diversity of inward migration (based on the Shannon population mixing index). Results of these studies have been conflicting. In this new study association between ALL, socio-economic status, migration and a novel measure of diversity in small-area based socio-economic status is analysed.

Method: Data on childhood acute Leukaemia was obtained from the Northern Region Young Persons’ Malignant Disease Registry, which is fully population-based. Case details of all 120 cases of ALL that were diagnosed during the period 1996–2005 were extracted from the registry. A new Shannon index of diversity of socioeconomic status was constructed using small-area socio-economic deprivation measures. The putative association between the incidence of ALL and three different measures of variation in socioeconomic status (diversity of socioeconomic status, population mixing and the Townsend deprivation score) was analysed using a fully Bayesian (Besaq-York-Mollie) hierarchical model. Relative risks (RRs) and credible intervals (CIs, which are the Bayesian analogue of confidence intervals) were obtained. The analyses were implemented using Markov chain Monte Carlo (MCMC) methods in WinBUGS software.

Results: A negative association with the incidence of ALL was most marked with the new diversity index of socioeconomic status (RR = 0.54; 95% CI 0.46–0.64) and less pronounced with population mixing (RR = 0.82; 95% CI 0.78–0.86) and the Townsend deprivation score (RR = 0.98; 95% CI 0.94–1.00).

Conclusion: Findings from this study suggest that areas that have populations that have the most diverse socioeconomic origins have the most reduced relative risk of ALL. Putative reasons for the association are that higher diversity leads to earlier exposure to a diverse range of infections. We suggest that this may be protective against subsequent development of ALL in genetically predisposed children.

PP007

CANCER AMONG TEENAGERS AND YOUNG ADULTS IN SWEDEN 2000–2008

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Purpose: In the world today there is a focus on cancer care among teenagers and young adults, TAs. There are several studies describing the situation for TAs with cancer in different parts of the world. The purpose of this study is to analyze the current situation for TAs (15–29 y) with cancer in Sweden.

Method: Incidence, survival rate and diagnose information were gathered from the National Cancer Registry in Sweden and the NSOHR registry. Data were collected on cancer patients, 15–29 y, diagnosed in Sweden between the years 2000–2008. Patients were divided in groups according to age (15–18, 19–23 and 24–29 y) and diagnosis. The groups were divided in these groups mainly because patients in the age of 15–18 are treated at pediatric oncology centers and 19–29 at adult units. Cancer types were defined using the International Classification of Diseases for Oncology (ICD-10) classification.

Results: The most common cancer types in the age group 15–18 y: lymphomas (28%), CNS tumors (27%) Leukemia and bone tumors (11%), among 19–24 y: testicular cancer (26%), lymphomas (55%) and skin melanomas (22%) and among 25–29 y: skin melanomas (27%), testicular cancer (26%) and lymphomas (15%). Analysis of the result is currently in working progress, the overall 5 year survival will be described. Among 15–18 y all are treated at university hospitals with national and/or international treatment protocols. Regarding 19–29 y, treatment approaches varies between the different diagnoses and will be further described.

Conclusion: The conclusion shows the diagnosis, the places of care, existing treatment plans and survival for TAs with cancer in Sweden. To further explore TAs opinions on hospital care we are continuing the study with focus group interviews.

PP008

THE ARGENTINE PEDIATRIC ONCOLOGY REGISTRY ROHA-INSTITUTO NACIONAL DEL CANCER: A TOOL TO IMPROVE CANCER CARE IN CHILDREN

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Purpose: Cancer registries are a known strategy to improve cancer care in developing countries. We report the experience of ROHA, a population-based pediatric cancer registry that started in 2000. Since 2010, ROHA has been incorporated into the National Cancer Institute.

Method: ROHA collects and consolidates data about cancer diagnosis, treatment, and survival in children aged 0 to 14. The registry was developed following IARC guidelines for hospital-based registries and provides direct feedback to reporting centers. Cross-validation with the national mortality database is conducted annually. Standardized incidence cancer rates (SIR) were estimated for the period 2000–2008. In addition, we report on treating institutions’ characteristics and need of migration for treatment.

Results: From 2000–2008 ROHA registered 11,445 new childhood cancer cases in Argentina. It is estimated that the registry covers 90% of the country’s cases for a base population of 10 million children (Census 2001). Data sources include pediatric oncology services (n = 40) and private practices (n = 36) throughout the country, regional cancer registries (N = 12), and cooperative groups (n = 2). The SIR for all histological types combined is 128.5 per million; for Leukemias 47.5 and for CNS Tumors 23.5. 86% of children were cared for in public institutions and 53% of these cases were treated in 4 tertiary level hospitals. Migration to get treatment at tertiary care centers varied by tumor type (39% for Leukemias/lymphomas vs. 55% for solid tumors, p-value < 0.001).

Conclusion: Since 2000 ROHA provides a relevant and reliable portrait of the epidemiology of pediatric cancer in Argentina. ROHA in this middle-income country are comparable to those from high-income countries. Pediatric cancer care is centralized in a few public institutions and migration a frequent event for families. ROHA is an invaluable aid for the development of pediatric cancer control programs throughout the country.

PP009

PRENATALLY DIAGNOSED MALIGNANT SOLID TUMORS IN RUSSIAN FEDERATION

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Purpose: The aim of the study was to assess epidemiological and clinical features of prenatally diagnosed solid tumors in Russian Federation (RF).

Method: Infants with malignant solid tumors first detected prenatally were included in the study. The data on patients were collected as a part of multicenter (22 centers) study investigating malignant solid tumors in infants in RF for the period 2006–2010.

Results: 18 (5.6%) cases of prenatally diagnosed tumors were revealed among 321 cases of malignant solid tumors in infants. The median gestation age at the time of detection was 32 weeks (range 22–39). 3 (16.7%) patients had congenital anomalies. 11 cases (61.1%) were located in the retroperitoneal space, 2 cases (11.1%) in the brain, head and neck region and pelvic area. 1 case (5.5%) in posterior mediastinum. The most common tumor was neuroblastoma - 9 (50%) cases, followed by germ cell tumors - 4 (22%), Wilms tumor - 2 (11%), soft tissue sarcomas - 2 (11%), glioblastoma - 1 (6%). Age at the time of histological confirmation of diagnosis was less than 15 days in 3 patients, 1 month in 15 patients, 2 months - 1 patient, 3 months -1 patient 6 (33%) patients had stage I, 4 (22%) stage II, 8 (45%) - stage III–IV. Tumors in stage I patients were only surgically removed. Patients with stage II–IV were treated by surgery and chemotherapy. 14 patients are alive with the median follow-up of 8 months (range 1 month - 4.9 years). 2 patients died because of the disease, 2 - lost to follow-up.

Conclusion: Our study showed that solid malignancies detected prenatally belonged to embryonal tumors, neuroblastoma was the most common. The obtained data can be used for planning timely cancer care for children in the early neonatal period.

PP010

EPIDEMOLOGICAL SPECTRUM OF PAEDIATRIC MUSCULOSKELETAL TUMORS AT A TERTIARY REFERRAL CENTRE IN INDIA

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Purpose: To study characteristics at presentation of paediatric musculoskeletal tumors (PMST).

Method: All PMST (< 18 years) presenting to Bone & Soft Tissue disease management group of our institute from January to December 2010 were included.

Results: 396 cases of PMST were seen during this period. Male to female ratio was 1.7:1. Thirty seven cases did not return for review after the first visit. 281cases (72.8%) were malignant lesions while 53 cases (14.7%) were benign. 25 (6.9%) non-neoplastic lesions were seen. There were 277 (98.5%) primary malignant tumors. Among primary malignant bone tumors (226 cases), the commonest tumors were Osteosarcoma 121 cases (53.5%) and Ewing sarcoma/PNET 88 cases (39%). Among primary malignant soft tissue tumors (51 cases), the commonest tumors were Ewing sarcoma/PNET 15 cases (29.4%) and synovial sarcoma 13 cases (25.4%). Complete metastatic work-up was possible in 248 primary malignant tumors. 183 (73.7%) were localised and 65 (26.2%) were metastatic at presentation with the incidence being similar for bone and soft tissue sarcomas. The commonest benign bone tumors were giant cell tumour 12 cases (22.6%) and aneurysmal bone cyst 10 cases (18.8%).

Conclusion: Our comparison with our data with SEER analysis (Surveillance, Epidemiology and End Results, US) for paediatric bone tumors. Our malignant to benign bone tumor incidence was found only among age-group 15–19 years. Although this is a small study an association between ART and risk of childhood cancer may be inferred. Larger population based studies would be required to further establish the link if any of this interesting observation.

PP012

SOCIOECONOMIC STATUS AND LYMPHOMAS INCIDENCE IN CHILDREN AND ADOLESCENTS IN BRAZIL

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Purpose: To analyze the incidence rates of lymphomas in children/adolescents (0–19 years) and their correlation with socioeconomic status (SES) in Brazil.

Method: All cases of Hodgkin (HL), non-Hodgkin (NHL), Burkitt lymphoma (BL) were extracted from 15 Population-based cancer registry (PBCR) in five different geographical regions, during 2000–2005. Cases were assigned using the International Classifications of Disease for Oncology (ICD-O, 1996–2004; ICD-O, 2005). The subtypes of lymphomas were grouped according to the International Classification of Childhood Cancer (ICCC).

Conclusion: This study showed that mothers of children with cancer used ART more frequently and had a higher incidence of abortions and infertility as compared to the control group. Although this is a small study an association between ART and risk of childhood cancer may be inferred. Larger population based studies would be required to further establish the link if any of this interesting observation.

PP013

EPIDEMIOLOGY OF CHILDHOOD CANCER IN KENYA: A REPORT FROM THE DOCTOR2DOCTOR TWINNING PROGRAM

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Purpose: Basic epidemiologic information on childhood cancer in Western Kenya is lacking. This is an important pitfall in improving the care and cure for these children in this part of the world. Our study aims to provide an overview of childhood cancer in Western Kenya.

Method: A retrospective analysis of childhood malignancies in Western Kenya was carried out using information from three private databases at the Moi Teaching and Referral Hospital. All patients between 0–19 years with a newly diagnosed malignancy were included. First presentation of patients occurred between January 2006 and January 2010.

Results: A total of 437 children with cancer were registered in the period. There were 257 (59%) boys and 180 (41%) girls with a male/female ratio of 1.4:1. The group aged 6–10 years contained most children (29%). Median age at admission was 8 years. Non-Hodgkin lymphoma was the most common type of cancer (34%), followed by acute lymphoblastic
Leukemia (15%), Hodgkin lymphoma (8%), nephroblastoma (8%), thalassemia (7%), retinoblastoma (5%) and Kaposi sarcoma (5%). Only 4 (1%) children with brain tumors were documented. Ewing sarcoma was not diagnosed.

Conclusion: Our study provides an overview of childhood malignancies in Western Kenya. It gives useful information about the local challenges. The distribution of malignancies is similar to findings in other equatorial African countries and differs markedly from studies in high-income countries. The new comprehensive cancer registration should be continued and extended to establish an evidence-based oncology program. Eventually this may lead to better clinical results.

PP014
THE IMPACT OF PREDICTORS OF CO-MORBIDITY AND TREATMENT INTENSITY ON SURVIVAL FROM CHILDHOOD LEUKAEMIA IN ENGLAND AND WALES, 1980–2006
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Purpose: To evaluate the impact of birth-weight and congenital malformations on five-year survival, and to ascertain whether these factors are predictors of co-morbidity in children who were diagnosed with Leukaemia.

Method: Records for children aged 0–14 years diagnosed with Leukaemia while resident in England during 1980–2006 were identified in the National Registry of Childhood Tumours. Their registry records were linked to birth records for birth weight data, and Children’s Cancer and Leukaemia Group records and Hospital Episode Statistics (HES) available from 1998 onwards for information on congenital malformations. Relative survival was estimated by birth weight (< 2,500 g, 2,500–4,000 g, > 4,000 g), presence of a congenital malformation, age at diagnosis (< 1, 1–4, 5–9, 10–14 years), sex, type of Leukaemia and clinical trial entry. Multivariable analysis will be used to model the impact of demographic factors and predictors of co-morbidity on survival.

Results: Children with a low or high birth weight (< 2,500 g and > 4,000 g) had slightly poorer five-year survival than other children (80% vs 83% during 2000–06), but the difference was never significant. Children with a congenital malformation had lower survival of at least 10% compared with other children. Children under one year at diagnosis consistently had poorer survival at least 15% compared with older children. Children with lymphoid Leukaemia had higher survival than children with other types of Leukaemia (87% vs 64% during 2000–2006). Children who entered into clinical trials had higher survival of at least 10% compared with other children throughout the study.

Conclusion: Initial findings suggest that birth weight is not an independent prognostic factor for childhood Leukaemia survival. Presence of a congenital malformation, age at diagnosis, type of Leukaemia and non-entry into a clinical trial are all predictors of a poorer outcome in children with Leukaemia. Final conclusions based on multivariable analyses will be presented.

PP015
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Purpose: To estimate five-year survival and the proportion of patients ‘cured’ of acute myeloid Leukaemia (AML) and the survival of the ‘uncured’ by age at diagnosis, and to compare estimates for England with those observed in Sweden.

Method: This population-based study included records of 47,250 adult patients within the National Cancer Registry who were diagnosed with AML in England during 1971–2006. Relative survival and cure mixture models were used to produce estimates and predictions of outcome.

Results: Five-year survival and the proportion ‘cured’ increased for those under the age of 70 years at diagnosis during 1971–2006, but the magnitude of the increase varied with age. Increasing age at diagnosis was associated with poorer outcome. The most dramatic increase in five-year survival occurred in those aged 15–24 years, from 7% to 50%, but for those over the age of 70 years it remained less than 5%. The proportion ‘cured’ is predicted to increase to 46% for those aged 15–24 years and 13% for those aged 60–69 years at diagnosis in 2006. The median survival of the ‘uncured’ increased from 0.41 years in 1975 to 0.93 years in 2000 in those aged 15–24 years, and from 0.19 years to 0.38 years in those aged 60–69 years at diagnosis.

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Conclusion: Improvements in the long-term outcome of patients with AML have been age-dependant, with dramatic improvements seen in those diagnosed under the age of 25 years. Whilst these improvements are welcome, long-term outcome of adults with AML in England is still poorer than in Sweden, especially in those under the age of 40 years.

PP016
RATIONAL MANAGEMENT AND PREDICTORS OF ADVERSE OUTCOMES OF FEBRILE NEUTROPENIC EPISODES IN CHILDHOOD MALIGNANCIES
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Purpose: Among neutropenic children with cancer, infection is the major antyopy defined cause of death. Identifying febrile neutropenic episodes where children are at low risk of adverse outcome may lead to successful out-patient management and better utilization of resources. This study was designed to identify predictors associated with adverse outcomes (culture positivity/ hemodynamic instability/ mortality alone or in combination) in pediatric febrile neutropenic episodes and to determine the common organisms and their antimicrobial sensitivity in such children.

Method: 155 episodes of childhood febrile neutropenia were enrolled. Admission information pertaining to proposed risk factors was obtained which included age & sex of child, maternal education, primary diagnosis, severity of fever, time since last chemotherapy and blood transfusion, being on oral antibiotics, number of previous febrile neutropenic episodes, anemia, thrombocytopenia, severity of neutropenia and abnormal Chest Roentgenogram. These children received treatment according to our center protocol till they reached the final outcome, which was either adverse outcome or discharge from hospital.

Results: Out of the 155 episodes adverse outcome occurred in 53 episodes; majority were due to invasive bacterial infection. Univariate analysis identified time since last chemotherapy and last blood transfusion, number of previous episodes, fever duration, being on oral antibiotics and Chest X Ray abnormality as significant predictors. On Multivariate analysis significant variables associated with adverse outcome were: more than three such previous episodes being on oral antibiotics and abnormal Chest X Ray at presentation. The prevalence of bacterial infection was 18.7%. Gram negative infections (Escherichia coli) were more frequent than gram positive infections (Staphylococcus aureus). Sensitivity pattern of micro-organisms to antibiotics was established.

Conclusion: This preliminary study provides useful information on predicting adverse outcomes in episodes of febrile neutropenia, prevalence of blood stream infections, prevailing microbial organisms and their sensitivity pattern in this select group of patients.

PP017
CHILDHOOD CANCER MORTALITY TRENDS IN NAIROBI PROVINCE KENYA 2003–2006
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Method: Data on cancer incidence and mortality was extracted from Nairobi Cancer Registry. Population data on deaths was obtained from register of deaths at Civil Registration Department.

Results: During the period under review, 7730 new cases of cancer were reported and of these, 542(7%) were childhood cancers. Over the same period, 81985 deaths were registered in Nairobi. Of the deaths registered, 3.42% (2864) were cancer-related. Childhood cancers made up 15.7% (442) of these deaths with haematological malignancies being the leading cause of death and accounting for 15.4%(68%). This was closely followed by Burkitt lymphoma comprising 15.1% (67%). Non-Hodgkin lymphoma was the third leading cause of childhood cancer-related deaths making up 8.1% (36+) and followed by nephroblastoma at 7.6% (35+). The 0–4 year age band registered the highest number of deaths and accounted for 34.1% (126) of all deaths.

Conclusion: Haematological malignancies were the leading cause of childhood cancer-related deaths closely followed by Burkitt lymphoma. These two types of cancer make up a significant proportion (30.5%) of all causes of childhood cancer-related deaths.

PP018
INCIDENCE AND CHARACTERISTICS OF PAIN IN CHILDREN WITH SOLID MALIGNANT TUMORS- OUR RESULTS
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SIOP ABSTRACTS

PP001
FIRST OUTCOME ANALYSIS OF THE NEW ZEALAND CHILDREN'S CANCER REGISTRY

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Purpose: To report the development and first outcome analysis from the New Zealand Children’s Cancer Registry.

Method: We developed a national online children’s cancer registry (NZCCR) integrated with our national late effects assessment programme database - LEAP-IT. Our fully relational database (MS SQL) has registered all childhood cancer diagnosed in New Zealand since 2000. NZCCR captures core demographic data, including geographic location, ethnicity, recurrence, secondary cancer, cancer predisposition, disease status and outcome. Cancers are coded according to the ICD-0 fields and the ICC3. We capture extended diagnostic data including disease stage, risk stratification, treatment and treatment related events.

Results: Over the 8-year period 2000–2007, 1170 cases of cancer were registered and verified. The median age at diagnosis was 4 years, with an equal gender ratio (male 51%, female 49%). Māori and Pacific Island children account for 28.8% of diagnoses (Māori 17.6% and Pacific 11.1%). Acute Leukaemias were 31% of registrations, ALL 26%, and AML 5%. Lymphomas were 8.4% of diagnoses and Brain tumours including pilocytic astrocytoma, 18.1%. Neuroblastoma and bone sarcoma were both 7% of diagnoses and soft tissue sarcoma 5.4%. There were 227 deaths reported giving a 3 year overall survival for the whole cohort of 80.6%, and disease specific survival for ALL 88%, AML 55% and brain tumours 71%. There was a 99.5% concordance of registrations for malignant cancers with the New Zealand Cancer Registry.

Conclusion: We have established a national online children’s cancer registry and report on the first national analysis for the 8 year period 2000–2007, including the first overall outcome analysis for childhood cancer in New Zealand. Māori and Pacific Island children account for 28% of diagnosis but the overall pattern of childhood cancer in New Zealand is similar to other Western Populations. Overall survival for childhood cancer in New Zealand compares favourably with other international reported outcomes.

PP002
EVIDENCE-BASED PRACTICE AND SPECIFYING OUTCOMES FOR CHILD CANCER ORGANIZATIONS

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PP003
LEUKEMIA AND LYMPHOMA TRENDS IN CHILDREN IN ALBERTA: A 22 YEAR POPULATION-BASED STUDY

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Purpose: There is paucity of published literature on epidemiological data addressing childhood acute Leukemias and lymphomas from Canada. Hence this study was designed to describe epidemiology of children and young-adults (< 20 years) diagnosed with acute lymphoblastic Leukemia (ALL), acute myeloid Leukemia (AML), Hodgkin lymphoma (HL), and non-Hodgkin lymphoma (NHL) in Alberta, Canada over 22 fiscal years.

Method: The high resolution Alberta Cancer Registry was used to extract epidemiologic and demographic information on all ALL, AML, HL, and NHL diagnosed between 04-01-1982 and 03-31-2004. Population data for Alberta were also obtained. Splus 8 statistical software was used for descriptive statistical analyses.

Results: During 22 years, 525, 117, 257, and 111 children (total 1,101) were diagnosed with ALL, AML, HL, and NHL, respectively. The median ages at diagnosis were 4, 11, 16, and 12 years for ALL, AML, HL, and NHL, respectively. The majority were male for ALL (287/525, 55%), AML (64/117, 55%), and NHL (81/257, 73%), and female for HL (133/257, 52%). A median of 23 cases were diagnosed annually (range: 1-63). The crude rates per 100,000 children were very low, with significant trends, over time and for each diagnosis; the median annual rates, per 100,000 children, were 3.00 (range: 1.87–3.75) for ALL, 0.62 (range:0.26–1.27) for AML, 1.42 (range:0.76–2.67) for HL, and 0.54 (range:0.24–1.40) for NHL. A few potential spatio-temporal clusters were identified by Besag and Newell, and Kulldorff and Nagawalla tests. They are likely due to small number of cases and plausibly clinically insignificant.

Conclusion: Overall, childhood Leukemia and lymphoma rates in Alberta have remained relatively stable with no clear epidemiological trends and no significant spatiotemporal clustering. Further investigations are warranted to see if such stability continues and if spatiotemporal patterns arise from studies in larger geographic regions with a larger sample size; whilst analysing for other causal/associated factors, individual susceptibilities and disease outcomes.

PP004
CANCER INCIDENCE AND MORTALITY IN INDIGENOUS AUSTRALIAN CHILDREN, 1997–2006

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Method: The data were obtained from cancer registries within the Indigenous Cancer Information System (ICIS). ICIS is a multi-cancer registry, linked to the National Cancer Database (NCDB). The incidence and mortality data were extracted from the ICIS and NCDB databases and linked using a unique personal identifier. The data were stratified by age, sex, and Indigenous status (Indigenous and non-Indigenous). The incidence and mortality data were analysed using the Surveillance, Epidemiology, and End Results (SEER) database.

Results: The incidence and mortality rates for cancer among Indigenous Australian children from 1997 to 2006 were calculated. The incidence rates were highest for non-Indigenous children, while the mortality rates were highest for Indigenous children. The most common types of cancer among Indigenous children were leukaemia, lymphoma, and solid tumours. The incidence and mortality rates were highest for non-Indigenous children, while the mortality rates were highest for Indigenous children. The most common types of cancer among Indigenous children were leukaemia, lymphoma, and solid tumours.
Purpose: To report the patterns of incidence and mortality of cancers among Indigenous children diagnosed with cancer during 1997–2006 and compare these with corresponding rates for non-Indigenous children.

Method: Utilising data from the Australian Paediatric Cancer Registry (APCR), one of the few population-based national registries of childhood cancer in the world, age-specific cancer incidence and mortality rates were calculated for all cancers and by selected cancer diagnostic groups. Rates were age-standardised to the WHO World Standard Population. Indirectly standardised incidence ratios (SIRs) were also produced, by applying age-specific incidence rates for non- Indigenous children to the population data for Indigenous children to calculate the expected number of cases. The SIRs were then obtained by dividing the observed number of cases by the expected number. A similar process was used to derive standardised mortality ratios (SMRs). Confidence intervals for the SIRs/SMRs were calculated at the 95% level of certainty (denoted as 95% CI).

Results: A total of 181 cancers were identified among the population of Indigenous children, representing an incidence rate of 97.3 per million per year. Of these, Leukaemias and tumours of the central nervous system were the most common cancers, responsible for 53% of all new cases. Overall, Indigenous children were 37% less likely to be diagnosed with cancer (SIR 0.63, 95% CI 0.54–0.73) than non-Indigenous children. Forty four children died from cancer from the Indigenous cohort during the follow-up period, corresponding to a mortality rate of 23.3 per million per year. The SIR for all cancers for Indigenous Australians compared to other children was 0.83 (95% CI 0.60–1.11).

Conclusion: Trends in incidence and mortality can be monitored over time, now that baseline data have been established. Monitoring mortality rates is particularly important given the estimates were based on a relatively small number of children.

PP025

EARLY CANCER DEATHS IN ARGENTINEAN CHILDREN: DATA FROM THE ARGENTINEAN PEDIATRIC ONCOLOGY REGISTRY

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5Matero Infanti San Juan Bautista Hospital, Oncology projects. The project results focus on legal issues concerning the legal, ethical, technical and clinical handling of consent in Europe and to identify existing practices and problems encountered in translational research throughout Europe.

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PP024

LEGAL, ETHICAL, TECHNICAL AND CLINICAL HANDLING OF CONSENT IN EUROPEAN PROJECTS DEATING WITH VULNERABLE PATIENT GROUPS

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PP026

THE IMPACT OF RURALITY AND ETHNICITY ON HOSPITAL UTILIZATION IN FRENCH EDERMIC CANCER PATIENTS

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Purpose: Data flow between care and research is fundamental for translational research. As the data to be exchanged are in most cases personal data, data protection is of utmost importance. Obtaining informed consent to the processing of data from patients is part of a data protection framework of which physicians are aware. Issues of informed consent will be addressed by CONTRACT (COntent in a TRiAL & Care environment), a project funded within the 7th Framework Programme of the European Union. It seeks to establish methods to understand the impact of consent on the success of translational research.

Method: CONTRACT has chosen to focus on projects and stakeholders dealing with consent issues in clinical trials involving vulnerable patient groups in particular. A survey showing how European and national translational projects deal differently with consent issues was undertaken to define good practices, to give policy recommendations and to offer a help desk for partner projects on consent issues. A developed questionnaire was divided into 6 different sections (general, clinical care, research, IT related, legal and ethical issues, handling) with 123 questions altogether.

Results: 8 different stakeholders groups (Clinicians and Care providers, Chairpersons of research projects or trials, Basic Researcher, Computer Scientists, Legal Experts and Ethics, Data Manager and Statisticians, European Policy makers) and 221 projects were contacted of which 184 (83%) were European or national projects. The project results focus on legal consent as a fundamental precondition for the legal processing of personal data. One problem of consent is the number of different consent forms, the complexity and the increasing load of information provided by these forms.

Conclusion: The results of the questionnaire allow to analyse the current situation concerning the legal, ethical, technical and clinical handling of consent in Europe and to identify existing practices and problems encountered in translational research throughout Europe.

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Purpose: Rural pediatric cancer patients may live great distances from specialized care centers, creating challenges for delivering therapy and managing toxicities. Hispanic ethnicity may also be associated with unique barriers to care for children with cancer in the US. This study investigates how rurality and Hispanic ethnicity impacts hospital utilization in these patients.

Method: We utilized an integrated regional hospital network database to determine 3-year hospital, emergency department (ED) and PICU admission rates for children diagnosed with cancer at a regional tertiary hospital from January 1995 to December 2008. Fisher’s exact and Mann-Whitney rank sum tests were employed to evaluate associations.

Results: We analyzed 3139 patients, 2366 (75%) were considered urban, 773 (25%) rural, 2429 (77%) white and 316 (10%) Hispanic. The geographic and ethnic groups did not differ in age or cancer type. After adjusting for ethnicity, urban patients were more likely to have had an ED encounter than were rural patients (46% vs. 23%, p = 0.001), with no differences in hospital admissions (46% vs. 42%, p = 0.13) or PICU encounters (11% vs. 8.4%, p = 0.09). Urban patients had a greater median number of ED visits (2 vs. 1, p = 0.02) while median number of hospital admissions and PICU encounters did not differ. Hospital and PICU length of stays did not differ in rural patients, nor did median inpatient and ED costs. White patients were more likely to be admitted to a hospital than Hispanics (47% vs. 39%, p = 0.01), but not more likely to have an ED (38% vs. 38%, p = 0.90) or PICU encounter (11% vs. 12%, p = 0.49). For those accessing the ED, median number of ED visits was 3 for Hispanics and 2 for whites (p = 0.009).

Conclusion: Rurality and ethnicity may be associated with hospital utilization patterns. Ongoing analysis of other morbidity indicators and mortality rates in this cohort will provide further insight into potential disparities.

PP001

SHARING THE CARE: AN INNOVATIVE HEALTH PROGRAM FOR CHILDHOOD AND ADULT CANCER SURVIVORS BETWEEN THE LATE EFFECTS CLINIC AT PETER MACCALLUM CANCER CENTRE AND THEIR GP’s.

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Purpose: Cancers survivors are increasingly more aware of their need for ongoing medical surveillance, psychosocial support and management of late effects. With this increased awareness and growing population of cancer survivors there is a need to develop sustainable models of survivorship care. This prospective audit sets out to identify appropriate and feasible models of long term care according to clinical need and risk of late effects.

Method: A prospective audit of all current patients on the Peter MacCallum Cancer Centre (PeterMac) Late Effects database will occur. Evidence based guidelines will be used to stratify patients into one of four levels of surveillance group. Level 1 patients will include those with complex needs and at high risk of late effects, requiring at least yearly multidisciplinary review, with level 4 being patients who are eligible for discharge from the clinic with care returned to their General Practitioner (GP). All patients and GPs will be given a Survivorship Care Plan and Long Term Follow Up recommendations.

Results: Since the 1st of October 2010, 235 patients have been reviewed in the Late Effects Clinic at Peter Mac. Of those, 79% of patients fell into level 1, n = 126, 14% into level 2, n = 22, 6% into level 3, n = 9 and 1% into level 4, n = 2.

Conclusion: This audit will help inform a sustainable and tailored model of long term follow up care for cancer survivors at risk of late effects.

PP002

UTILISING A REQUIREMENTS ANALYSIS APPROACH TO INTEGRATE USER AND PROFESSIONAL VIEWS INTO THE DESIGN OF A CANCER SURVIVORSHIP SERVICE

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Purpose: Mechanisms for incorporating user views into clinical service design are poorly defined. We utilised Requirements Analysis, a systems engineering process, in designing a shared care survivorship programme. The Bristol Aftercare service supports adult survivors of childhood cancer in a population of 4.5m. Care is currently centralised at the paediatric oncology centre but the project aims to help patients transition to safe and effective care, in an adult setting, as close to home as possible.

Method: In order to design a service based on user views, data was sought by postal questionnaires and focus groups (patients, n = 245), on-line questionnaires (professionals, n = 47) and by geographical analysis. Key findings (n = 140) were submitted to Requirements Analysis to define and prioritise work needed to address their expectations. Each finding was assessed for implications (Requirements) on a new survivorship service. 59 requirements (reduced from 202 by de-duplication) were first evaluated against factors chosen to reflect health policy and practical applicability, including: Benefits considered achievable in areas of Quality, Innovation, Productivity, Prevention & Personalised Care (QIPP); Priority (Must, Should, Could, Would do); Scope; Difficulty (Very Difficult to Very Easy); Benefit (None/Very Low to High). These were then allocated to a category of activity (e.g. Process, Patient Knowledge) and to aspects of service function (e.g. Clinic Consultation, Training/Education). The methodology ensured that an audit trail linked each Requirement to a final activity that would inform service design.

Results: Requirements related to Quality or Innovation; 76% were defined as Must/Should do activities; 66% as having High/Significant benefit; but 36% were considered Difficult/Very Difficult to achieve. Greatest impacts were predicted on activities affecting patient knowledge (34%) and processes relating to direct patient contact (42%).

Conclusion: Requirements Analysis offers an effective way to prioritise patient and professional views in clinical service design. A new Aftercare service is being implemented utilising these findings.

PP003

SECOND MALIGNANT NEOPLASMS IN CHILDHOOD CANCER SURVIVORS IN A TERTIARY PAEDIATRIC ONCOLOGY CENTRE IN HONG KONG

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Purpose: To report the first analysis of outcome for indigenous Maori and Pacific Island (PI) children with cancer in New Zealand.

Method: Maori and Pacific Island children have higher infant mortality and preventable deaths compared to New Zealand children as a whole. Similarly, adult Maori and Pacific Islanders have significantly worse outcomes for cancer compared to European adults. We analysed the New Zealand Children’s Cancer Registry to describe the spectrum of cancer and 3-year overall survival of Maori and PI children over and 8-year period from 2000–2007. All cancer diagnoses were classified according to the International Childhood Cancer Classification 53.0.

Results: Of 1170 verified and validated cancer registrations, 207 were Maori (17.6%) and 130 were Pacific (11.1%). Age, gender and diagnosis for Maori and PI were comparable to the whole cohort except for ALL, which was less frequent in Maori (19%) compared to PI (24%), and overall 26% and medulloblastoma where Maori children had higher risk disease at diagnosis. Neuroblastoma was uncommon in PI at 2.0% of diagnoses (Maori at 6.7%, overall 6.9%) and Retinoblastoma more common (5.3%) compared to Maori (2.8%) and overall of 2.6%. Of 226 deaths, 50 were Maori and 22 PI. The 3-year overall survival were 80.6% for the whole cohort, Maori 76% and PI 83%.

Conclusion: In this first analysis of cancer Maori and Pacific Island children, the spectrum of cancer is comparable to the whole population with the exception of ALL, high risk medulloblastoma neuroblastoma and retinoblastoma. Cancer outcomes for Maori and Pacific Island children are similar to the whole population with differences in overall survival attributable to relative mortality of cancer diagnosis. This important observation implies culturally appropriate health care by child cancer services can achieve excellent outcomes for children with cancer regardless of their cultural or ethnic origin.
**Purpose:** To evaluate the incidence, risk factors and outcome of second malignant neoplasms in childhood cancer survivors in a tertiary paediatric oncology centre in Hong Kong.

**Method:** Retrospective review of patients treated in Childrens Cancer Centre in Prince of Wales Hospital between May 1984 and March 2011. Case records of patients developed second malignant neoplasms were reviewed.

**Results:** Total 1471 new cases were treated in this 26-year study period. Thirteen cases developed second malignant neoplasms with 10-year and 20-year cumulative incidence of 1.3% and 2.9% respectively. Another 4 cases were referred to us from other centres for the management of second malignant neoplasms. The median age of second malignancies was 12.9 years (range 5.5–21 years). The most frequent second malignant neoplasms were acute leukemia or myelodysplastic syndrome (n = 6) and central nervous system tumor (n = 4). Median time interval between diagnosis of primary and second malignant neoplasms was 7.4 years (range 2.1-13.3 years). Median interval was shorter for second Leukemia or myelodysplastic syndrome of 4.2 years compared to second solid tumor of 9.1 years. Nine patients died of progression of second malignant neoplasms, mainly resulting from second central nervous system tumor and osteosarcoma. Radiotherapy significantly increased the risk of development of second solid tumor in patients with acute lymphoblastic Leukemia (p = 0.027). Eight patients developed second solid tumor within the previous irradiated field. All patients who developed acute Leukemia or myelodysplastic syndrome as second malignant neoplasms had prior use of chemotherapy with alkylating agents, topoisomerase II inhibitors or platinum compounds. Seven out of 17 patients who developed second malignant neoplasms died of progression of second malignant neoplasms, mainly resulted from second solid tumors. 5—Despite the poor prognosis of SMN, second therapy is advisable considering the possibility of achieving long survivals in our setting.

**Conclusion:** Radiotherapy was associated with second solid tumour among patients with acute lymphoblastic Leukemia up to 12.3 years after completion of treatment. Patients developed second brain tumor and osteosarcoma had poor outcome.

**Conclusion:** Radiotherapy was associated with second solid tumour among patients with acute lymphoblastic Leukemia up to 12.3 years after completion of treatment. Patients developed second brain tumor and osteosarcoma had poor outcome.

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**SECOND MALIGNANT NEOPLASMS IN CHILDHOOD: 23 YEAR EXPERIENCE IN A SINGLE INSTITUTION IN ARGENTINA**

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**Purpose:** Improvement in childhood cancer survival results in development of long term sequelae being second malignant neoplasms (SMN) one of the most serious complications.

**Method:** From August-1987 to March-2011, with a mean annual accrual of 350 new malignancies, fifty-four out (M:30/F:24) cases were defined as SMN. Patients were classified according to whether first malignant neoplasms (FMN) was hematological (ALL, AML, NHL and HL). 24 cases were neuroblastoma, 28 sarcoma family tumours, 13 second leukemias and 20 solid tumors, including 2 Ewing sarcoma-family tumors, 3 osteosarcoma, 3 malignant schwannoma, 2 thryroid carcinoma and 1 rhabdomyosarcoma, fibrohistioctytic sarcoma. Nine tumors occurred in non-irradiated areas. Treatment was administered to 52 SMN. Forty-three patients achieved complete remission (CR), 5 died during induction and 6 were resistant to treatment. From the 43 patients who achieved CR, 18 presented relapses or progressive disease and 5 died in CR. Twenty-one patients remain in CR with a median follow-up of 62 months (range: 2–264 mo).

**Conclusion:** 1-SMN is an infrequent event in pediatric oncology. 2-AL presented increased risk of developing SMN, followed by retinoiblastoma. 3-Occurrence of solid tumors is not always related to radiotherapy. 4-Latency for developing AL is significantly shorter than for solid tumors. 5-Despite the poor prognosis of SMN, second therapy is advisable considering the possibility of achieving long survivals in our setting.

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**CONSEQUENCES OF TREATMENT ON THE FOOD PREFERENCES AND DIETARY HABITS OF CHILDHOOD CANCER SURVIVORS**

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**Purpose:** Rates of childhood cancer are increasing, yet so are survival rates. Loss of fertility is an expected consequence of most cancer treatments. This study sought to identify and compare the specific reproductive concerns of adolescent girls with cancer and their parents using an 8-item survey instrument.

**Method:** 13 pairs of adolescent girls aged 12–17 and their parents (n = 26) were interviewed. Families were from FL and CA. We assessed the level of agreement between parent and adolescent response on the items. Overall, there was 47% agreement between parents and daughters; 55% agreement on meaning; and 35% agreement on distress. For example, the item “If I cannot have a baby in the future I would blame my cancer” was described as “well understood” by 93% of the teens. However, only 57% of parents thought that their daughter would understand this item (thus, agreement rate = 75%). On this same item, 14% of the girls said it was not relevant to their life but 100% of their parents thought their daughter would find this relevant. 86% of parents thought their daughter would be distressed by this item, yet 29% of teens said they felt distress.

**Conclusion:** Parents may not have accurate predictions about their daughter’s perceptions of reproductive concerns. These data indicate the desire to learn about risks and risk reduction including infertility by teen girls but also acceptance of the idea that they may not be able to have a child. Parents had less acceptance of that concept and were less willing to consider fertility preservation for their daughters. As a result of this study, the instrument was refined and a guide for administration was developed. The guide emphasizes the need for trained staff to administer the instrument and the importance of fertility discussions.
PREVALENCE OF THE METABOLIC SYNDROME IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER. A PILOT SINGLE CENTRE STUDY

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Purpose: To assess the prevalence of metabolic syndrome (MS) in a cohort of adolescents (10–16 years) long term survivors of childhood cancer (CCS), by using recent diagnostic criteria set by the International Diabetes Federation.

Method: Adolescents attending our long-term follow-up clinic were evaluated by body mass index (BMI), waist circumference, blood pressure, fasting glycaemia, fasting insulinemia and lipid profile. MS was diagnosed if BMI > 90 centile and ≥ 2 of the following risk factors: systolic pressure ≥ 130 mmHg, diastolic pressure ≥ 85 mmHg, triglycerides ≥ 150 mg/dl; cholesterol HDL < 40 mg/dl; waist circumference > 90 centile; fasting glycaemia > 100 mg/dl. Study type: 2 diabetes.

Results: 68 patients (55 males; 33 females) were evaluated: 36 (53%) were treated for a solid tumour, 32 (47%) for Leukaemia or lymphoma. Median age at cancer diagnosis was 5.1 years (range 0.3–19.0 years). MS was diagnosed in 23 patients (34%) at follow-up visit was 13.5 years (range 10.2–16.9 years). Treatment included alkylating agents or anthracyclines in 53 subjects (78%); radiotherapy to the abdomen, head or TBI in 16 (23%). No physical activity was reported in 20 survivors (29%). MS was diagnosed in 12 patients (18%) in 33 (48%) at least one risk factor was found; the remaining 23 survivors (34%) had no risk factors. Only gender was found to be significantly correlated with MS, occurring in 29% of males (n = 10) and in 6% of females (n = 2)(P = 0.04; chi-squared test). No other significant correlation was found between MS and treatment variables related with physical activity.

Conclusion: One fifth of adolescents survivors of solid tumour, Leukaemia or lymphoma appears to have MS, almost 50% of them have already 1 or 2 risk factors for MS. In these patients preventive interventional strategies including lifestyle changes should be implemented. The cohort needs to be enlarged in order to allow more detailed analyses.

PQ009

PRESERVATION OF OVARIAN FUNCTION CHILDLREN AT RISK FOR OVARIAN FAILURE

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Purpose: Chemotherapy and radiotherapy can damage the ovary in children. The option that enables fertility to be preserved is cryopreservation of ovarian tissue. There is a classification of subfertility risk (Wallace et al., 2005b) that should be considered.

Method: To report our experience regarding indications for cryopreservation, age, technique-related complications, delay of cancer treatment, re-implantation, and analysis of patients’ opinions. Methods: Thirty-nine girls and adolescents diagnosed (2006–2011) with neoplasm, 12 of whom were peripuberal. Five had a high risk of ovarian failure due to Hodgkins disease (4) and metastatic rhabdomyosarcoma (1), and one patient had an intermediate risk due to osteogenic sarcoma. All were offered cryopreservation and accepted; cryopreservation could not be carried out in one patient due to poor initial performance status.

The data corresponding to the end of treatment are analyzed (data regarding menstruation, hormone study, re-implantation, replacement therapy, and the patient’s attitude toward the preserved tissue, as per a questionnaire). The procedure was performed by laparoscopy, under general anesthesia at the reference center. There were no incidents in the patients 1–3 days later, without delaying cancer treatment initiation. The patients expressed a very good opinion with respect to the procedure. After cancer treatment: Current age Menstruation pre/post Treatment FSH mIU/ml/E2 estradiol pg/ml Risk of ovarian failure Primary ovarian failure Replacement Therapy Hormid: Hodgkin, 20 yes/no, 74/6 high no no no; Hodgkin, 15 yes/no, > 2005 yes E+P no; Hodgkin, 14 yes/es., high no no no; Hodgkin, 16 yes/es., high no no no and chose not to restrict their child.

Similar parental concerns about portion size and high fat/sugar intake were less apparent in the comparison group. Parents of cancer survivors also reported that they should have been more proactive in encouraging consumption of healthier foods during treatment.

Conclusion: The qualitative framework of Miles and Huberman was used to guide data analysis. The results from this study provide insights into the long-term change in dietary habits of child cancer survivors. This study highlights key areas for preventative nutritional interventions during and soon after treatment which may help to decrease the risk of later effects in adult survivors of childhood cancer.

PQ010

INTESTINAL PERMEABILITY IN CHILDREN WITH SOLID TUMOURS

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Purpose: It was well known that anti-cancer treatment may result in the damage of bowel mucosa. The aim of this study was the measurement of intestinal permeability in children after multidrug chemotherapy for solid tumors.

Method: 49 pediatric patients with cancer (26/23 F/M, aged from 2 to 20 years), who were diagnosed and treated in the Department of Pediatrics, Hematology, and Oncology, Medical University of Gdansk, Poland, in the period from 2008 to 2010 were enrolled in the study. They had no gastrointestinal symptoms, infections and nephropathy. Intestinal permeability was assessed by measurement of urinary lactulose/mannitol after oral challenge by the enzymatic analyses.

Results: There was statistical significance in lactulose and mannitol urine excretion compared to the controls (p = 0.006 for lactulose and p = 0.0053 for mannitol). Cancer patients excreted less mannitol (mean 8.04 vs 10.46) than the controls (mean 10.6%). Excretion of lactulose in the oncological group increased (mean 0.455%) compared with the control (mean 0.28%). The ratio of lactulose to mannitol, which is an estimation of intestinal wall permeability, was significantly higher in children with cancer (mean 0.166) than for the controls (mean 0.353) (p < 0.0001).

Conclusion: Intestinal barrier is damaged in pediatric cancer patients after chemotherapy. This method is non-invasive, safe and easy to perform. It may be useful in clinical practice to establish the proper diet and apply the treatment according to protocols without delay.

PQ011

PULMONARY OUTCOMES FOLLOWING TREATMENT FOR CHILDHOOD CANCER WITH LUNG IRRADIATION

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Purpose: To describe the prevalence of pulmonary complications in pediatric oncology patients treated with lung irradiation.

Method: Eligible patients at Children’s Hospital Los Angeles from 1999–2009 were identified from the radiation oncology database. Patients who received total body irradiation were excluded. Clinical features, radiographic findings, pulmonary function tests and radiation therapy data were retrospectively ascertained.

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Results: 139 patients (93 male) were identified. Median age at irradiation was 13 years (range 0.0–21 yrs) with a median follow-up of 2.5 yrs (range 0.2–192 yrs). Median radiation dose was 34 Gy (range 12–82 Gy). Diagnoses were equally divided between lymphomas and other solid tumors. Chemotherapy that could potentially contribute to pulmonary toxicity included bleomycin in 46.7% and cyclophosphamide in 78.4%. Chronic cough was noted in 7.9% (gr 1 = 5%, gr 2 = 2.9%) and dyspnea in 9.4% (gr 1 = 2.9%, gr 2 = 1.4%, gr 3 = 3.6%, gr 4 = 1.4%). Radiation pneumonitis developed in 7.2% of patients and 33.1% experienced at least one episode of pneumonia. Chest wall deformity was detected clinically or by radiography in 12 (8.6%). Radiographic evidence of intestinal lung disease was present in 33% of patients (gr 1 = 27.3%, gr 2 = 5%, gr 3 = 0.7%). The probability of developing at least one of the above findings at 5 years was 50.7% (95% CI: 40.6–60.6%). Results of pulmonary function tests following irradiation were available for 48 patients. FEVI and TLC were decreased in 30% and 16.3% respectively. DLCO was decreased in 7%. There was no significant difference in the prevalence of adverse pulmonary outcomes between the irradiation only and irradiation + pulmonary toxic chemotherapy groups by log rank analysis (p = 0.65).

Conclusion: One-third of patients receiving pulmonary irradiation for the treatment of childhood solid tumors had at least one radiation related long-term complication. In this cohort of patients, chemotherapy did not additionally contribute to pulmonary toxicity.

PQ012
ENDOCRINE DYSFUNCTION AS LATE EFFECTS IN CHILDHOOD MEDULLOBLASTOMA: A COMPARISON BETWEEN PATIENTS TREATED WITH DIFFERENT RADIOTHERAPY DOSES OVER A 13 YEARS PERIOD

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Purpose: The outcome of medulloblastoma has significantly improved recently with radiotherapy as an integral part of the treatment and endocrine dysfunction as one of the late effects. Current approach in clinical trial is to reduce the dose of craniospinal radiotherapy to reduce the late effects. This study is to evaluate the effect of reduction of radiotherapy dose on the incidence of endocrine dysfunction among medulloblastoma survivors.

Method: This is a retrospective review of 74 children with medulloblastoma treated at our institute in between 1996 to 2008. We compared the incidence of endocrine abnormalities between two groups treated with different doses of craniospinal radiotherapy including 36 Gy (Grays) 23 Gy and those children who did not receive radiotherapy.

Results: We noticed that reduction in the dose of craniospinal radiotherapy did not reduce the incidence of endocrine dysfunction. Out of 74 patients, 62 (88%) received radiotherapy include 34 (46%) 36 Gy and 28 (38%) 23 Gy. In patients who received 36 Gy, growth hormone deficiency was noticed in 18 patients (53%), hypothyroidism in 15 (44%), precocious puberty 3 (9%), delayed puberty 1 (3%) steroid deficiency 2 (6%). However, in patients received 23 Gy, the number of growth hormone deficiency was 16 (57%), hypothyroidism 9 (32%), precocious puberty 4 (14%), delayed puberty 1 (4%), steroid deficiency 1 (4%). One patient, out 12 who did not receive radiotherapy also developed growth hormone deficiency. However this patient had previous traumatic brain injury which might have caused growth hormone deficiency. We could not find any other hormone deficiency in patients who did not have radiotherapy.

Conclusion: This study shows that endocrine dysfunctions are still a significant late effect among medulloblastoma survivors. Reducing the craniospinal radiotherapy did not decrease the incidence. There can be other factors which cause endocrine late effect among medulloblastoma survivors. We recommend prospective study among medulloblastoma survivors.

PQ013
BONE MINERAL DENSITY AND BONE FORMATION ACTIVITY IN CHILDREN WITH MEDULLOBLASTOMA AND BRONCHIAL ASTHMA IN COMPARISON WITH THE HEALTHY PEERS

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Purpose: To compare bone mineral density and bone formation activity in children treated for medulloblastoma (MB) and bronchial asthma (BA) with healthy peers.

Method: We have examined 31 patients with MB, 91 patients with BA and 84 healthy peers (CG). All MB and BA patients presented surgical treatments, chemotherapy and craniospinal irradiation. Among BA patients 25 of them were treated with inhalation and systemic steroids, 66 did not receive them. Bone mineral density of the L1-L4 spine region was assessed in all children using densitometry device Lunar Prodigy GE. Z-score equal or less than -2SD indicated low bone mass (LBM). Ostacalcin (OC) level in plasma was assessed in all children with the immunoelectrochemiluminesence. Alkaline phosphatase (AP) activity in plasma was assessed with the colorimetric method of Bessey, Lowry and Brock. Shapiro-Wilk’s test (1), Mann-Whitney test (2) were used for statistical analysis. Data were expressed as M(SD), Me(LQ-U).

Results: LBM was determined in 22.6% (7/31) patients with MB, in 11.6% (9/91) patients with BA and in 6% (5/84) of CG. LBM frequency was higher in MB when compared with both BA (2 = 0.014) and CG (2 = 0.010), no difference in LBM frequency was found between BA and CG (2 = 0.196). OC level in MB comprised 64.7 (30.4) ng/ml, p = 0.091, in BA 98.8 [70.4:137.1] ng/ml, p = 0.000, in CG - 89.9 [69.1:127.0] ng/ml, p = 0.000. AP activity in MB was 389 [284:529] IU/l, p = 0.005, in BA - 556 (202) IU/l, p = 0.061, in CG - 456 (207) IU/l, p = 0.196. OC level was lower in MB in comparison with CG (p = 0.001) and BA (p = 0.000). AP activity was lower in MB in comparison with BA (p = 0.001).

Conclusion: Low bone mass and low bone formation activity is more prevalent in MB patients in comparison with BA patients and healthy peers and puts patients treated for medulloblastoma at high risk for osteoporosis in the adult life.

PQ014
LONG-TERM FOLLOW-UP OF NUTRITIONAL STATUS, PANCREATIC FUNCTION, AND MORPHOLOGICAL CHANGES OF THE PANCREATIC REMNANT AFTER PANCREATIC TUMOR RESECTION IN CHILDREN

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Purpose: The objectives of the present study are to determine nutritional status, pancreatic exocrine function, pancreatic endocrine function, and morphological changes of the pancreatic remnant following pancreatic tumor resection in children.

Method: The nutritional status was evaluated by the patterns of growth. Pancreatic exocrine function was evaluated by using a questionnaire and the Bristol stool form chart. Pancreatic endocrine function was evaluated by the serum levels of fasting blood glucose and hemoglobin A1c (HbA1c). Morphological changes of the pancreatic remnant were evaluated by computed tomography (CT), magnetic resonance image (MRI), or magnetic resonance cholangiopancreatography (MRCP).

Results: The present study consisted of 6 pancreatic tumor patients (5 solid pseudopapillary tumors of the pancreas; SPT, 1 pancreatoblastoma). Tumor enucleation was performed in 3 patients (2 head of the pancreas and 1 tail of the pancreas), distal pancreatectomy with splenectomy in 1 patient (tail of the pancreas), and pylorus-preserving pancreaticoduodenectomy (PPPD) in 2 patients (2 head of the pancreas). At a median follow-up of 98 months (36 to 192 months), none of patients received pancreatic enzyme supplements. All patients achieved normal growth. There was no patient with severe steatorrhea. Incidence of postoperative diabetes was 0%, but the serum levels of HbA1c have been gradually elevated in all of two patients with PPPD. A significant decrease in pancreatic parenchymal thickness and dilatation of the main pancreatic duct were observed on CT, MRI, or MRCP in all of two patients with PPPD.

Conclusion: After pancreatic tumor resection, children can grow normally. Endocrine pancreatic insufficiency after PPPD may be explainable by obstructive pancreateatitis after operation. Taken together the results of pancreatic endocrine function and morphological changes of pancreatic remnant after PPPD, tumor enucleation should be considered as surgical approach in children with pancreatic head tumor whenever possible.

PQ015
LONG-TERM OUTCOME OF CHILDREN WITH CANCER SURVIVORS -PERSONAL EXPERIENCE

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Purpose: An experience of increasing number of long-term survivors of children’s cancer brings many new challenges to pediatric oncologists. It is essential to know long-term outcome of children with cancer, whom we treated by ourselves, in order to give them better care.

Method: All children with cancer who were treated by author’s group and whose outcomes are known are enrolled. Among them, patients who are surviving at least 10 years after diagnosis are evaluated for late effects.

Results: The outcome of 534 out of 643 children with cancer are known and 189 patients (35.4%) (10-year survivors) survive more than 10 years after diagnosis. Median of ages of 10-year survivors is 29 years (range: 11 to 52 years, 3 months to 53 years 4 months). The kinds of cancers of children whose outcome is known are proportional to those of whole children but more than half of 10-year survivors had acute lymphocytic Leukemia (ALL) (55.0%). Forty one patients (21.7% of 10-year survivors) have one or more late adverse effects. The second primary neoplasms were seen in 9 patients. These are meningioma, breast...
carcinoma, rectal carcinoma, thyroid carcinoma and adenoma and acute myelogenous Leukemia. Ten 10-year survivors died. Median of their survival time was 15 years 9 months (range: 10 years 10 months to 35 years 9 months). The causes of death were relapsed primary disease, respiratory failure, heart failure and rectal carcinoma. Three patients with ALL relapsed and died long after continuous complete remission. These patients had been in CCR for 15 years, 19 years and 33 years before the first relapses.

Conclusion: Although prognosis of children’s cancer excellent, possibility of late death cannot be ignored. Particularly, good risk ALL can relapse long after continuous complete remission. Therefore, careful long follow up is important for children with cancer.

PQ016

REPRODUCTIVE OUTCOME IN MARRIED YOUNG ADULT SURVIVORS OF CHILDHOOD CANCERS ATTENDING AFTER COMPLETION THERAPY (ACT) CLINIC

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Purpose: To assess the reproductive outcome in married young adult (Age ≤ 35 yrs) survivors of childhood cancers registered in After Completion of Therapy (ACT) Clinic between Feb. 1991 to Feb 2011.

Method: ACT Clinic database was analyzed for reproductive outcome in married young adult survivors. Risk factors for infertility such as diagnosis at age, diagnosis and treatment modalities were reviewed.

Results: 1200 survivors (> 2 years off therapy and disease free) were registered in ACT Clinic from Feb 1991 to Feb 2011. 971/1200 (80.9%) are survivors of hematological malignancies, 206/513 (40%) are survivors of solid tumours.

Conclusion: Our study indicates that management of fertility is an essential part of survivorship care. Male:female ratio was 3:1 (381:132). 307/513 (60%) are survivors of hematological malignancies, 206/513 (40%) are survivors of solid tumours. 71/513 (14%) are married. Further data was obtained from 49/71 (69%) married survivors who are following up regularly. Male:female ratio of 3:1 (36/13) survived pregnancy after therapy. 1/4 of the survivors were infertile, 1/4 had spontaneous abortions, 1/4 had recurrent spontaneous abortions. 1/4 of the survivors had hydrosalpinx and 1/4 had peritonitis.

PQ017

LONG-TERM FOLLOW-UP OF CHILDREN AFTER ANTICANCER TREATMENT IN POLAND- STRUCTURE, PROBLEMS AND FIRST RESULTS

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Purpose: To assess the reproductive outcome in married young adult (Age ≤ 35 yrs) survivors of childhood cancers registered in After Completion of Therapy (ACT) Clinic from Feb.1991 to Feb 2011.

Method: ACT Clinic database was analyzed for survivors (<18 yrs) of childhood cancers registered in After Completion of Therapy (ACT) Clinic between Feb. 1991 to Feb 2011.

Results: 1200 survivors (> 2 years off therapy and disease free) were registered in ACT Clinic from Feb 1991 to Feb 2011. 971/1200 (80.9%) are survivors of hematological malignancies, 206/513 (40%) are survivors of solid tumours. 71/513 (14%) are married. Further data was obtained from 49/71 (69%) married survivors who are following up regularly. Male:female ratio of 3:1 (36/13) survived pregnancy after therapy. 1/4 of the survivors were infertile, 1/4 had spontaneous abortions, 1/4 had recurrent spontaneous abortions. 1/4 of the survivors had hydrosalpinx and 1/4 had peritonitis.

Conclusion: Our study indicates that management of fertility is an essential part of survivorship care. Male:female ratio was 3:1 (381:132). 307/513 (60%) are survivors of hematological malignancies, 206/513 (40%) are survivors of solid tumours. 71/513 (14%) are married. Further data was obtained from 49/71 (69%) married survivors who are following up regularly. Male:female ratio of 3:1 (36/13) survived pregnancy after therapy. 1/4 of the survivors were infertile, 1/4 had spontaneous abortions, 1/4 had recurrent spontaneous abortions. 1/4 of the survivors had hydrosalpinx and 1/4 had peritonitis.

PQ018

SURVIVING CHILDHOOD NEUROBLASTOMA: AT WHAT COST?
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Purpose: To evaluate late effects of therapy in survivors of Neuroblastoma (NB) registered in After Completion of Therapy (ACT) Clinic at Tata Memorial Hospital in context of therapeutic approaches.

Method: ACT Clinic database was analyzed for survivors (> 2 years off therapy and disease free) of NB for late effects of therapy, which was reviewed in context of NB database from 1987–2008. Era1 (1987–1998), Era2 (1998–2008) were identified based on availability of optimal treatment components (intensive induction therapy, surgery, 13 C retinoic Acid, I131 MIBG & ABMT).

Results: Of 1020 survivors registered in ACT Clinic between 1991 and 2008, 73(7%) are survivors of NB. M: F 2:1(47:26). Median time since cessation of treatment was 5 years 2 (2–19). Median duration of follow up in ACT clinic 2 years (0–18) yrs. Median age at last follow up is 29 yrs indicating they are in the prime of reproductive life. Out of 36 married men,34(94%) are azoospermic while 2(6%) have normal semen analysis.13(34%) have children through assisted reproduction.1/4(3%) have adopted while 16/34(47%) are awaiting. 1/3(33%) have normal menstrual cycles and 9/13(69%) have conceived normally.

Conclusion: Our study indicates that management of fertility is an essential part of survivorship care. Male:female ratio was 3:1 (36/13) survived pregnancy after therapy. 1/4 of the survivors were infertile, 1/4 had spontaneous abortions, 1/4 had recurrent spontaneous abortions. 1/4 of the survivors had hydrosalpinx and 1/4 had peritonitis.

PQ019

ASSESSMENT OF BRACHIAL ARTERY REACTIVITY, CAROTID INTIMA MEDIA THICKNESS AND ADHESION MOLECULES IN PEDIATRIC SOLID TUMOR PATIENTS WHO RECEIVED ANTICANCER CYCLES

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Purpose: Appropriate follow-up of pediatric cancer survivors is essential for applying preventative measures and early treatment to potential organ-related side-effects of received treatment.

Method: In 2008 a Polish nationwide data base of pediatric cancer survivors was created. Personal data, information on diagnosis, stage, type of treatment applied, acute side effects and current functioning of organs and systems are collected. Since 2009 maintenance of this system is funded from Health System as a part of National Program for Cancer Prevention. As parts of this project a standard summing-up information letter for cancer survivors was designed and educational booklets for parents and teenagers were printed.

Results: 1 So far 721 pediatric cancer survivors were registered. Following percentage of sequelae after anticancer therapy were reported: 17.0% in cardiac, 16.6% in renal, 7.2% in liver, 15.9% in thyroid and 33.9% in gonadal function; 11.4% in respiratory, 16.8% in digestive, 14.2% in neurologic, 10.4% inocular and 13.6% in immune systems, 9.1% in hearing perception, 18.7% in stature. 374(17.2%) survivors presented at least one long-term side effect of treatment. 2 Long-term follow-up of survivors who became adult and those who moved from the given pediatric oncologic center region is still a significant problem in Poland. They stay under the supervision of GPs and their close follow-up related to secondary cancers and other sequelae is very difficult.3 Meetings with general practitioners and pediatricians, educational programs for pediatric cancer survivors and their parents, are way to raise awareness of possible long-term complications of anticancer treatment and necessity of follow-up.

Conclusion: Observed problems in organs functioning after treatment in childhood and long-term follow-up system of survivors (especially of teenagers) indicate that multidisciplinary centers for medical care of this population are needed.

Pediatr Blood Cancer DOI 10.1002/pbc
Purpose: In this study, we aimed to determine the endothelial dysfunction and subclinical atherosclerosis in pediatric solid tumor patients who received anthracyclines. We used carotid and brachial artery Doppler ultrasonography (USG) and measured serum adhesion molecules levels to assess the cardiovascular disease risk in these patients.

Method: Fifty patients who were in remission, and 30 healthy children were included in the study. We measured the cumulative value of doxorubicin per m2 for each patient. Patients were evaluated in 3 groups. Cumulative anthracycline dose $< 100$ mg/m2, cumulative anthracycline dose $100-300$ mg/m², and $> 300$ mg/m². Patients with hyperlipidemia, obesity, hypertension, atherosclerotic cardiac disease and congestive heart failure were excluded from the study. The brachial artery reactivity, right and left carotid intima media thickness (IMT) were measured in order to determine the endothelial function and were compared with control group. We also measured the serum adhesion molecule levels in our patients and controls.

Results: The brachial artery reactivity of the patients with cumulative anthracycline dose $> 300$ mg/m² was significantly lower than the patients with cumulative anthracycline dose $< 100$ mg/m² and healthy controls ($p = 0.003$ and $p = 0.005$, respectively). Also, there was a negative correlation between brachial artery reactivity and increasing cumulative anthracycline dose ($r = -0.287$, $p = 0.044$). No statistically significant difference was detected between the serum levels of sICAM-1, sVCAM-1, sE-selectin of the patients and the control. There was also no statistically significantly different fort the serum adhesion molecules between patients groups of different cumulative anthracycline dosages. We found significant difference between the mean IMT of the patients and the healthy children ($p = 0.041$).

Conclusion: In conclusion, this study supported that the use of anthracyclines in pediatric cancer patients could result in increase of the carotid IMT and endothelial dysfunction. Cancer patients who received anthracyclines should be followed for vascular toxicity and early atherosclerosis.

**PO202**

ENDOCRINE LATE SEQUELAE IN LONG-TERM SURVIVORS OF CHILDHOOD NON-HODGKIN LYMPHOMA

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Purpose: Aim of this study was to investigate the long-term endocrine side effects of treatment for childhood non-Hodgkin Lymphoma (NHL).

Method: A single centre cohort of 84 survivors (22 females), treated for childhood NHL between 1975 and 2003, was included in this retrospective study. Median age at diagnosis was 7.9 yrs (range 1.5–16.0 yrs), and at follow-up 21.3 yrs (8.9–40.0 yrs). Time after cessation of therapy was 12.4 yrs (4.4–29.9 yrs). Body mass index (BMI) was calculated. Percentage of ideal body mass (LBM), bone mineral content (BMC), bone mineral density of total body (BMD-TB) and lumbar spine (BMD-LS) were measured using DXA-scan. Serum levels of AMH and Inhibin-B were measured. Results were compared with Dutch age and gender matched controls, and were expressed as standard deviation scores (SDS).

Results: Height was lower in NHL survivors at follow-up (median SDS $-0.31$, $p = 0.002$), but analysis at age of diagnosis suggested shorter stature was already present (median SDS $-0.064$). BMI, percentage fat, BMC, BMD-TB, BMD-LS and BMAD-LS in survivors were not different from controls. LBM was lower in survivors (median SDS $-0.26$, $p = 0.014$), especially in male survivors (median SDS $-0.18$, $p = 0.034$) and in non-B-NHL survivors (median SDS $-0.14$, $p = 0.042$). NonB and B-NHL survivors did not differ with respect to these parameters. TSH, FT4 and TFG-I were normal in all survivors. Three adult females had low AMH levels and 23 adult males had low Inhibin-B levels.

Conclusion: Twelve years after cessation of therapy, survivors of NHL are not at higher risk of developing adiposity, osteopenia or osteoporosis or thyroid disease. Male NHL survivors seem to be at risk for infertility.

**PO203**

FIRST EXPERIENCES WITH BARIATRIC SURGERY IN THE TREATMENT OF CHILDREN WITH CRANIOPHARYNGIOMA AND MORBID OBESITY

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Purpose: The aim of this study was to investigate the late effects of childhood cancer treatment on thyroid functions.

Method: 120 relapse-free survivors of childhood cancer (84 M, 36 F) followed up in Gazi University Hospital between November 1992 and April 2010, were included in this study. The diagnosis of patients were: Lymphoma, Leukemia, Brain tumors, Rhabdomyosarcoma, Nasopharyngeal carcinoma and others. Patients were divided into two groups depending on the treatment. Group I: chemotherapy only (n = 52), Group II = chemotherapy and radiotherapy (head/neck/thorax) (n=68). Thyroid function tests, urine iodine levels and thyroid ultrasound examinations were evaluated in both groups.

Results: The median age of the patients was 16.25 years. The median age of the patients at diagnosis was 8.12 years and median follow up time was 6.66 years. The patients in group II developed hypothyroidism (n=31), morphological pathologies (e.g. nodules, parenchymal heterogeneity) (n=38), autoimmune thyroiditis (n=20) and secondary thyroid cancer (n=3) during follow-up. The median interval from the time after radiation therapy until the recognition of hypothyroidism, thyroid nodule and secondary thyroid malignancy was 5 years, 9.16 years and 11.75 years respectively. In Group I, patients developed autoimmune thyroiditis (n=16), morphological pathologies (n=19). The overall incidence of hypothyroidism was 25.6%, morphological pathologies was 47.5%, autoimmune thyroiditis was 30%. The incidence of hypothyroidism and thyroid nodules in Group II were significantly higher than in Group I (p < 0.001). In Logistic regression analysis, mantle radiotherapy (RR 4.2), cervical radiotherapy (RR 22) and 5000-6000 cGy radiotherapy (RR 22) were found to increase the development of hypothyroidism significantly (p < 0.05).

Conclusion: While the incidence of hypothyroidism, nodule formation and secondary thyroid malignancy were increased in patients who received chemotherapy and radiotherapy, the use of only chemotherapy does not seem to be associated with an increased incidence of primary hypothyroidism.
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Purpose: There is a high risk of non-ocular tumours occurring in survivors of heritable retinoblastoma. Non-ocular tumours, osteosarcoma is the most common second malignancy seen in retinoblastoma survivors. Purpose of this study was to evaluate clinical features and outcome of treatment of secondary osteosarcoma following retinoblastoma.

Method: In Korea, we surveyed the survivors of retinoblastoma in 4 hospitals, and found 7 survivors of retinoblastoma who had secondary osteosarcoma. We retrospectively reviewed the record of 7 patients.

Results: Retinoblastoma was bilateral in all 7 cases. Patients had been treated with a combination of surgery, chemotherapy, and radiation. Average age at diagnosis of secondary osteosarcoma was 8.9 years (5.4–14.8 years). Average interval between the two malignancies was 8.3 years. One of 7 patients refused the treatment and died of disease progression. 6 of 7 patients received multimodal management. Three of the six patients were dead, because of disease progression (1 patient) and septic shock in neutropenia (2 patients). 3 of the six patients are still alive without disease for 10 months, 1 year 5 months, and 2 years respectively; One received the conventional treatment and 2 patients received high dose chemotherapy with peripheral blood stem cell rescue.

Conclusion: Prognosis of osteosarcoma in retinoblastoma patients remains poor as compared to conventional high grade osteosarcoma despite multimodal management. High dose chemotherapy with stem cell rescue might be good to improve the outcome.

PR002

Unpredictable Consequences of Brain Tumors, Complex Analysis by Neuropsychological Assessment and FMRI

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Purpose: Neurological and cognitive problems are frequent late effect associated with childhood brain tumors. Symptomatology and consequences of brain tumors are largely dependent upon tumor location. In our sample we observed small subgroup, in which that relation between localization of brain damage (as a consequence of tumor) and dysfunction is complex and mechanism not clear. The aim of the study was to find causes of unpredictable disability not correlated with tumor location. We search for broad spectrum of coexisting and causes of unpredictable physical and/or sensory dysfunction were excluded and detailed analyzed.

Method: A prospective study was undertaken analyzing the full psychological outcome in 350 patients with malignant brain tumors treated with neurosurgery, chemotherapy and radiotherapy. Study utilizing long-term observation and repeated psychological testing was performed in patients with physical and/or sensory problems associated with brain tumors. Not clear mechanism of impairment in some cases, was also analyzed by neuropsychological assessment correlated with FMRI.

Results: Psychological testing was performed in 350 childhood brain tumor survivors (various type and localization of tumor) to determine the effect of brain tumors. Age at psychological diagnosis ranged from 6 to 26 years. From this group 30 patients with unpredictable physical and/or sensory dysfunction were excluded and detailed analyzed.

Conclusion: The research allowed put the hypothesis about the probable causes and mechanisms of injury beyond the location of the tumor. Also may be an important voice in the debate on development and plasticity of the brain.

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PR003

Something’s Gotta Give, Changing Work Practices to Reduce Cytotoxic Exposure

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Purpose: As Cytotoxic Drugs meet the Australian criteria for Hazardous Substances, the Royal Children’s Hospital (RCHB) is required to meet workplace health and safety requirements.

Method: We have worked closely with the RCHB health and safety management and the occupational health and safety team to implement and evaluate a new role for the occupational health and safety nurse (OHN). The OHN is a health professional with specialist knowledge and experience in the management of workplace health and safety risks.

Results: The OHN plays an important role in the management of workplace health and safety risks. The OHN is responsible for implementing and maintaining a comprehensive workplace health and safety program for the RCHB. The OHN is also responsible for providing advice and support to the RCHB health and safety management and the occupational health and safety team.

Conclusion: The implementation of the OHN role has been successful in reducing the workplace health and safety risks at the RCHB. The OHN is an important resource for the RCHB health and safety management and the occupational health and safety team.
legislative requirements. To achieve this and to align with the best practice recommendations in Queensland, a project was initiated by the Queensland Children’s Cancer Centre. This paper outlines the project achievements along with the education roll-out strategies and outcomes.

Method: The project performed a gap analysis (literature search; review of existing RCCH policies and procedures; practice audits; risk assessments) where existing practices at RCCH was compared with the legislative requirements and best practice recommendations. Recommendations from the project were incorporated into: nursing standards, procedures, and work instructions; staff education programs, resources and multidisciplinary implementation plans; and parent education resources. Collaboration with representatives across the organization occurred throughout the project. An implementation plan was developed with consideration to all disciplines and to the legislative requirements for training.

Results: The project has successfully implemented Standards and Procedures in the organization which meet the current legislative requirements and best practice recommendations. Training requirements have also been met for induction training, and ongoing training requirements have been achieved in the Nursing discipline. There is now parent information and extensive educational/support resources available for staff. A health monitoring program has been established and processes are now in place for ongoing reporting, review, and management of exposure incidents.

Conclusion: Whilst achieving these results, there is an ongoing need for the organization to meet legislative training requirements across all disciplines. Future trials of clinical equipment need to be considered by the organization to further reduce the risk of exposure to workers when preparing/administering cytotoxic drugs. Risk assessments will need to be repeated to meet legislative requirements. Ongoing clinical practice audits will assist in identifying compliance to standards and ensuring consistent practice across the organization.

PR004
MALNUTRITION IN PEDIATRIC ONCOLOGY: PREVALENCE AND SCREENING

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Purpose: Nutritional assessment is an essential component of the initial assessment of children with cancer. The prevalence of malnutrition in pediatric oncology depends on the type of the malignancy and the treatment intensity. The aim of this study is to evaluate the prevalence of malnutrition in children with cancer in Tunisia and to identify predictive factors of major weight loss during treatment.

Method: Nutritional status of 40 children aged less than 15 years with newly diagnosed malignancy between November 2008 and January 2009 was evaluated by anthropometric parameters. The Reilly score was used to assess nutritional risk.

Results: A total of 40 patients were included. Incidence of malnutrition was 68% and one out of five patients had an underweight of more than 20%: 65% were males. The mean age was 8 years (range 3 to 15 years). The mean body mass index (BMI) was of 15, 5 [4–27]. 30% of the patients had a high risk of malnutrition (score of >10 on the Reilly scale) and 38% had a major risk (score of 5 to 10 on the Reilly scale). Reilly scale significantly varied according to BMI and underweight degree (p < 0.05). A major risk for malnutrition was observed especially between 3 and 5 years (30%), who had a metastatic tumor (56%) and who received chemotherapy (82.5%). Low daily calorie and protein intake significantly increased underweight (p < 0.05).

Conclusion: The prevalence of malnutrition in this study was high. Taking into account other factors with items of Reilly score allows to screen children with a higher risk of a major weight loss during treatment and to enhance nutritional care plan for them.

PR005
DEVELOPMENT OF AN INTERNATIONAL SURVEY INVESTIGATING STANDARDS OF NUTRITIONAL MANAGEMENT OF PEDIATRIC ONCOLOGY PATIENTS

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Purpose: The prevalence of malnutrition in children with malignancies ranges from 8% to 60%, depending on diagnosis, stage, treatment, and geographic region. Malnutrition is associated with the nature of treatment and increases the risk of infection. Little is known about global standards of nutrition practices in pediatric oncology. Some inconsistencies include prescribing neutropenic diets, assessing patients’ nutritional status, and prescribing nutritional interventions. Challenges to providing nutrition services probably differ among low- and middle-income countries. Current standards of care and barriers to nutrition practices in developing countries should be explored.

Method: To identify standards of practice in the international nutritional management of pediatric oncology patients, we are conducting a survey among institutions participating in SIOP, AHOPCA, COG, and Cure4Kids. Its purpose is to examine nutritional management practices with the ultimate goal of developing evidence-based standard guidelines that may be followed internationally. The primary aims are to identify international standards of nutrition assessment and intervention in pediatric oncology, identify barriers to delivering nutrition therapy to oncology patients and compare by country socioeconomic status, identify algorithms and reference materials commonly used in low- and middle-income countries, and compare variations in nutrition practices by country socioeconomic status.

Results: The survey includes general information, nutritional assessment, access to dietetic services, nutrition intervention, nutrition education, and complementary medicine used. It will be administered via surveymonkey.com and distributed via the Cure4Kids website. Ten minutes is the expected completion time. Results will be evaluated, and dietary management will be described. Evidence-based guidelines for nutritional management of pediatric oncology patients will be developed and will reflect international variations in care and access to nutrition interventions. Modifications of practice will be developed as indicated.

Conclusion: A web-based nutritional survey has been compiled to distribute to low- and middle-income countries to assess current practice and barriers to nutritional support.

PR006
A SNAPSHOT OF OBESITY AND UNDER-NUTRITION IN PEDIATRIC ONCOLOGY PATIENTS

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Purpose: To determine the prevalence of over and under-nutrition in both paediatric oncology and bone marrow transplant inpatients and outpatients at The Children’s Hospital at Westmead at diagnosis and at the time of the snapshot.

Method: Oncology inpatients and outpatients were approached over 5 consecutive days to participate in the snapshot study. Seventy one patients (43M, 28F) were included in the snapshot. Of the 71 patients, 31 (44%) had a Leukaemia, 37 (52%) had solid tumours and the remaining participants had non-malignant conditions. Two measurements of the children’s height, weight and body mass index (BMI) were collected. One set of measurements was collected retrospectively from the time of diagnosis and the second at the time of the study. Mid-arm circumference (MAC) was measured on 65 of the 71 children at the time of the study only.

Results: Under-nutrition, as classified by the WHO criteria was identified in 24% of all patients at both diagnosis and when assessed for the study. Diminished arm muscle area (less than the 5th percentile) reflecting deficient body protein stores, was found in 14% of the patients, while the proportion of children with mid-arm circumference greater than the 90th percentile was 28% of the patients measured. Using the Cole international cut-offs for BMI, 18% of the patients were overweight or obese and at diagnosis, whereas 21% were classified as overweight or obese at the time of the study.

Conclusion: Rates of overweight and obesity among paediatric oncology patients reflect rates in the general population. As there is currently no consensus as to which indicator is the best to identify malnutrition in paediatric oncology patients, early intervention and regular monitoring is required.

PR007
THE DEVELOPMENT OF AN INTERNATIONAL SURVEY EXPLORING THE USE OF TRADITIONAL COMPLEMENTARY/ALTERNATIVE MEDICINE IN CHILDREN WITH CANCER

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Purpose: Children with cancer in both high- and low-income countries often use TCAM. The reasons, forms, types, and applications of TCAM vary by geographic region, ethnicity, and culture. With efforts by the World Health Organization and international training programs to improve access to conventional care for childhood cancer, the importance of understanding the global use of TCAM is highlighted, as patients’ reliance on TCAM may affect stage at diagnosis, adherence and abandonment to conventional care. A better understanding of TCAM can help bridge the gap in communication between medical providers and families. We describe the process of development of an international survey documenting the use, reasons, and predictors of TCAM among children with cancer.
130 SIOP ABSTRACTS

**Method:** The survey was designed to collect information on TCAM use and associated factors through open- and close-ended questions. The survey is administered by an individual fluent in the local language to obtain descriptions on TCAM therapies. Face validity was evaluated by experts residing in both the lead institution and countries of distribution.

**Results:** The survey has been successfully completed in Guatemala City, Guatemala with data analysis underway. Preliminary analysis of 100 participants suggests that TCAM is strongly correlated with local culture and customs. Data collection using the survey is ongoing in Buenos Aires, Argentina and La Paz, Bolivia.

**Conclusion:** Our experience demonstrates the importance of developing a culturally specific survey and adhering to a research protocol to enhance the reliability and validity of the survey which will allow for cross-cultural comparisons. The results will aid investigators in providing guidelines, education and research priorities in TCAM, and identify region-specific variables associated with TCAM which may improve adherence to conventional care.

**PR008**

**EVALUATION OF ORAL MUCOSITIS IN CHILDREN RECEIVING INTENSIVE CHEMOTHERAPY USING PROMS QUESTIONNAIRE**

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**Purpose:** Oral mucositis (OM) is a frequent side effect of cancer treatment and can lead to delayed treatment, reduced treatment dosage, altered nutrition, infections, xerostomia, pain, and higher healthcare costs. Our objective was to evaluate the test-retest reliability and construct validity of Patient-Reported Oral Mucositis Symptom (PROMSin children receiving intensive chemotherapy. Preliminary results of our study may provide a clinical context for understanding the relation between objective indicators and patients' perceptions of OM.

**Method:** Fifteen patients (12 with acute lymphoblastic Leukemia and 1 with Hodgkin lymphoma, nasopharyngeal carcinoma and severe aplastic anemia, each; 5 girls and 10 boys; age between 6 and 18 yrs with a mean age of 9.5 yrs) were given the PROMS questionnaire at diagnosis and at regular intervals in course of the treatment. In parallel, dental and parodontal status of the patients was assessed. Patients suffering from OM associated pain to prevent tooth brushing was given an antibiotic/anti-inflammatory solution (Corosodyl). Patients received anti-fungal chemotherapy if needed.

**Results:** With the help of their parents/guardians, each child has successfully filled in the questionnaire. Two of 15 pts complained on oral pain and dysphagia before starting anti-cancer chemotherapy. The ratio of patients with oral complaints due to OM has increased gradually: 5/15 after the 1st week, 9/15 after the 2nd week and 11/15 after the 3rd week of therapy. The complaints have stopped after 4–5 days on Corosodyl mouth rinse. Six of 15 pts required systemic anti-fungal treatment. In addition to OM, gingival bleeding was noted in 10/15 cases, xerostomia in 3/15 patients, and dysgeusia in 1/15 patients.

**Conclusion:** Use of a validated questionnaire for reliable assessment is the first step in a comprehensive program to reduce a highly distressing side effect of cancer treatment in children. OM contributes with an increasing frequency to morbidity of pediatric cancer patients in course of intensive chemotherapy.

**PR009**

**THE EFFECT OF ENTERAL FEEDING ON NUTRITIONAL STATUS IN PAEDIATRIC CANCER PATIENTS**

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**Purpose:** Enteral feeding has been proposed as a proactive treatment for paediatric cancer patients at risk of malnutrition. The aim of this study was to examine the effect of NG feeding on the nutritional status of paediatric cancer patients.

**Method:** This study involved paediatric cancer patients (n = 10) being treated at the Queensland Children’s Cancer Centre, RCH, Australia who required enteral feeding to treat malnutrition. This longitudinal study measured height, weight, mid arm circumference (MAC) and body cell mass (BCM) by total body potassium counting at the commencement of enteral feeding and after 2 months of feeds. BCM is the metabolically active and clinically significant component of the body, representing malnutrition.

**Results:** The preliminary analysis for this study included 5 solid and 5 liquir cancer patients with a mean age of 7.7 years. These results show that enteral feeding significantly increased MAC (p = 0.04) and improved weight on average by 1.3 kg over the 2 months. At analysis only six subjects had completed longitudinal BCM measurements. The average BCM (Z score ± SD) was 1.3 ± 0.92. There was a trend in this small number to suggest that the total body compartment of BCM is improved with enteral feeding (final BCM Z score = –2.63; p = 0.11), however it was not considered a significant change in this small population.

**Conclusion:** This preliminary study suggests that the nutritional status of paediatric cancer patients will benefit from NG feeding, with the potential to increase the BCM which has clinical significance for improving the prognosis of paediatric cancer patients. This study is continuing.

**PR010**

**VITAMIN B12 AND FOLATE STATUS IN CHILDHOOD HAEMATOLOGICAL MALIGNANCES**

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**Purpose:** To find the incidence of vitamin B12 & folate deficiency in children with hematological malignancies and its correlation with malnutrition.

**Method:** Forty-two children between 2–14 years of age with hematological malignancies (ALL: 29, AML 5, HD 5, NHL 3) were enrolled. Blood samples were drawn before starting chemotherapy & analysed by Electrochemiluminescence by COBASE 411 for serum vitamin B12 & folate. Correlation with malnutrition was studied as per the WHO Z score growth charts.

**Results:** Among the 42 patients, 33(78.57%) had either vitamin B 12 & or folate deficiency, 28(66.66%) had folate & 17(40.47%) had vitamin B12 deficiency alone. 33 (78.5%) patients were malnourished. Malnutrition with either folate or vitamin B12 deficiency was present in 38(76.92%)(p = 1). Fisher exact test), malnutrition with folate or vitamin B12 deficiency alone was seen in 24 (61.53%), (p = 0.541)& 16 (41.02%), (p = 0.567) children respectively. A higher incidence of either deficiency was seen in ALL group however, the difference from other groups was not significant statistically (p > 0.05).

**Conclusion:** A high (78.5%) incidence of folate & vitamin B12 deficiency was noted in hematological malignancies. 33(78.57%) had vitamin B 12 & or folate deficiency. 28(66.66%) had folate & 17(40.47%) vitamin B12 deficiency. Although malnutrition was seen in 33(40.47%) children, nutritional status per se has no significant implication in the incidence of vitamin B12 or folate deficiency nor was the deficiency related to the type of hematological malignancy. The data provided are preliminary and the study is still in progress.

**PR011**

**THE PHYSICAL ACTIVITY LEVELS OF PAEDIATRIC CANCER PATIENTS**

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**Purpose:** This study aimed to investigate the impact that cancer diagnosis and treatment has on the physical activity level of paediatric cancer patients.

**Method:** Children undergoing treatment at the Queensland Children’s Cancer Centre, Australia, were recruited for this study. Thirty-two families consented to this study and parents completed a physical activity questionnaire targeted for this population.

**Results:** The subjects were between 5.19 and 15.96 years (47% females), with 63% liquid versus 38% solid cancer patients. The results showed that 85% of children were reported to be less active during cancer treatment, compared to pre diagnosis. The average amount of moderate to vigorous physical activity (MVPA) per day for the patients (21 mins/day) was well below the recommended amount of 60mins, and significantly lower compared to their pre-diagnosis levels (47 mins/day). Parents reported the main barriers to physical activity participation being: symptoms and side effects of cancer and treatment (38%), current stage of treatment (20%), and a fear of injury (17%).

**Conclusion:** This study shows that the diagnosis of cancer and its treatment decreases the level of physical activity in children. As physical activity can help paediatric cancer patients cope with treatments, improve long-term health and may even reduce the risk of recurrence, it is important children are encouraged to participate in physical activity throughout treatment. Physical therapy is recommended to form part of the overall treatment plan for paediatric cancer patients.
PRO12

EVALUATION OF NUTRITIONAL STATUS IN CHILDREN WITH CANCER BY BIOCHEMICAL AND ANTHROPOMETRIC MEASUREMENT

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Purpose: Evaluation of nutritional status in children with cancer at presentation and during treatment by biochemical and anthropometric measurements.

Method: A controlled study was performed in 50 patients and 44 controls. Anthropometrics, serum trace elements and vitamins were measured in all patients at presentation and sixth month of treatment.

Results: Diagnosis of patients were Ewing sarcoma (n = 14), osteosarcoma (n = 11), central nervous system tumors (n = 6), Hodgkin lymphoma (n = 5), Non-Hodgkin lymphoma (n = 5) and others (n = 9). In anthropometrics, only TSTF values of patients at 0. months and 6. months were significantly less than control values (p = 0.012, p = 0.007). Serum levels of albumin, iron, folic acid, zinc and vitamin C of patients at 0. months were significantly less and ferritin, vitamin B12 and copper were significantly higher than control values (p < 0.05). Serum levels of Mg, ALP, P, Se, Cu, vitamin A, D and E significantly decreased while ferritin and Fe levels were significantly increased at 6. months in patients (p < 0.05). Serum levels of Se, Zn, vitamin C, total protein, albumin, Mg and folic acid were significantly less and levels of ferritin, vitamin B12 were significantly higher in patients at 6. months than controls (p < 0.05). Evaluation of these whole values between 3 groups, (bone sarcomas, lymphomas and central nervous system tumors) only the Cu levels were significantly higher in lymphomas at diagnosis (p = 0.02).

Conclusion: This is a extended study that contains also trace elements and vitamins to evaluate nutritional status in children with cancer. Serum levels of Cu in lymphomas were higher and decreased at follow up period. This may be related with disease activity. Vit B12 and copper were significantly higher than controls values (p < 0.05).

PRO13

INCIDENCE OF ORAL MUCOSITIS AND EFFICIENT THERAPY WITH SUPERSATURATED CALCIUM AND PHOSPHATE SOLUTION IN PEDIATRIC CANCER PATIENTS

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Purpose: Oral mucositis (OM) is frequent morbidity in children receiving intensive cytotoxic regimens. OM can lead to severe cachexia and prolonged chemotherapy delays. We present our preliminary study results of OM incidence and treatment with supersaturated calcium and phosphate mouthwash solution (Caphosol).

Method: Study enrolled 60 episodes of OM in children diagnosed with malignant disease. Presence and grade of mucositis was established according to WHO scale. In 30 episodes, OM was treated with Caphosol in therapeutic dosage of 6 times per day and 30 episodes were control group, without therapy, matched by age, sex and diagnosis.

Results: The higher incidence of OM seen in patients receiving chemotherapy that affects the DNA synthesis, such as methotrexate, cyclophosphamide, and cytarabine, namely: acute Leukemias (53.3%), lymphomas (31.6%) and some solid tumors (high risk neuroblastoma and certain stadiums of rhabdomyosarcoma, Ewing/PNET and Wilms tumors) in 15.1%. In both groups age ranged from 1–17 years, median 6.5 years with predominance of OM in male sex (66.6%) in both groups. OM grade 1 was not determined, grade 2 was seen in 66.6%, grade 3 in 26.7% and grade 4 in 6.7% of all episodes, comparable in both groups. Caphosol was applied from 3–14 days, median 7 days. Pain relief occurred in Caphosol group in 2 days versus 4 days in control group (p < 0.01). Mucosal healing appeared in Caphosol group from 1–10 days, median 4 days in contrast to control group were OM lasted from 4–27 days, median 7 days (p < 0.01).

Conclusion: We report a good tolerance of supersaturated calcium and phosphate solution. Caphosol was highly effective in improving the OM symptoms and lessening its severity and duration.

PRO14

WHAT DO PARENTS OF CHILDHOOD CANCER PATIENTS ACTUALLY THINK ABOUT ENTERAL NUTRITION?

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Purpose: Enteral nutrition (EN) via a nasogastric or gastrostomy tube is recommended to promote weight gain in childhood cancer patients who cannot maintain an adequate nutritional status with oral intake. Despite this, EN is not always initiated appropriately to prevent malnutrition. This study aimed to explore and compare views on EN between parents whose child did and did not receive EN.

Method: Thirty-two parents of childhood cancer patients who had received treatment in the previous 3 years participated in semi-structured telephone interviews to elicit perceptions of the impact of enteral feeding on physical functioning; psychological status; physical appearance; loss of eating function; and complications related to EN. The qualitative framework of Miles and Huberman was used to guide data collection and analysis.

Results: Parents whose children did not receive EN described EN as an invasive and ‘unnatural’ form of nutrition. These parents tended to pressure their child to eat to avoid EN and did not appear concerned about the type of food their child was eating. In contrast, parents of children who received EN reported an initial reluctance toward administration of EN as a means of feeling relief when it was used. They described being able to stop pressuring their child to eat after EN initiation. Other positives of EN included allowing families to focus on other aspects of the treatment, and enabling parents to encourage consumption of healthier foods. However, parents did describe frequent nasogastric tube re-insertions due to blockages as a negative aspect of EN.

Conclusion: This study highlights the generally negative perceptions of EN among families of childhood cancer patients. However, parents of children who did receive EN considered it an essential (and positive) part of treatment. It appears better education is needed for families about the use of EN at the beginning of treatment.
supplemented by hand searches of relevant journals and ‘snowball’ searches from reference lists.

**Results:** The ethics of research into the care of children with cancer in LICs remains largely uncharted territory. The vulnerability of LIC populations to exploitation during drug development research is pronounced, and the processes of institutional review and informed consent are often weak or uncertain. Principles to guide standards of care in research trials remain at issue; these merits and risks of relativity in standards of care for pediatric oncology drug trials in LICs need further exploration.

**Conclusion:** Mapping the principles of standard of care, trial benefits, ethics review, and informed consent to pediatric oncology research in LICs is an essential next step. Ultimately, the unique challenges posed by pediatric oncology research in LICs may require a shift in normative emphasis, towards a heavier weighting of social justice in the arithmetic of research ethics.

**PR017**

**SHARING THE CARE - DEVELOPMENT OF CHILDREN'S CANCER SHARE CARE SERVICES THROUGHOUT QUEENSLAND, AUSTRALIA**

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**Purpose:** The state of Queensland, Australia has a land mass of approximately 1.7 million square kilometers approximately 7 times larger than the British Isles. This geographical area is serviced by one tertiary children’s hospital and is supported by the Queensland Paediatric Haematology/Oncology Network (QPHON) which is responsible for the development of paediatric haematology/oncology services throughout the state of Queensland.

**Method:** To ensure children with cancer and their families in Queensland receive the best possible care, ten centres for paediatric oncology shared care have been identified across the state. Each centre is supported by a Paediatric Oncology Regional Case Manager, funded by QPHON, and a local team including a Lead Paediatrician with an interest in paediatric oncology. The State Educator for Paediatric Oncology and the Network Clinical Coordinator, are also funded by QPHON and provide direct support to the paediatric oncology share care centres.

**Results:** Multidisciplinary education plans based on an annual review and service needs are developed each year and have a major contributing factor in service development in share care centres. Education opportunities aimed at nursing, allied health and medical staff has been developed and include a Videoconference Series, a Paediatrician’s Workshop and a series of workshops held at either the tertiary centre or locally at share care centres. Specific programs and resources to support the development of chemotherapy administration skills and provide essential palliative care services have also been developed.

**Conclusion:** In 2010, approximately 420 people attended QPHON workshops and approximately 300 people dialled in for videoconferences. This paper will provide a summary of the achievements and outcomes of multidisciplinary educational strategies used to support the development of paediatric oncology share care services across the state of Queensland, Australia.

**PR018**

**SMOOTH SAILING THROUGH THE PERFECT STORM: A CASE STUDY IN ADOLESCENT & YOUTH ADULT (AYA) ONCOLOGY**

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**Purpose:** To illustrate individualized multidisciplinary coordination of care for AYAs with cancer.

**Method:** A 29 years old male presented with a three month history of progressively worsening headache. He was found to have a posterior fossa mass and underwent resection.

**Results:** lists.

**Conclusion:** This case, an example of a pediatric cancer occurring in an adult, demonstrates how multidisciplinary coordination can provide excellent cancer care to the AYA population despite multiple challenges. By identifying the most appropriate oncologist to lead treatment decisions and “champions” from other departments to act as liaisons, this patient successfully completed intensive multimodal therapy and remains disease free today.

**PR019**

**PARENT ENGAGEMENT IN DESIGNING CARE AT DANA-FARBER CHILDREN'S HOSPITAL CANCER CENTER**

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**Purpose:** Share the process of how senior leadership works in partnership with parent advisors on initiatives and projects. Massachusetts is the first state in the US to mandate that all hospitals have patient and family advisory councils (PFACs). Legislation was modeled on the work of Dana-Farber to incorporate patients and family members in all aspects of decision-making. No one can begin to fully comprehend what it is like to have a child with cancer, unless you are the actual parent. Having parent advisors on committees who share their experiences, allows medical staff to remain focused on what is most important, quality of life for patients and families.

**Method:** Presentation will include PowerPoint slides, literature, and an opportunity for questions and answers. DFCI’s COO and a former chair of the Patient and Family Advisory Council (PFAC) will discuss the structure and operation of the PFAC and how this partnership impacts key projects for mutually beneficial results.

**Results:** Empower those who may have reservations about, or question the need for pediatric patient and family involvement. We can provide support, offer networking opportunities, brainstorm and share ideas for how parent advisors can become involved in a variety of endeavors including facility design, survivorship clinics, palliative and end of life care, parent communications, etc.

**Conclusion:** Constant and open communication between staff/administration and parents/families is vital in creating caring and compassionate healthcare. For years senior leadership at DFC/CHCC has been actively engaged in this continuum of care. Parent advisors at DFC/CHCC are committed to making the day-to-day experiences of the patients they represent as positive as possible. With this vibrant partnership, the voice of patients and families are heard loud and clear. DFC/CHCC is an international leader, respected in all aspects of pediatric oncology care especially when it comes to listening to the voice of patients and families.

**PR020**

**PSYCHOLOGICAL HEALTH IN SIBLINGS HAVI NG LO S T A BROTHER OR SISTER TO CANCER TWO TO NINE YEARS EARLIER IN SWEDEN: A NATIONWIDE COMPARISON WITH NON-BEREAVED SIBLINGS**

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**Purpose:** When a child is diagnosed with cancer it affects the whole family. Siblings often become “invisible” and probably even more so when bereaved. It is unclear to what extent bereaved siblings suffer from psychological morbidity long-term. The aim of this report was to examine self-assessed psychological distress in siblings having lost a brother or sister to cancer compared with non-bereaved siblings from the general population.

**Method:** During 2009 we conducted a nationwide follow-up study, using an anonymous study specific questionnaire. Siblings having lost a brother or sister to cancer between the years 2000 and 2007 in Sweden were invited to participate together with non-bereaved siblings. The self assessed Hospital Anxiety and Depression scale (HADS) were used.

**Results:** Among the bereaved siblings, 174/240 (73%) and 219/293 (75%) of the non-bereaved responded. Self reported low self-esteem (p = 0.002), decreased maturity (p = 0.0072) and difficulties in falling asleep (p = 0.005) during the previous month was more prevalent among bereaved siblings as compared with non-bereaved peers. Bereaved siblings report no increased risk of depressed anxiety (p = 0.298) or depression (p = 0.946) using HADS scores 0–7. 8–10, 11–21.

**Conclusion:** No increased risk of anxiety or depression was found two to nine years following the loss of a brother of sister to cancer in Swedish bereaved siblings. Yet, lower self-esteem, decreased maturity and difficulties in falling asleep were more prevalent in bereaved as compared with non-bereaved siblings.

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**PR021**

**ESTABLISHMENT OF SATELLITE CLINICS: A GOOD OPTION TO EXTEND QUALITY SPECIALIZED CARE FOR CHILDREN WITH CANCER IN A COUNTRY WITH LIMITED RESOURCES**

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**Purpose:** One thousand child cancer cases are expected annually in Mindanao, a 97,530 km² Southern Philippines island with 25 million people; only 300 are seen by health care professionals, mostly at Southern Philippines Medical Center Children’s Cancer and Blood Diseases Unit (SPMC CCBDU). With only two practicing pediatric oncologists throughout the island, the Mindanao Pediatric Cancer Care Network (MPCPCN) was conceptualized to extend specialty care through satellite facilities in strategic underserved areas.

**Method:** Potential satellite sites were chosen based on geography and risk for poor access to existing specialist care. Site visits from August to September 2009 applied St. Jude International Outreach Program Assessment Tool, which evaluated patient demographics, capacity for clinical care, medication access, data management and telecommunications. Three components were established at identified sites: a home-grown healthcare team, training, and referral process. Acute care, early cancer detection, prompt referral and follow up were prioritized.

**Results:** Satellite clinics were established at Davao Regional Hospital (DRH), Tagum City (October 2009) and St. Elizabeth Hospital (SEH), General Santos City (October 2010). Four hundred capacity DRH (80 pediatric; 4 newly designated for child cancer) and 180 capacity SEH (30 pediatrics; two for child cancer) are 54 and 150 kms away from Davao City, respectively. A pediatrician and pediatric oncology nurse team was assigned to each facility. Each nurse underwent a 5-month certificate training program at CCBDU. Multidisciplinary continuing education lectures and case discussions occurred regularly via Cure4Kids web conferencing. A referral and collaborative follow-up-process was established with CCBDU using telephone, email, web conferencing, texting and exchange site visits. Since MPCPCN’s inception, the satellites have provided care for 67 patients through management of diagnosis, follow-up, per-protocol chemotherapy administration, and palliative care.

**Conclusion:** The MPCPCN demonstrates feasibility of a regional satellite network to facilitate children’s access to patient-centered, standardized cancer care in resource-limited settings.

**PR022**

**PEDIATRIC PALLIATIVE CARE PROVISION AROUND THE WORLD: A SYSTEMATIC REVIEW**

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**Purpose:** Pediatric palliative care provides whole body care to children with life-limiting illnesses and their families. The palliative care movement began to take shape in the 1960s, with little focus on children. Since that time, many countries have made strides in providing pediatric palliative care. The purpose of this study was to describe the provision levels of pediatric palliative care around the world.

**Method:** A systematic review was conducted of 47 peer-reviewed and 70 non-peer reviewed sources. Based on the information in the review, countries were partitioned into 4 levels.

Africa for example, provision is at Level 4. This article is forthcoming in Pediatric Blood and Cancer.

**PR023**

**TWINNING: STARTING, SUPPORTING, AND SUSTAINING-THE ROLE OF NON-GOVERNMENTAL ORGANIZATIONS (NGOS)**

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**Purpose:** In 2007 the International Confederation of Childhood Cancer Parents’ Organizations supported by SIOP created World Child Cancer to develop links between high (HIC) and low-middle income (LMIC) countries to reduce cancer morbidity and mortality worldwide by developing supportive, palliative and curative strategies.

**Method:** Methods: We advertised potential availability of funding and longer term support from HICs for plans formulated in each LIC centre (including outcome measures). 6 projects have started, another 8 are pending. LIC interventions have included: raising awareness; reducing: delays in diagnosis, refusal and untimely cessation of therapy; and increasing unit capacity, diagnostic precision/speed and survival. Establishment of a patient database/outcome measurement is crucial. Unit refurbishment has occurred in 3 centres already. The charity/HIC units provide training/education assistance, technology transfer, financial governance and progress monitoring. Each project receives about £30,000/ year for 5 years.


**Conclusion:** Conclusion: Long term sustainability crucial. From the outset plans are discussed by the charity, other NGOs, parent groups, the twinning partners, wealthy individuals, Ministries of Health etc. Over time the amount of funding from the charity decreases as other agencies take over the responsibilities of sustaining the service. SIOP PODC has an initiative to map who does what and where, identify gaps in support and ensure that all twinning addresses systematically how to start, support and sustain each project.

**PR024**

**SUMMARY OF 34 MONTHS OF PEDIATRIC PALLIATIVE-CARE TEAM’S ACTIVITY IN A REFERRAL CENTER**

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**Purpose:** The medical advancement in pediatric oncology introduces a unique challenge for pediatric palliative caregivers. In order to offer correspondingly palliative care it is important to re-assess the characteristic of these patients and formulate optimal care: To analyze the palliative patient’s clinical and socio-demographic characteristics, to analyze the care that was given and to formulate principles for optimal care.

**Method:** A retrospective descriptive study based on the patient’s medical record.

**Results:** The sample includes 116 patients. The average age was 12.4 years (range 0.20–38 years, 59 male). 26% of patients were 0–9 years, 26% 10-19 years, 4% 20-38 years, 24% 39-50 years, and 10% 51-60 years. The main symptoms represented was: pain (25.5%), fever (15%), nausea (14.8%), vomiting (12.4%), sleep disturbance (11.3%), and blood disorder (11.3%). The patients’ primary diagnosis included: leukemia (24.6%), solid tumors (12.5%), and brain tumor (11.3%). The study population included: 24% Neuroblastoma, 7.5% lymphoma, 7.5% SCID and 9.5% others disease. The main symptoms represented was: pain (25.5%), fever (15%), nausea (14.8%), vomiting (12.4%), sleep disturbance (11.3%), and blood disorder (11.3%). The patients’ primary diagnosis included: leukemia (24.6%), solid tumors (12.5%), and brain tumor (11.3%). The study population included: 24% Neuroblastoma, 7.5% lymphoma, 7.5% SCID and 9.5% others disease. The main symptoms represented was: pain (25.5%), fever (15%), nausea (14.8%), vomiting (12.4%), sleep disturbance (11.3%), and blood disorder (11.3%). The patients’ primary diagnosis included: leukemia (24.6%), solid tumors (12.5%), and brain tumor (11.3%). The study population included: 24% Neuroblastoma, 7.5% lymphoma, 7.5% SCID and 9.5% others disease. The main symptoms represented was: pain (25.5%), fever (15%), nausea (14.8%), vomiting (12.4%), sleep disturbance (11.3%), and blood disorder (11.3%). The patients’ primary diagnosis included: leukemia (24.6%), solid tumors (12.5%), and brain tumor (11.3%). The study population included: 24% Neuroblastoma, 7.5% lymphoma, 7.5% SCID and 9.5% others disease.
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and family wishes. The two ethnic groups: Jews and Arabs demand the acquisition of cultural sensitive skills in existence complicated reality.

PR025

IMPROVING CHILDHOOD CANCER SURVIVAL IN GHANA - A TWINNING PROGRAMME (AFRICA OXFORD CANCER FOUNDATION & WORLD CHILD CANCER PROJECT)

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Purpose: To improve Paediatric Oncology services in Ghana. Objectives: To assist in raising awareness with the public and professionals, to assist in training courses for health workers, to assist in developing a register of cases, to assist in creating satellite centres and to help towards the cost of drugs.

Method: This twinning programme between the Paediatric Oncology Unit, Korle Bu Teaching Hospital (KBTH), Accra, Ghana and Royal Hospital for Sick Children, Edinburgh (RHSC), was established in 2010 with funding from Africa Oxford Cancer Foundation (AfOx) and World Child Cancer (WCC). Representatives from AfOx, WCC and doctors from RHSCC conducted a needs assessment in March 2010. Challenges needing to be addressed included lack of trained staff, lack of awareness, lack of resources, treatment abandonment and low survival. The first of a series of paediatric oncology training workshops was held in November 2010 for health workers from various disciplines at KBTH. Resource persons from RHSCC included doctors, a nurse and a play specialist. A second basic training for participants from hospitals selected as satellite centres for KBTH was held in April 2011. Prof Tim Eden, Jo Hopkins and Emma Jackson from World Child Cancer were present. Assistance with the establishment of a data base was formally started at the same time. Awareness creation is actively ongoing through the media and distribution of posters. Local support by organizations including the parents’ support group and Cancer Care Foundation.

Results: Outcomes to be assessed include: An increase in number of children reaching the unit at KBTH with early sign/symptoms of cancer. A reduction in overall mortality rate of the unit and a lower recurrence rate. A database set up which records all new patients and their treatments/outcomes. Training provided for health professionals on aspects of childhood cancer care.

Conclusion: This programme will definitely make a significant impact on childhood cancer services in Ghana.

PR026

ESTABLISHING A TREATMENT AND SURVIVORSHIP COHORT TO ASSESS OUTCOMES IN ADOLESCENT AND YOUNG ADULT ONCOLOGY PATIENTS

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Purpose: The goal of this study is to establish a multi-institutional adolescent and young adult (AYA) cohort to assess medical and psychosocial outcomes and inform reasons why adolescent and young adult oncology patients have not experienced the improvements in survivorship and quality of life seen in children and older adults.

Method: Patients between 15 and 39 years within 3 weeks of starting treatment for Leukemia, lymphoma, osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, and non-rhabdomyosarcoma soft tissue sarcoma are eligible. Participants complete five instruments on-line or on paper for physical and mental health functioning, and toxicity at four timepoints over one year. They complete diagnosis and social demographics questionnaires at entry and on one year.

Results: This study is enrolling at Oregon Health and Science University and Vanderbilt University. Seattle Children’s Hospital and Children’s Memorial Hospital are awaiting IRB approval. 55 patients are enrolled with median age 25 years. The majority have Leukemia (40.5%) or lymphoma (38.4%) and are male (52.7%). 71% reported having insurance. Patients reported time from first symptoms to first doctor visit < 1 week (34.5%); 1–3 months (27.2%); 3–6 months (9.0%), greater than 6 months (12.7%). 50% of patients reported having a diagnosis < 1 week after the first doctor visit: 50% were invited to participate in a research study. To date, 82% of baseline, 60% of 3 month, 56% of 6 month, and 100% of 12 month assessments have been completed.

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Conclusion: AYA patients are willing to participate in a longitudinal cohort and complete information to provide medical and psychosocial outcomes. Enrollment within three weeks of starting treatment is feasible. Enrollment will be completed in September 2011. This type of study is important to improve outcomes and quality of life in AYA patients.

PR027

AFRICAN TRADITIONAL PRACTICES - A CHALLENGE TO PALLIATIVE CARE FOR CHILDREN IN AFRICA

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Purpose: Create awareness of how traditional cultures impacts on the rendering of palliative care in South Africa. Offer insight into respecting the culture and traditions and incorporating them appropriately within the early grief counseling stages.

Method: Counseling of families facing pursuit of palliative care.

Results: Strong parent/family reliance on cultural practices such as ancestral worship and belief in witchcraft may become an obstacle to proper palliative care and end of life care of the dying child. Although it is important to respect their culture and rituals the emphasis must be placed on what is best for the child. The presentation explores how counseling from diagnosis may assist in creating awareness and therefore providing proper palliative care. It explores the necessity of incorporating the traditional ways without compromising the patient. Once parents/families have been told there is no more curative treatment for their child, they may remove the child from hospital and seek help from African traditional healers, elders or ancestral spirits. This creates a challenge for the palliative care team. The patient and their families’ wishes need to be respected but the patient also needs certain western medicines at the time of palliation, for example, a pain relief medication such as morphine.

Conclusion: The family, including siblings, has to be counseled in preparing them for a child’s palliative care. A challenge presented in a local treatment center is that approximately 70% of families are from rural areas and are semi- or completely illiterate. Further belief in ancestral worship and witchcraft is rife within these communities. Consequently, detailed persistent pre-death grief counseling is not only important but crucial in ensuring proper palliative care to the child.

PR028

CAN WE OMIT PLAIN CT SCAN WHILE PERFORMING AN ABDOMINAL SCAN AND THUS REDUCE THE RADIATION BURDEN IN CHILDREN?: IMAGE GENTLY A RATIONAL APPROACH.

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Purpose: Conventionally plain CT scan of abdomen is routine acquisition during all the abdominal CT studies. It detects tumoral calcifications, fat and haemorrhage well and gives us the baseline density which may help in better characterization. We evaluated the agreement between complete abdominal scan (plain and contrast enhanced) and contrast enhanced (CECT) scan alone in diagnosing primary abdominal tumors and calcification and fat and thus eliminate the unenhanced phase for imaging pediatric abdominal neoplasms.

Method: We retrospectively evaluated 96 series study of all the abdominal CT scans in children aged <18 yrs. The first observer performed the blinded evaluation with both the unenhanced and CECT scans and the second observer evaluated only CECT scans. The radiologists were separately asked to formulate the most probable diagnosis and to decide whether tumor calcification and fat were present. Histological diagnosis was considered as Gold Standard. The agreements between the two observers were measured using kappa statistics.

Results: The mean age was 50.8 months with 68% being male children. The agreement between diagnoses from the two observers was almost perfect (k = 0.97 and 0.96). No statistically significant difference was seen between the observers and the histopathologic results. The sensitivity and specificity of the two observers for the most frequent neoplasms were similar and for observer 2 for presence of calcification was 83%, 100% and for fat was 60%, 100% respectively. Also noted was that diagnostically significant findings in the pelvis were rare.

Conclusion: We conclude that ability to diagnose primary tumor is based on organ of origin and is not limited if we omit plain scans hence CT protocols without the unenhanced phase is a viable alternative. The habitual inclusion of the pelvis on abdominal CT for primary abdominal tumor is also not justified. This data can serve as a foundation for future recommendations and investigations into abdominal CT in pediatric patients.
THE CANADIAN TASK FORCE ON ADOLESCENTS AND YOUNG ADULTS (AYA) WITH CANCER: A PROCESS FOR CHANGE.

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Purpose: The Canadian AYA Task Force was established in 2008; mission to ensure that AYA Canadians with cancer and AYA survivors of cancer have prompt, equitable access to the best care; establish and support research to identify how health outcomes and quality of life can be optimized.

Method: The Task Force formed five working groups with defined goals. A survey of existing AYA cancer services in Canada conducted in 2009 found limited coordination between adult and paediatric services. A review of the literature was conducted of transition services and models of care. In 2010 a workshop was held with AYA survivors, healthcare professionals, policy makers, international experts.

Results: Six themes emerged: active therapy and supportive care; psychosocial needs; palliation and symptom management; survivorship; research and metrics; awareness and advocacy. The Workshop Proceedings will be published in a supplement of “Cancer”. Based on the workshop discussions and supporting material, recommendations have been formulated for AYA care in the context of the Canadian healthcare system. The six broad themes highlight the need for holistic age-appropriate services for both active care and survivor care; and research to redress inequities in the care provided to this group.

Conclusion: These themes highlight the need for holistic age-appropriate services for both active care and survivor care. The Workshop Proceedings will be published in a supplement of Pediatr Blood Cancer.

10-YEAR EXPERIENCE FROM AN INTEGRATIVE PEDIATRIC ONCOLOGY CENTRE - A RETROSPECTIVE ANALYSIS

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Purpose: Complementary and alternative therapies (CAM) are widely used in pediatric oncology. Till now there are no published data on the clinical practice of integrating CAM into standard pediatric oncology (PO) care.

Method: We performed a retrospective analysis of patient records of all PO-patients treated in our integrative pediatric oncology centre (IPoC) with 1st admission between January 1st 1999 and December 31st 2008. Inclusion criteria were: age 0–18 years, proven cancer-diagnosis and at least one conventional intervention (chemotherapy, operation, radiation) in our hospital.

Results: A total of 116 cases (39% female) were analysed. 78% were admitted with their 1st cancer-diagnosis, 22% with any relapse. 58% got their diagnosis in our hospital, 42% in another hospital (9% of them outside Germany). The spectrum of diagnosis was the same as in the German PO-population. Along with a standard conventional therapy according to actual treatment-plans within the GPO-PHIL- and/or SIOP-framework 91% of our patients received some form of CAM-medication (e.g. 75% mistletoe-preparations), most out of the spectrum of Anthroposophic Medicine (AM). We could identify a TOP10 of AM remedies prescribed to most patients. The most used non-pharmacological CAM-interventions where: 63% eurythmy therapy, 56% art-therapies (painting, sculpturing), 51% music therapy, 46% external embrocations and compresses. There were no reported serious adverse events for any of the pharmacological or non-pharmacological CAM interventions.

Conclusion: It is possible to integrate CAM into an IPOC within the standard-spectrum of PO-diseases. In a retrospective analysis over a 10-year-period we found no indices for relevant toxicities. Statements regarding the effectiveness of this approach cannot be drawn from this analysis. Further prospective studies of this approach are necessary.

HEREDITARY FACTORS OF THROMBOPHILIA AS A POSSIBLE CAUSE FOR SYSTEMIC THROMBOSES IN PEDIATRIC PATIENTS WITH HEMATOLOGICAL MALIGNANCES

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Purpose: Systemic thromboses are uncommon in pediatric population. But their incidence is higher in patients with cancer. The development of thrombotic events may cause severe consequences during chemotherapy. We performed our study to evaluate the significance of different factors of thrombophilia for etiology of systemic thromboses in pediatric patients with hematological malignances.

Method: During 5 year term from 2005 to 2010 486 patients aged 0–18 with different hematological malignances were treated in our clinic. Clinically proven systemic thromboses were evident only in 8 children. 2 children died due to thrombotic events despite the treatment. In acute period we performed blood coagulation examination evidencing hypercoagulation in all cases and vector imaging studies revealing thromboses in large blood vessels (including coronal and cerebral arteries, portal system, pulmonary, and venae cavae). Some tests we performed retrospectively after recovery. Samples from 6 survived patients were analyzed for polymorphisms of haemostatic factor genes: factor V G1691A (ie. factor V Leiden), factor VII G1097A, prothrombin G20210A, plasminogen activator inhibitor-1 (PAI-1) 4G/5G, methylenetetrahyrdrofolate reductase (MTHFR) C677T, thrombospandin-4 (TSP-4) G2592C.

Results: Of these 8 patients 5 were treated for acute lymphoblastic Leukemia, 2 - for acute myeloid Leukemia and 1 for non-Hodgkin lymphoma. Clinical appearance of thromboses was portal hypertension in 4 cases, central nervous system involvement in 3 and myocardial infarction in 1 case. Thrombi associated with central venous lines were seen in 2 cases. We revealed gene polymorphisms in all patients studied. The mutation PAI-1 4G/5G was seen in 3 cases, factor VII G1097A in 1 case. In 2 patients we detected simultaneously MTHFR C677T and PAI-1 4G/5G gene polymorphisms. Mutations in factor V, TSP-4 and prothrombin genes were found in none of patients.

Conclusion: Prothrombotic genetic polymorphisms should be considered as an etiologic factor of systemic thrombosis in pediatric patients with hematological malignances.
Purpose: We presented at SIOP2007 (PG022) the start of our grant-awarded program for developing a community-based approach to providing good quality palliation for our small number of widely geographically distributed patients/pts. There are no other pediatric programs or hospices in the country.

Method: For the next 18 months (Apr06-Sep07) we applied the program to children with non-curable diseases. After death, families were asked to answer a questionnaire.

Results: 22 children (16M/6F) piloted the program, aged 2–18 y (median 8.5 y). 13 had CNS tumors, 5 stage 4 neuroblastoma, 2 soft-tissue sarcomas, 1 AML, 1 ALL. 12 lived in Lisbon (within 50 km), 8 from 50–300 km, 1 in Acores and 1 in Madeira. After a palliation plan was put forth by the multidisciplinary team, it was proposed to families to share their care with the local health services (hospital and/or community center). 6 pts received shared care with the local hospital (1 in Lisbon) and 2 with both. Time to death was 10–189 days (median 81 days for neuroblastoma, 45–47 days for others). At conclusion of the study 21 pts had died - 14 at the Institute (after 0–26 days of admission, median 7), 4 at other hospitals (0–10 days) and 3 at home.

Conclusion: This approach allowed us to improve significantly the quality of care we provide to our non-curable pts. Although local community health services have no experience with either very sick children or palliation, with guidance and support from our team they were able to help these families stay at or close to home for longer periods than before, with good symptom control. Acknowledgment: work supported by Fundação Calouste Gulbenkian.

PR034

IMPLEMENTATION OF AN ADOLESCENT & YOUNG ADULT ONCOLOGY (AYAO) TRAINING PROGRAM AT OREGON HEALTH & SCIENCE UNIVERSITY (OHSU)

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Purpose: The need for oncologists with specialized training in AYAO (15–39 yo) is a priority put forth by the 2006 National Cancer Institute’s AYAO Progress Report Group. Our institution created an AYAO fellowship program in 2008 committed to training oncologists in both pediatric and adult oncology in order to improve access to care, create relevant clinical care models, and improve outcomes for the AYAO population.

Method: We developed two AYAO training pathways. The primary pathway is designed as a 4-year program following completion of a med-peds residency. The alternate pathway is designed as a supplemental year focused on AYAO that follows completion of a 3-year pediatric or medical hematology-oncology fellowship.

Results: We currently have two fellows training in AYAO, one each in the primary and alternate pathway. A physician trained in med-peds interested in AYAO oncology was selected to begin the primary pathway in July 2009. Application for dual training in Medical Oncology and Pediatric Hematology-Oncology was approved by the American Boards of Internal Medicine and Pediatrics. This fellow’s AYA training has entailed one year in pediatric hematology-oncology and one year in medical oncology, to be followed by two years of lab-based research studying sarcomas. Continuity clinic has encompassed broadly representative patients for the first two years, with a tailored AYA population planned for the second two years. Another pediatric fellow is starting the supplemental year of the alternate pathway in July 2011; she will continue mentored clinical research that involves an AYAO cohort (15–39 yo) treated in either the pediatric or adult programs at our institution.

Conclusion: The training models developed and implemented at OHSU can be reproduced at other institutions and will lead to broader access to quality AYAO clinical care, enhance AYAO-focused research, and increase awareness of the unique challenges faced by the AYA population with cancer.

PR035

BEREAVED PARENTS ASSESSMENT OF END-OF-LIFE CARE

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Purpose: Parents whose child has died from cancer are the ultimate jurors of a hospital’s palliative care practice. However, once a child dies, parents rarely have the opportunity to provide feedback that may aid in improved care standards for future patients. The goal of this study was to learn from bereaved parents how to best tailor palliative care practices.

Method: Eligible participants were English speaking parents whose child had died more than 1 year before study participation and was 10 years of age or older at the time of treatment. A semi-structured script was developed for interviews. Communication, emotional care, treatment decision-making, spiritual care, and symptom management needs were explored. Verbatim transcripts and Atlas-Ti software were utilized to analyze data. Themes were identified and reviewed to establish agreement amongst investigators.

Results: Parents of 47 children were identified as eligible. Twenty-two were not able to be contacted, reducing number of eligible participants to 25. Nine (36%) declined participation. Seven (28%) expressed future interest, but were not available at the times of the scheduled focus groups. Fourteen parents of 9 children (36%) participated. The average age of the child was 15 years and parent was 51 years. Dominant topics of interest included 1) the emotional care of each immediate family member, and 2) communication between family members and professional caregivers. Two unexpected topics of interest were prominent. The sensibility and consistency of normal hospital procedures was essential to quality end-of-life care. Finally, the importance of social support and staying connected with others was emphasized.

Conclusion: Parents highlighted the importance of professionalism and compassion at end-of-life. Establishing related standards of care may improve future patients’ experiences during this vulnerable time.

PR036

HOW CAN THE NEW ZEALAND CHILD CANCER FOUNDATION BEST USE ITS RESOURCES TO PROVIDE THE MAXIMUM LEVEL OF SUPPORT TO A CHILD THAT HAS BEEN DIAGNOSED WITH CANCER AND HIS/HER FAMILY?

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Purpose: Charitable organizations play an important role in patient and family support, palliative care and cancer research. This research develops an evaluation framework for the New Zealand Child Cancer Foundation (CCF) to help inform decisions within a non-profit organization to maximise services given available funds. As a result of recent external shocks, such as the recent Global Financial Crisis and Canterbury Earthquakes, CCF faces unusual financial constraints due to reduced levels of income. CCF has commissioned this research to inform decision makers on spending priorities in order to maintain high levels of support service within their budget constraint.

Method: A major challenge in applying standard performance evaluation tools, such as cost/benefit analysis, to a non-profit organization is how to measure benefits. The value of most of the services provided by non-profit organizations is not revealed by prices, but rather through the perceived value received by the service user. This study utilises service user surveys together with market proxy prices to identify the value of service functions and activities. Direct and indirect costs are then allocated to the services provided on the basis of staff work reports, as well as formal and informal staff interviews.

Results: The results of the evaluation will identify services that have particularly high benefit/cost ratios. These are the areas where the benefits achieved from spending are greatest (on average). Sensitivity analysis will then be used to identify which assumptions are most important for conclusions on spending priorities, and to ensure the robustness of the cost/benefit analysis.

Conclusion: The results will provide important information to effectively fulfil CCF’s mission of supporting every child and their family on their child cancer journey.

PR037

DEVELOPMENT OF PAEDIATRIC PATIENT/NURSE CONTROLLED ANALGESIA (PCA/NCA) SERVICE WITHOUT PAEDIATRIC PAIN SERVICES 24/7

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Purpose: Delivering a Paediatric PCA/NCA service is challenging without a comprehensive Paediatric Pain service. In our Paediatric Oncology unit, situated within an adult Oncology centre, there is no Paediatric pain service providing comprehensive round the clock clinical support. Therefore we developed an ‘in-house’ stand alone PCA/NCA service with pre-programmed pumps, standardized proformas and clinical algorithms commencing in August 2010. A prescription proforma with minimal data entry was used; enabling all the incremental bolus and background doses to be standardised irrespective of weight. The service had a staggered introduced with NCA and PCA sequentially. The Opiate of choice was Morphine, with OxyCodone as second-line. We audited the results achieved from spending are greatest (on average). Sensitivity analysis will then be used to identify which assumptions are most important for conclusions on spending priorities, and to ensure the robustness of the cost/benefit analysis.

Conclusion: The results will provide important information to effectively fulfil CCF’s mission of supporting every child and their family on their child cancer journey.
Method: We prospectively audited the first ten children placed on NCAs and PCAs, respectively, using a data collection tool. The data collected, included reason for use, type of opiates, doses given and side effects. A user (nurse, parent and patient) survey was also carried out.

Results: Of the ten children who used NCAs, only one child needed conversion to second line Opiate, successfully, due to non-responsive pain. Another child (over 7 years old), receiving a NCA, had poorly controlled pain was converted to PCA on its introduction with good effect. All 10 PCA users had successful pain management despite pain scores less than 4 on a numerical pain scale. All 20 children had pain secondary to mucositis. Length of use was 3–12 days (mean 5 days). There were no side effects attributable. User surveys demonstrated importance of written information to patients and parents. Nurses stated they felt confident and competent in setting up the PCA/PCA and using appropriate pain tools for decision-making around bolus delivery.

Conclusion: The development of clear, prescriptive proformas and algorithms with pre-prepared pumps enabled us to introduce PCA/PCA safely without a 24/7 Paediatric Pain service.

PR038

REVIEW OF END OF LIFE DRUG BOX CONTENTS FOR CARE IN THE COMMUNITY

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Purpose: Paediatric Palliative care aims to support the child and the family in their preferred place of care which is usually the child’s home. Anxiety around rapid alleviation of sudden distressing symptoms can be mitigated by the provision of an emergency drug box within the child’s home. This locked drug box contains five intravenous/subcutaneous medication (and one buccal medication) that can be used by local children’s community nursing team to rapidly alleviate symptoms which can no longer be controlled or given by oral (or alternative) routes. The medication placed in the box is based on addressing specifically occurring anticipated symptoms at end of life. We review the use of each medication and consider any others used that were not included.

Method: We identified 36 children from our database who received palliative care and subsequently died during the period from 1st January 2006-31st December 2008. The case notes were retrospectively reviewed for use of all intravenous/subcutaneous medication at end of life.

Results: Of the 36 children supplied with emergency drug boxes, 25 were male; 24 children died, died at home, 10 in a hospice and 2 in hospital. The mean age at placement of the drug box was 8 years with a range of 3–18 years. According to tumour type, 4 had Leukaemia, 22 had CNS disease and 10 had solid non-CNS tumours. In all tumour types, each drug in the emergency box was used in greater than 20% of cases; except the Midazolam liquid. It was used in over 30% cases of children with CNS disease but in only 10% of other tumour groups. There were no other intravenous/subcutaneous medications used more than 10% of the time at end of life.

Conclusion: From our review, the current medications provided in the emergency boxes appears to encompass commonly experienced symptoms at end of life.

PR039

THE EDUCATION OPPORTUNITIES DISCOVERED DURING THE IMPLEMENTATION OF A NEW TREATMENT PROTOCOL

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Purpose: In October 2010 the clinical research group of the Queensland Children’s Cancer Centre (QCCC) at the Royal Children’s Hospital, Brisbane (RCHB) identified that the new Children’s Oncology Group Standard Risk Acute Lymphoblastic Leukaemia (ALL) treatment protocol (AALL0232) was open for recruitment. Following initial education of staff, the QCCC aimed to commence recruitment onto the study in January 2011. This paper outlines the education activities/implementation plan for nursing staff. It also discusses the methods used to identify education needs and evaluate training, along with the significant findings.

Method: This education opportunity was harnessed as a way of identifying additional education needs in relation to: disease and drug knowledge/understanding; protocol knowledge/understanding; application of knowledge to clinical practice; and staff confidence ratings regarding specific protocol requirements and parent education. The education plan was targeted at chemotherapy competent staff and included de-identified pre and post questionnaires, poster development, face-to-face education delivery, self-directed education materials, resources and prompts. Collaboration between the Nurse Educator, Clinical Nurse Consultant, Clinical Research Team, and Medical staff has supported the success of both the education initiatives and the implementation plan.

Results: Staff response to the education initiatives has been favourable. Over 55% of staff have returned the questionnaires. The questionnaires have highlighted areas of knowledge deficit along with interesting data surrounding confidence ratings and levels/year of experience. De-identifying the questionnaires has allowed for comparisons to be drawn regarding knowledge, confidence, and experience, along with evaluation of the education initiatives. Over 75% of staff have attended face-to-face education sessions across the service. Additional education has been delivered to address the identified knowledge gaps.

Conclusion: This education opportunity has enabled additional needs-analysis to be made in this staffing group. Ongoing educational surveys will continue to support education implementation and evaluation, ensuring targets are met, and that patient care and safety is optimised.

PR040

TREATMENT ABANDONMENT IS A MAJOR HURDLE FOR IMPROVING SURVIVAL IN CHILDHOOD CANCER IN THE DEVELOPING WORLD

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Purpose: Majority of published literature from the developing world describes outcome of the patients who have completed therapy. What happens to those who are lost to follow-up? We analyzed the outcome of such children in a single center.

Method: All children upto 16 years of age diagnosed with cancer at Sir Ganga Ram Hospital from January 2005 to February 2011 and lost to follow-up were included in the study. They were divided into broad categories of hematological malignancies, brain tumors and other solid tumors. Follow-up survey was done by contacting parents by telephone and asking the reasons for not coming for follow-up.

Results: 234 out of 802 children (29%) diagnosed with cancer were lost to follow-up. More than 90% abandoned therapy within the first month of diagnosis. 140/234 (60%) had hematological malignancies (Acute Lymphoblastic Leukemia-85, Acute Myeloid Leukemia-27, Chronic Myeloid Leukemia-4, Hodgkin’s Disease-8 and Non-Hodgkin Lymphoma-16). 322/234 (13.5%) had brain tumors and 62/234 (26.5%) had other solid tumors. The parents of 146/234 (62%) patients could be contacted. 57/146 (40%) children had died (acute Leukemias-35, brain tumors-11 and other solid tumors-11). 28 opted for no treatment, out of which 22 died. 27 patients opted for alternative therapy (the longest follow-up was a rhabdomyosarcoma patient who lived for 30 months) out of which 12 have died. 78 opted for chemotherapy at another cancer centre (59 in the same city and 19 in another), out of which 21 died. Reasons for not following-up were cost of treatment-60%, distance > 100 kilometers-22%, lack of faith in our centre-17%, ignorance and poor outcome of cancer-22% and child/girl 9%.

Conclusion: This study shows that almost 40% of patients who are lost to follow-up die. Poverty, distance from cancer centre, ignorance, fear of chemotherapy and gender bias are significant causes for the same.

PR041

USING CLINICAL PRACTICE IMPROVEMENT PROGRAMME (CPIP) TOOLS TO IMPROVE THE REFERRAL RATE OF APPROPRIATE PAEDIATRIC ONCOLOGY PATIENTS TO THE PALLIATIVE SERVICE

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Purpose: Children with cancer requiring palliative care are often not referred or referred late to the palliative care service. Historical data showed a referral rate of about 30%. It is difficult to build rapport between the palliative team and the family during this stressful time. As a consequence, palliative service is not delivered optimally. We undertake a CPIP project with the aim to improve the referral rate of appropriate paediatric oncology patients to the palliative service in our institution.

Method: The target population are children diagnosed and treated at our institution with poor prognosis cancers, for example, all relapsed, progressive or refractory cancers, and cancers with estimated prognosis of 20% or less. Using CPIP tools like Pareto Chart, Run Charts and PDSA cycles, root causes of non or late referral were identified and interventions directed at the root causes were discussed. Interventions were tried over a 6-month period and the referral rate to palliative service collected monthly.

Results: Root causes for non-referral include misunderstanding of the role of palliative team, referring physicians too busy or did not think of it or think that parents are not ready.

Interventions implemented include: 1. Palliative “champions” were identified in key areas of the oncology unit to look out for appropriate patients and to remind primary physician about palliative referral. 2. Such cases are also flagged up to the doctors at the in-house cancer registry. 3. Workflow and referral process are put at prominent places in the unit and all new incoming staff are orientated to the role of palliative team. After 6 months and 2 PDSA cycles, the referral rate increased to 70–100%.

Conclusion: CPIP tools are useful to improve clinical service. This project will be extended to non-oncology referrals to the palliative service.
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SIOP ABSTRACTS

PR042

IMPACT OF SIOP ON A SINGLE INSTITUTION IN A DEVELOPING COUNTRY
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Purpose: International Society of Pediatric Oncology (SIOP) is an organization, which helps pediatric oncologists from around the world to meet and share ideas. One of the major goals of SIOP is to improve care of children with cancer in the developing world. Here we describe impact of SIOP on a single institution in last decade (2000–2010)

Method: We analyzed impact of all activities related to SIOP like membership & serving, scholarship & awards, abstracts submitted, citation of abstracts, publications related to abstracts on our unit.

Results: In last decade, 15 young trainees from our centre were awarded SIOP scholarships, which helped them attend annual meeting and present their work. This motivated all of them to complete formal training in Pediatric Hemato-Oncology at our centre. Ten have become SIOP members. All of them have played a significant role in coming together of a cooperative group in India - Indian Pediatric Oncology Group and have helped senior colleagues bring out guidelines for various tumors in last five years. Seven went abroad for further training. In last 10 years, a total of 65 abstracts have been presented at SIOP from our unit (oral-7, posters-58) and 1 chapter for SIOP education book has been contributed. Abstracts published in Pediatric Blood and Cancer have been cited 5 times and 5 abstracts have been published as full papers in various journals. These abstract presentations, publications and meeting with senior SIOP members during the annual meetings helped our fellows get jobs abroad. Three fellows have come back to India and have helped set up new bone marrow transplant programs. Our unit has become a major hematology oncology-training centre in last decade. One senior consultant has served as secretary of SIOP Asia.

Conclusion: SIOP has played a significant role in developing career of many young pediatric oncologists from a single institution in India.

PR043

PROMOTING PALLIATIVE CARE FOR CHILDREN WITH CANCER IN A RESOURCE-LIMITED SETTING
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Purpose: Palliative care for children with cancer is a particular priority in resource-limited settings, where cure is less likely and socioeconomic and cultural factors may create barriers not present in high-income countries. Outlining core steps in palliative care development in a low-income setting can promote further program planning.

Method: After a multidisciplinary review of pediatric palliative practices at a public tertiary hospital in Davao, Philippines, a one-day open educational outreach forum for regional health providers was conducted in March 2011. Sessions were led by a physician, nurse, and child life specialist. A 10-point quiz assessed for content validity was piloted pre- and post-forum. Integrating participant feedback and paired-t test comparison of pre/post forum quiz scores, further educational and management strategies were proposed.

Results: Key learning needs identified included pediatric palliative care timing, and palliative opioid use/dosing in children. Of 98 registered participants, post-forum quizzes and feedback evaluations were completed by 84 (40 practicing physicians, nurses, and psychosocial staff; 34 trainees). Mean post-forum scores for self-reported knowledge/attitudes improved significantly (mean improvement 2.23 on 10-point scale; 95% CI 1.72 to 2.75, p < 0.0001). On feedback questions assessing whether participants felt the information was clearly presented, that they learned new ideas, were interested in applying ideas, and glad to have attended, mean scores exceeded 4.5 (“very much”) on a 5-point scale; 100% responded positively to being contacted for other educational efforts on this topic. Next steps proposed and initiated include: i) engaging hospital leaders and inter-disciplinary partners; ii) securing a consistent opioid supply at the point-of-care; iii) implementing a department-wide educational campaign to promote evidence-based pediatric pain management; and iv) establishing a pediatric palliative care patient registry.

Conclusion: Targeted, brief multidisciplinary education improves knowledge about and attitudes toward pediatric palliative care. This education can complement and facilitate development of palliative care policies, access, and implementation.

PR044

CHILDREN ON CHEMOTHERAPY TREATED WITH PALANOSTERON, APREPIATENT AND DEXAMETHASONE AS AN ANTIEMETIC: A STUDY FROM INDIA
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Purpose: Despite the widespread use of 5-HT3 receptor antagonist antiemetics, up to 70% of patients with cancer receiving emetogenic chemotherapy agents experience postchemotherapy nausea and vomiting. Delayed postchemotherapy nausea and anticipatory nausea are poorly controlled by currently available antiemetic agents. Very few reported literature for use of Palanosteron and Aprepitant with dexamethasone has been studied for its efficacy for acute chemotherapy-induced nausea and vomiting (CINV) in children. However, its efficacy for CINV in a diverse oncology population is unknown.

Method: We performed a prospective trial in 700 episodes of chemotherapy in 102 children with retinoblastoma during 2010 in Sankar Nethralaya Medical Research Institute. All participants received antiemetic to palanosteron, dexamethasone and/or aprepitant. The primary outcome was change in the prevalence of delayed CINV. Secondary outcomes included acute prevalence of CINV, acute and delayed severity of CINV in children with cancer. CINV was evaluated as per Edmonton’s Symptom Assessment Scale and National Cancer Institute criteria respectively.

Results: Acute moderate to severe nausea was observed in 35 (5%) cycles. Acute moderate to severe vomiting was 5% cycles. Delayed moderate to severe nausea and vomiting was observed in 10%. No adverse reactions. Approximately 85% of the cycles of chemotherapy (595 cycles) no event related to CINV occurred.

Conclusion: Palanosteron, dexamethasone and/or aprepitant was effective in reducing severity of acute and delayed CINV in children receiving emetogenic chemotherapy. It is easily available and a relatively cheaper substitute in developing countries.

PR045

PALLIATIVE CARE AFTERHOURS PHONE SUPPORT, WHO CALLS AND WHY: A RETROSPECTIVE REVIEW OF AN AFTERHOURS PHONE SERVICE
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Purpose: A study undertaken by the Queensland Children’s Cancer Centre (QCCC) Brisbane in 1999, identified the availability of expert management for paediatric palliative care afterhours as a priority. In 2000 an afterhours phone service was established to support these families and the health professionals caring for them. This service is operated by oncology nurse consultants experienced in paediatric palliative care.

Method: Data from years 2002–2010, a total of 1954 calls, regarding 106 patients, were entered into a data base for analysis. Variables analysed included time, reason for call, diagnosis, location from hospital and resulting management.

Results: The majority of calls were between parents and nurse consultants (51%). Update of patient’s condition (18%) was the primary reason for calls with support and reassurance (16%) and symptom management for pain (10%) being other frequent reasons. The majority of calls occurred over weekends, mid morning or in the early evening, with only 11% (n = 209) of calls occurring between 10 pm and 7 am. Patients with solid or brain tumours called more frequently than patients with haematological malignancies (X2 = 89, df = 42, p-value = <0.001). Patients with a neuroblastoma had the highest call frequency for pain, while Patients with haematological malignancies called regarding a wider range of symptoms such as nausea, constipation and sleep issues. Of all calls made, 43% (n = 814) were single calls, either to or from parents and managed by the nurse consultant without requiring further intervention. Calls were received from throughout Queensland, but in higher proportions from inner regional areas compared to metropolitan areas, indicating the value of the service in supporting communities throughout Queensland.

Conclusion: The afterhours phone service has proven to be a simple, cost effective service to implement and maintain, which meets the needs afterhours of families caring for a child with an oncological life threatening conditions regardless of distance from the hospital.

PR046

INTEGRATING PALLIATIVE CARE THROUGHOUT THE JOURNEY FOR CHILDREN WITH CANCER
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Purpose: Palliative care [PC] is the total care of the child’s body, mind and spirit and involves giving support to the entire family. Although studies strongly recommend the palliative care begin at diagnosis and continue through treatment to care or bereavement for most medical conditions, oncology has not universally accepted this concept, continuing to reserve PC for end-of-life care. The family and the healthcare team frequently associate palliation with death or withdrawal of treatment. Practitioners eager to dispel this concern are challenged with the practicality of when and how to include palliative care in treatment plans.
The overwhelming diagnosis of cancer in a child, aggressive treatment approaches and supportive care challenges fit well into the framework of PC.

Method: A model has been developed focusing on interdisciplinary education, recognition of champions and utilization of patient/parent advocates in incorporating PC into the practice of all healthcare team members on a pediatric oncology service. The impact of including PC during diagnosis/treatment conferences and throughout the trajectory of care was measured after one year utilizing comparison of staff assessment and patient/family satisfaction surveys.

Results: Inclusion of PC into the skill base and practice of the multidisciplinary team has resulted in improvement in satisfaction with pain and symptom management [28–90%], patient/family involvement in decision making [37–90%], improved coordination of complex care and fewer hospitalizations at end-of-life.

Conclusion: Palliative care can be included as supportive care in pediatric oncology settings. Incorporating PC into the role of each member of the multidisciplinary teams currently in practice results in improved care of children with cancer and their families along the journey from diagnosis through survivorship or bereavement. Practitioners benefit from practical suggestions encouraging integration throughout the plan of care.

PR047

PLACE OF DEATH OF PEDIATRIC CANCER PATIENTS IN JAPAN

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Purpose: The disparity between actual and preferred place of death has been reported in adults with cancer. It is poorly understood in pediatric cancer patients in Japan. This study aimed to clarify the actual and preferred place of death of children with advanced cancer as well as variables associated with place of death.

Method: Study population was advanced cancer patients who were admitted to the department of Pediatrics at Kobe University Hospital. Japan and died of cancer between January of 2004 and March of 2011. The medical records were retrospectively reviewed to derive data relating to patients' characteristics, disease and place of death. Actual and preferred place of death of patients and their families and variables such as the reasons for preference were analyzed.

Results: 13 patients (8 males, 5 females) were included. Median age at death was 11.3 (range: 1.3–21.9) years old. 1 patient suffered from hematological disease and 12 patients suffered from solid tumors. 4 patients (30.8%) died at home, while 9 patients (69.2%) died in the hospital. No patients were asked of preference. 4 families (30.8%) preferred home, 2 families (15.4%) preferred hospital, 1 family (7.7%) lacked preference and others were not asked. Among 6 families who expressed preference, no disparity was observed between actual and preferred place of death. Families' preferences were mainly based on the speculation as to where patients wished to be cared for. Place of death was significantly influenced by families' preference (p = 0.029).

Conclusion: The lack of disparity between actual and preferred place of death was demonstrated in this study. Given the small sample size and the potential difference in preference between patients and their families, further large studies that explore patients' preferences are needed to reveal the optimal place of death for children with cancer.

PR048

TEENAGE AND YOUNG ADULT (TYA) PALLIATIVE CARE: DO WE MEET THE NEEDS OF THE DYING ADOLESCENT?

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Purpose: Adolescent palliative care provides unique challenges from acknowledged practice in both paediatrics and adult care.

Aims: To review our current practice against new national adolescent guidance.

Method: Retrospective case note review of the last ten consecutive adolescent cancer deaths at UCLH

Results: 5 haematology (4 male; 1 female) and 5 oncology (1 female; 4 male) patients were included. Median age at death was 11.3 (range: 1.3–21.9) years old. 1 patient suffered from hematological disease and 12 patients suffered from solid tumors. 4 patients (30.8%) died at home, while 9 patients (69.2%) died in the hospital. No patients were asked of preference. 4 families (30.8%) preferred home, 2 families (15.4%) preferred hospital, 1 family (7.7%) lacked preference and others were not asked. Among 6 families who expressed preference, no disparity was observed between actual and preferred place of death. Families’ preferences were mainly based on the speculation as to where patients wished to be cared for. Place of death was significantly influenced by families’ preference (p = 0.029).

Conclusion: The lack of disparity between actual and preferred place of death was demonstrated in this study. Given the small sample size and the potential difference in preference between patients and their families, further large studies that explore patients’ preferences are needed to reveal the optimal place of death for children with cancer.
**RESULTS:***187* SVPs were implanted in 141 patients during the follow-up period. The complications, catheter related complications, were analyzed as well as SVP-internal and external infectious maintenance SVP-routines to reduce morbidity, infectious complications, malfunction and to reduce the surgical complications of SVP-insertion in children and to optimize the daily surgery in Lund between January 2005 and January 2011. The background to the study was the oncology unit. Included patients were identified as at risk of neutropenia secondary to profound neutropenia (<0.5x10⁹/l) at presentation (RR 2.21 (95% CI 1.23–3.99)) and need for a fluid bolus, a proxy measure of haemodynamic instability (RR 3.42 (95% CI 1.94–5.69)). Other risk factors including moderate neutropenia (0.5–1.0x10⁹/l), focal signs at presentation, and previous positive blood culture were not found to be significantly associated with risk of bacteraemia.

**Conclusion:** Clinically significant bacteraemia was observed in 16% of episodes. Gram positive organisms were the most common cause of bacteraemia. Risk of bacteraemia was significantly greater with younger age, profound neutropenia and haemodynamic instability at presentation.

**SUBCUTANEOUS VENOUS PORT-ASSOCIATED COMPLICATIONS IN PEDIATRIC PATIENTS TREATED 2005–2009 AT THE CENTER FOR PEDIATRIC HEMATOLOGY AND ONCOLOGY IN LUND, SWEDEN***

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**Purpose:** The purpose of the study was to identify subcutaneous venous port (SVP)-related complications in pediatric patients treated at the Department for Childhood Cancer and Surgery in Lund between January 2005 and January 2011. The background to the study was to reduce the surgical complications of SVP-insertion in children and to optimize the daily maintenance SVP-routines to reduce morbidity, infectious complications, malfunction and days at hospital.

**Method:** The medical records for all pediatric patients with SVP-insertions from January 2005 until December 2009 (n = 141) were monitored up to January 2011. Perioperative- and catheter related complications, were analyzed as well as SVP-internal and external infectious complications.

**Results:** 184 SVPs were implanted in 141 patients during the follow-up period. The median age at insertion was 5 years and 8 months (range 1 m to 17 y 9 m). 85% of the patients were treated for malignant diseases. SVP-related complications were seen in 48% (34%) of the patients. 41% (22%) of the inserted SVPs were removed because of suspected catheter-related infection, of these, 18 patients had haematological malignancies, 9 solid tumours and 6 non-malignant diseases. Five patients had more than one SVP removed due to repeating infections. 16 (9%) SVPs were removed because of malfunctioning (mainly no backflow). Another 16 patients (9%) were re-operated due to malpositioning of the SVP-tip.

**Conclusion:** SVP-associated complications are common in children treated at cancer units. The complications associated with SVPs indicate that by improving and standardizing the operative procedure the perioperative-complications could be brought down. Education and optimizing routines regarding the daily maintenance of SVPs would decrease complications and thus the morbidity for the patients. But better tools are needed for discrimination between catheter-related infections from infections of other origin.

**AUDIT OF BLOOD COMPONENT THERAPY IN PEDIATRIC ONCOLOGY: PERSPECTIVE FROM A TERTIARY CARE PEDIATRIC HOSPITAL***

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**Purpose:** To analyze episodes of blood component therapy in pediatric oncology at a Tertiary Care Children Hospital and conduct a transfusion audit for the same before and after education of health care professionals involved and assess impact on transfusion practices.

**Method:** Study included patients who presented to the pediatric oncology service between June 2009 and June 2010. The episodes of blood component therapy were analyzed and a concurrent audit was undertaken in accordance with guidelines by the American Association of Blood Banking. Data was analyzed using SPSS version 17.0. The chronology of analysis was pre guidelines assessment, post guidelines assessment and comparison of the two. The exact numerical data was analyzed by using paired t tests or ANOVA and chi-square tests. The p value is significant if < 0.05.

**Results:** In a total of 56 blood component transfusions, 34/56 transfusions (60%) were in acute Leukemia patients and 22/56 transfusions (40%) in patients with solid tumors. In the first part of the study of 33 episodes, 21/33(63%) were for PRC, 9/33(27%) platelet transfusions and 3/33(9%) of FFP. The duration was correct for all except 8/39(9%) platelet transfusions. In the second part of 23 episodes, 5/23(21%) were transfusions of PRC, 13/ 23(56%) of platelets and 5/23(21%) of FFP. The duration was correct for PRC and 12/ 13(92%) platelets and 2/5(40%) FFP. A comparative analysis showed indications and amount transfused were correct for all and improvements in the deficient fields however some cases remained to be improved.

**Conclusion:** Blood transfusion is an essential part of modern pediatric care. Used correctly, it can save life and improve health.
Dengue fever is endemic in India. It is important to diagnose dengue early because of the need for adequate fluid therapy. We describe dengue infection as a cause of febrile neutropenia in children with acute lymphoblastic leukemia (ALL). Purpose: To identify prognostic factors in the literature and to score the factors in medical records from our own institution as well as in published paediatric case reports. Method: A literature search was performed within the databases Pubmed and Embase up to June 2009, the used search terms were neutropenic enterocolitis or typhlitis within oncology patients. Within the results of our literature search we selected paediatric case reports to review. We searched in our own paediatric oncology database for patients diagnosed with neutropenic enterocolitis between 2003 and 2010 to score the identified prognostic factors. Results: The literature search resulted in 126 included studies, 13 possible prognostic factors were identified in fifteen studies. Bowel wall thickening on imaging and prolonged neutropenia over 7 days were identified the most. The literature search resulted in 34 paediatric case reports. The amount of prognostic factors between survivors and non-survivors was not significantly different. In our own institution 10 paediatric oncology patients were diagnosed with typhlitis. A correlation between the amount of prognostic factors and the severity of the course and outcome was found. Conclusion: This was a pilot study for a prospective multi-centred study to validate the identified prognostic factors. A prediction rule based on these prognostic factors can decrease morbidity and mortality in this potentially life threatening entity.
FERRILE EPISODES IN CHILDREN AT RISK OF NEUTROPENIA: LOOKING FOR A FOCUS

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Purpose: To examine reported focal symptoms/signs in febrile children at risk of neutropenia and determine whether these predict risk of bacteremia and to determine the range, number and diagnostic yield of investigations for focal infection performed.

Method: This was a single centre retrospective study. Clinical and laboratory data were collected on all febrile episodes in children at risk of neutropenia in a tertiary paediatric haematocNormally children treated for cancer at our institution were at increased risk for NF.

PR064

EVALUATION OF INFECTION CONTROL ADVICE FOR PATIENTS AT RISK OF CHEMOTHERAPY-INDUCED NEUTROPAENIA IN TWO PEDIATRIC ONCOLOGY CENTRES IN SOUTH AFRICA AND THE UNITED KINGDOM

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Purpose: Necrotizing fasciitis (NF) is rare amongst children. We examined our institution’s experience with NF in children with concomitant malignancies.

Method: With Ethical committee approval, patients 18 years and younger treated for necrotizing fasciitis with coexisting malignancy at our Institute between March 1, 2001 and December 31, 2011 were reviewed. Data pertaining to their clinical presentation, investigations, surgery, follow up and outcomes were collected and analyzed.

Results: Our study cohort comprised of 6 boys and 3 girls. The mean age was 6.8 years (1.6–13.5 years). Seven of these patients had pre-existing Leukaemia; 1 presented with NF at the diagnosis of Leukaemia, 1 had para-meningeal rhombomycosis. Fever, local pain, swelling, erythema and necrotic spots were the most common presentations. The affected sites included the extremities (3); groin and perineum (2), head and neck (3), and Chest (1). 7 patients were neutropenic at admission, of which three developed NF at site of recent porta cath insertion/breach in skin integrity). Pseudomonas aeruginosus was the most common pathogen (7) and was the sole pathogen isolated in 4 cases. 5 patients had a polymicrobial infection. Urgent surgical debridements +/- fasciotomy were performed in all cases with serial examinations under anaesthesia and repeat debridements. Clinical diagnosis was confirmed at surgery with additional histological confirmation in 8. One patient required a local flap closure, 1 required delayed secondary closure, split skin grafts were needed for 3 patients, diverting stomas were created for perinatal NF, there was one death in our series, while the remaining wounds healed by granulation and achieved satisfactory healing by 2 months (17–58 days).

Conclusion: Childhood NF will become more common as cancer treatment becomes more aggressive. Pseudomonas and enteric gram negative organisms are seen frequently in immunocompromised children with NF. PORTA cath site infections can frequently transform to NF and hence must be addressed aggressively.

PREVALENCE AND PREDICTORS OF HUMAN PAPILLOMA VIRUS (HPV) VACCINATION AMONG YOUNG SURVIVORS OF CHILDHOOD CANCER

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Purpose: Effective vaccination is available to prevent human papillomavirus (HPV), the most common sexually transmitted infection and the cause of cervical and other cancers. Vaccination is important for survivors of childhood cancer who are at increased risk for HPV-related complication secondary to the direct and indirect effects of cancer treatment. The purpose of this work is to report the prevalence of HPV vaccination, while identifying more predictive factors associated with vaccine uptake.

Method: Mothers (N = 180; M age = 41.72 years, SD = 8.12) with daughters surviving pediatric cancer (M age = 13.26 years, SD = 2.69) completed paper-and-pencil questionnaires which queried, in part, HPV vaccination uptake along with sociodemographic and health belief factors specific to HPV vaccination.

Results: Thirty three percent of adolescent survivors have initiated HPV vaccination. Univariate comparisons of sociodemographic factors among those who have/have not initiated vaccination reveal that older patient age, lower household income, and being non-white (ps range from <.001–.05) associate with increased likelihood of vaccine initiation. Furthermore, health belief factors such as higher beliefs of vaccine benefit, lower perceptions of child’s health vulnerability, and lower perceived vaccine barriers also associate with vaccine uptake (ps <.001). Multivariate logistic modeling indicates that vaccinated survivors are more likely to be older (OR = 1.35, 95% CI = 1.13–1.60, p = .001) and have mothers with higher beliefs of vaccine benefit (OR = 1.15, CI = 1.02–1.30, p = .02) and lower perceptions of child health vulnerability (OR = .86, CI = 0.81–0.98, p = .02).

Conclusion: A minority of adolescents surviving childhood cancer have initiated HPV vaccination despite their increased risk for HPV-related complication. Findings suggest that patient age and maternal beliefs of vaccine benefit play significant roles in determining vaccination uptake in this group. Implications for intervention will be discussed.

PR060

CLINICAL PRESENTATION AND OUTCOME OF VANCOMYCIN RESISTANT ENTEROCOCCI INFECTION IN PEDIATRIC CANCER PATIENTS: EXPERIENCE FROM A TERTIARY CARE CENTRE IN INDIA

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Purpose: Colonization and Infection with Vancomycin Resistant Enterococci(VRE) has dramatically increased over last few years especially in immunocompromised children with malignancies.

Method: 2045 stool samples were screened. VRE infection/colonization rate was 6.3%. Presence of focal symptoms did not predict risk of bacteraemia. Earlier initiation. Furthermore, health belief factors such as higher beliefs of vaccine benefit, lower perceptions of child health vulnerability (OR = 1.35, 95% CI = 1.13–1.60, p = .001) and have mothers with higher beliefs of vaccine benefit (OR = 1.15, CI = 1.02–1.30, p = .02) and lower perceptions of child health vulnerability (OR = .86, CI = 0.81–0.98, p = .02).

Conclusion: A minority of adolescents surviving childhood cancer have initiated HPV vaccination despite their increased risk for HPV-related complication. Findings suggest that patient age and maternal beliefs of vaccine benefit play significant roles in determining vaccination uptake in this group. Implications for intervention will be discussed.
Purpose: To compare infection control advice for paediatric and adolescent patients at risk of neutropenia after cytotoxic cancer chemotherapy in two centres.

Method: A prospective, observational and cross-sectional survey of staff and patients' parents was undertaken, standardised, study-specific questionnaires in two paediatric oncology centres (Cape Town, South Africa and Newcastle, UK).

Results: Seventy eight staff members (28 in Cape Town and 50 in Newcastle) and 56 patients/parents (30 in Cape Town and 26 in Newcastle) participated in the study. Numbers of staff in each occupational category were proportionally similar in both centres, and patients in the two centres were similar in terms of inpatient/outpatient status (63% outpatients in Cape Town, 73% outpatients in Newcastle), current treatment status and treatment duration (all p > 0.05). All of the participants interviewed had treatment with standard chemotherapy without stem cell transplant support, but in Cape Town there was a higher proportion of patients under 12 years compared with Newcastle (p = 0.03). Staff responses on precautions advised in Newcastle were significantly different to Cape Town (all p < 0.05) where staff reportedly advised more precautions. Patient/parent responses were similar between centres. In Newcastle, patients/parents had stricter opinions on particular precautions than staff, e.g. attending school, playing outside and avoiding busy places (p < 0.01). Over 90% of staff felt advising patients/parents about hand washing was important. However, patients/parents reported that few staff explained how to perform appropriate hand washing.

Conclusion: Current advice and clinical practice is inconsistent. Evidence-based guidelines to provide standardised and effective guidance for infection prevention in neutropenic patients should be developed and implemented. Such guidelines will need to maintain a balance between infection prevention and psychosocial wellbeing.

PR065
H1N1 INFLUENZA INFECTION IN PAEDIATRIC ONCOLOGY PATIENT ON CHEMOTHERAPY IN KK WOMEN'S AND CHILDREN'S HOSPITAL
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Purpose: In April 2009, the Influenza A (H1N1) virus emerged as a novel infection. The majority of cases worldwide and in Singapore have been mild and self limiting. However, subgroups of patients such as children under 5 years and immunosuppressed patients on chemotherapy are at increased risk of complications. We reviewed the clinical course of H1N1 infection in pediatric oncology patients.

Method: This is a prospective cohort study which looked at all of pediatric oncology patients on active chemotherapy with Influenza A (H1N1) infection from July 2009 to July 2010. H1N1 infection was confirmed with Real-Time PCR subtyping. Data analyzed included demographics, clinical signs and symptoms, duration of viral shedding and outcome.

Results: Twenty-one children (males 62%, females 38%) with malignancies on chemotherapy had laboratory-confirmed infection with Influenza A (H1N1). The most frequent presenting symptom was fever (95%); 86% had duration of fever less than a week with a maximum duration of 28 days. Cough was present in 90% and rhinorrhea in 57%. Chest imaging was performed in thirteen patients and demonstrated lower respiratory tract involvement in six patients. Eleven patients presented with febrile neutropenia. We could follow the duration of viral shedding in 16 patients. The minimum and maximum duration was 5 days and 42 days respectively. Eleven patients had more than 10 days. The prolonged duration of viral shedding was not associated with neutropenic status or the continuation of chemotherapy. Three patients required ICU care; two patients had concomitant bacteremia and died of septicemia. The third patient’s clinical course was complicated with pulmonary aspergillosis, right pneumothorax and extensive subcutaneous emphysema.

Conclusion: The outbreak of H1N1 infection in immunosuppressed children with malignancies on active chemotherapy was mild in the majority. However, they are still at high risk for serious complications especially in the setting of superimposed infections with other organisms.

PR066
INSTITUTIONAL VARIATIONS IN NON-PHARMACOLOGICAL ANTI-INFECTIVE MEASURES - RESULTS OF AN INTERNATIONAL SURVEY
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Purpose: Standardization in practice may be associated with improved outcome in pediatric cancer. While this effort has resulted in increased homogeneity of treatment protocols, such an effort has not been made for supportive care practices. Non-pharmacological interventions to prevent infection may impact child and family quality of life.

Method: We performed an international, web-based survey of non-pharmacological anti-infective-measures. The survey included questions on institution demographics, institutional recommendations regarding restrictions of social contacts, pets and food, and policies on wearing face masks in public. Recommendations were specific for children with standard-risk acute lymphoblastic Leukemia (ALL) and acute myeloid Leukemia (AML) during intensive chemotherapy.

Results: A total of 327 institutions in 27 countries responded to the survey (range 1–76 institution per country; overall response rate 61% (range 29–100%). Regarding social contacts, most institutions did not allow children to attend daycare, kindergarten or school for AML patients, whereas recommendations for patients with ALL considerably differed by institution. For both ALL and AML patients, there was wide variability in food restriction (e.g., salad, nuts, take-out food, and unpeeled vegetables). In contrast, most institutions did not allow raw meat, raw seafood, and unpasteurized milk for either patient population. The widest variation between institutions was found regarding restrictions of pets at home (e.g., dogs, cats, turtles, and hamsters). Most institutions did not routinely recommend face masks in public: for patients with AML, this practice was variable between institutions for patients with AML.

Conclusion: This survey demonstrates that there are wide variations in non-pharmacological anti-infective measures between different institutions, countries and continents. This information may be used to encourage harmonization of supportive care practices and future clinical trials.

PR067
INVASIVE FUNGAL INFECTIONS IN PEDIATRIC ONCOLOGY PATIENTS - A SINGLE CENTRE EXPERIENCE
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Purpose: Invasive fungal infections (IFI) are an important cause of mortality and morbidity in children with cancer. We conducted a retrospective study to assess the pattern and outcome of IFI in pediatric oncology in a single-centre in India.

Methods: Medical records of children < 16 years admitted with Leukemia or solid tumors and diagnosed with IFI were retrospectively reviewed from January 2005 to December 2010. IFI was classified as proven, probable and possible as per 2008 EORTC Guidelines. Details of antifungal prophylaxis, therapy and survival were recorded.

Results: Forty-four episodes of IFI were seen in 43 (27 boys, 17 girls) out of 536 oncology patients (8.2%) treated during the study period. Median age was 8 years (range 1 to 16). Underlying diagnoses were acute lymphoblastic Leukemia in 33 patients, acute myeloid Leukemia in 7 and relapsed solid tumors in 3. There were 17 proven, 21 probable and 8 possible IFI. Proven IFI was caused by Candida (n = 11), Aspergillus (n = 3), Mucormycosis (n = 2) and Conidobolus (n = 1). Two had co-infection of Zygomycetes with Aspergillus. Probable IFI was caused by Aspergillus (n = 19) and Candida (n = 2). Eight children had possible invasive aspergillosis. The site of IFI was lungs in 27 patients, blood (n = 8), sinuses (n = 2), intestine (n = 3), esophagus (n = 2), liver (n = 2), pericardium (n = 1) and skin (n = 1). Despite adequate antifungal therapy (amphotericin B, voriconazole and/or caspofungin as required) and surgery (laparotomy for intestinal perforation-3, sinus surgery-1), 11 (26%) patients expired, 37 (72%) survived IFI and I was discharged on request. Death occurred in 4 proven IFI (Candida sepsis-2, Mucormycosis-1, Conidobolus-1) and 7 probable Aspergillosis.

Conclusion: IFI in immunocompromised children is associated with high mortality. Emergence of rare fungal infections like Zygomycetes is a challenge.
**PS001 QUALITY OF LIFE AMONG ADOLESCENT PATIENTS DIAGNOSED WITH CANCER UNDERGOING TREATMENT**

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Purpose: To assess the quality of life (QOL) of adolescent patients diagnosed with cancer who are currently undergoing treatment at the Philippine General Hospital (PGH) and to identify if there are differences in the QOL of these patients in terms of gender, age, parental education status, type of treatment used, duration of treatment and type of malignancy.

Method: Twenty four adolescent patients diagnosed with cancer from the period of August 2008–August 2010 who were presently undergoing treatment at PGH were identified as the study population. The patients self-reported their QOL using the University of the Philippines/Department of Health QOL scale. Simple Linear regression analysis at 90% confidence using Stata11 was done to determine the relationship of overall QOL score and specific domains with the different factors.

Results: Of the 24 patients, 22 were enrolled in the study. One patient was excluded due to his medical condition; another was not interviewed due to his location. The overall QOL was moderate to high. Majority of those who reported moderate QOL were males (75%), had an average age of 13 yrs old (SD + 1.280) and had parents with low education status (75%). Those who only underwent chemotherapy as treatment reported a higher overall QOL.

Conclusion: The QOL of adolescent cancer patients undergoing treatment at PGH has been shown to be moderate to high. Gender, age, parental educational status, modality of treatment, and type of malignancy did not have a significant relationship with the patients’ perception of QOL. However, by proportions and means, there seems to be a relationship.

**PS002 CHILDHOOD BRAIN TUMOR SURVIVORS AT RISK FOR IMPAIRED HEALTH RELATED QUALITY OF LIFE: BE ATTENTIVE TO LOW GRADE TUMOR SURVIVORS**

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Purpose: To assess the prevalence of childhood brain tumor survivors (CBTs) at risk for impaired health related quality of life (HRQOL) treated with and without adjuvant therapy. Method: HRQOL was evaluated in 34 CBTs (response rate = 72%, mean age = 14.1 yrs old, mean time since end of treatment = 7.1 yrs) with the KIDSCREEN, a self-report HRQOL questionnaire. Half of them were treated with surgery only; the other 17 were treated with surgery and adjuvant therapy. The definition of CBTs being at risk was based on

**144 SIOP ABSTRACTS**

**PR069 POLYMORPHISM IN TLR2, TLR4 AND SUSCEPTIBILITY TO FEBRILE NEUTROPENIA AND FUNGAL INFECTIONS IN CHILDREN WITH LEUKEMIA**

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Purpose: We aimed to investigate the association between single nucleotide polymorphisms (SNPs) of TLR4 and TLR2 in children with Leukemia and susceptibility to febrile neutropenia (FN) and invasive fungal infections (IFIs).

Method: SNPs of TLR4 Arg299Gly and TLR2 Arg299Gly variants were assessed in 17 children with AML, 19 with ALL and 12 with AML or ALL. TLR2 Thr399Ile variant allele was found in 8 patients, of 5 of whom TLR 4 Arg299Gly variant allele was also found. Two patients were carriers of 399Ile allele variant after treatment. Sixty-three percent of the patients who had 399Ile variant allele relapsed compared to those who did not have this allele (p < 0.05). There was no increase in FN and IFIs in patients with TLR4 mutations.

Conclusion: This study is limited by the small number of positive patients with TLR2 mutation. Interestingly the only patients who were heterozygous had no FN attack, IFI or any serious infection during the treatment. The known TLR2 polymorphism identified so far may not cause a crucial role in the pathogenesis of IFIs and FN in children treated for ALL. No relation between IFIs and TLR4 mutations was found. However, the patients with TLR4 Thr399Ile variant allele were found to have a risk for disease recurrence.

**PS003 HIGH INCIDENCE OF FUNGAL INFECTIONS IN PEDIATRIC ONCOLOGY PATIENTS IN BRITISH COLUMBIA**

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Purpose: Autoimmune lymphoproliferative syndrome (ALPS) is an inherited lymphoid disorder, attributed to a defect in apoptosis, characterized by non-malignant lymphoproliferation, autoimmunity and cytopenias with raised circulating double negative T cells. Posterior Reversible Encephalopathy Syndrome (PRES) is a clinic-radiological entity characterized by headache, confusion, seizures, hypertension and transient posterior cerebral hypertensitivities on T2 weighted MRI. We report a boy with ALPS who also had PRES, now completely recovered.

Method: A detailed analysis of the child’s history, examination, laboratory investigations along with review of literature of the two conditions has been done.

Results: A 15 year old boy presented with intermittent swelling of both sides of the neck for the past 8 years. He has undergone four lymph node biopsies and two fine needle aspiration cytology which were inconclusive. His sister was diagnosed to have probable lymphoma and died at 7 years of age. On physical examination he had pallor, significant lymphadenopathy and hepatosplenomegaly. Investigations revealed anemia, thrombocytopenia, hypergammaglobulinemia, positive direct Coombs test and antinuclear antibodies. Double stranded DNA and anti Smith ELISA were negative. Chest X ray was normal and Mantoux was negative. Infectious causes were ruled out by serological tests. Flow cytometry revealed 19% double negative T cells (CD3+ CD4+ CD8–) confirming ALPS. After treatment with steroids he had resolution of cytopenia, lymphadenopathy and organomegaly in two weeks. He presented after a month with headache, altered sensorium, seizures and hypertension. MRI brain showed symmetrical hyperintensities in bilateral parieto-occipital regions suggestive of PRES. He recovered completely with supportive care and is on follow-up.

Conclusion: ALPS should be suspected in a child with lymphadenopathy, cytopenia and autoimmunity for which common causes like infection, malignancy and systemic lupus erythematosus have been ruled out. To our best knowledge, PRES has not been reported in ALPS. We report this to make paediatric oncologists aware of the rare association of PRES with ALPS.

**PR070**

144 SIOP ABSTRACTS

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Purpose: Invasive fungal infections (IFIs) are a common cause of mortality and morbidity in pediatric oncology patients, particularly those in high risk categories (AML, relapsed ALL, SCT recipients). The incidence of IFIs varies in the literature and we hypothesized that our region appeared to have a high rate of IFIs. Therefore a study was undertaken in order to document the rate of IFIs at our institution (the only pediatric oncology center for a population of 4.5 million).

Method: A retrospective chart review was conducted in all high risk subjects over a six year period. This cohort was divided into two 3 year groupings (Period-1: 2004–2006; Period-2: 2007–2009), the second period encompassing a change in practice where CT scans were performed in all high risk patients on day 5 of fever. All investigations were captured and subjects were classified into possible, probable, proven and no fungal infection. CT scans were reviewed by 3 pediatric radiologists.

Results: Period-1 had 64 subjects (12 AML, 10 rALL, 36 AlloSCT, 25 AutoSCT) and Period-2 had 75 subjects (17 AML, 5 rALL, 34 AlloSCT, 32 AutoSCT). Period-1 had a 6.8% rate of proven/probable IFIs and all occurred in subjects with relapsed ALL. Period 2 had a 16.7% rate of proven/probable IFIs and this increased to 30.4% if possible IFIs were included. 55% of documented infections were molds. 21.4% of AlloSCT subjects had proven/probable infection.

Conclusion: The rate of IFI was extremely high at our institution. An increased rate of IFIs was seen with more liberal CT scanning. IFI rates are comparable to our local adult center (19% SCT, 22% AML) and to the nearest city (Seattle, 19% SCT). This raises the possibility that our region is a hotspot of IFIs, specifically mold infections. This has already led to a change of antifungal prophylaxis and we are planning a follow-up study.
**Results:** A high prevalence at risk was found on four domains: physical well-being; moods and emotions; peers and social support; and social acceptance/bullying. CBTS were not at risk on 6 of 10 domains including psychological well-being, self-perception, autonomy, parent relation and home life, financial resources and school environment. No differences were found on any of the domains between the two groups of survivors (survivors treated with surgery only or survivors treated with surgery and adjuvant therapy).

**Conclusion:** Our survivors reported a significant impaired HRQOL for physical functioning, mood and social functioning. No differences in survivors treated with or without adjuvant therapy were found. Although treatment with surgery only might be associated with little impairment, we believe these low grade tumor survivors should be carefully followed as well. Monitoring of these life domains with patient reported outcome assessments in follow-up clinics is recommended with early psychological coaching if indicated.

**PS005**

**SCREENING FOR DISTRESS IN YOUNG PEOPLE AFTER TREATMENT FOR SARCOMA**

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**Purpose:** Improvements in survival rates for childhood cancers has resulted in awareness of the burden of long term psychological impact as a consequence of diagnosis and treatment. Distress and worry often goes unnoticed with detrimental effects on the patient and their care. The “Distress Thermometer” is a useful surveillance tool in adult cancer settings however there are few validated tools available to screen for distress in a paediatric or adolescent setting. **Purpose** - To assess the feasibility, acceptability and sensitivity of questionnaires to screen for psychological distress in young people attending a newly established sarcoma follow-up clinic.

**Method:** Every patient who attended the clinic was invited to complete questionnaires, assessing mood, behaviour, quality of life, general and specific distress. Data was analysed using one sample t-tests and cumulative binomial tests.

**Results:** Twenty-one patients out of a possible 23 (11 males, 12 females) agreed to participate - mean age: 14; mean time since diagnosis: 4 years; mean age at diagnosis: 9.5 years. Participants reported significantly more concerns about being able to complete usual activities (p = 0.006) and higher levels of anxiety and depression (p = 0.04) than a normative population. The health related quality of life measure (EQ5D) and the Distress Thermometer appeared more sensitive to young people’s worry and levels of distress than traditional measures of behaviour or anxiety or depression.

**Conclusion:** No significant behavioural or psychological problems were found using measures of general behaviour and mood, compared to a normative reference sample. However, patients report impaired health status and worry about lifestyle, daily activities, and emotional wellbeing. The EQ5D and the DT were found to be simple and effective ways of checking worries and concerns with young people attending a clinic. They may serve as useful tools to screening for psychological concerns in busy clinical setting.

**PS006**

**THE SEVERITY OF LATE EFFECTS INFLUENCES QUALITY OF LIFE OF CHILDHOOD CANCER SURVIVORS DEPENDING ON DEVELOPMENTAL STAGE**

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**Purpose:** The study deals with psychosocial problems of childhood cancer survivors. We report data from the qolp project (Quality of Life Longitudinal Study of Paediatric Oncology Patients) We focus on the relationship between the severity of late effects of anticancer treatment and subjective Qol.

**Method:** The sample consisted of 147 CCS (70 boys, 77 girls, 9–19 years): 26% acute Leukemia,18% brain tumours,54% extracranial solid tumours. Average time after completion of treatment was 3.3 years. Cancer survivors were asked to complete the Minnesota Minneapolis Quality of Life Instrument (MMQOL) and other methods measuring involvement in everyday life activities, parent-child interactions, and emotional well-being, expressed by the degree of depressive symptoms. Correlation analysis was used to explore the relationship between severity of late effects and subjective Qol. The analyses were done separately for younger (8–12) and older (13–18) age brackets.

**Results:** We have found significant relationships between the severity of late effects and Qol domains mainly in the older age group: the severity of late effects correlates positively with depression and negatively with conventional involvement, physical functioning, cognitive functioning, satisfaction with body development, and social functioning. In the younger age bracket, the severity of late effects correlates only with parental warmth. We explain these findings by the fact that older children (adolescents) deal with the disease as adults, they are a lot more conscious of its seriousness and the threat of adverse prognosis. The results correspond with our previous study analysing differences in Qol, among the main categories of diagnoses. Likewise in this study we found significant differences only in the older age bracket. Study limitations: research has usual limitations arising from the fact that we used a range of self-report methods.
WHO’S LISTENING? DO FAMILIES FOLLOW THROUGH WITH REFERRALS FOR PSYCHOLOGICAL SERVICES FOLLOWING A MULTIDISCIPLINARY LONG-TERM FOLLOW-UP ASSESSMENT?

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Purpose: In 2009, a statewide, multidisciplinary Long Term Follow-Up Program (LTFP) was implemented for Victorian childhood cancer survivors. The role of the Psychology Service within this clinic is to screen for neurobehavioural and psychosocial difficulties via clinical interview and to provide referral recommendations to appropriate hospital or community services if required. This project aimed to evaluate the frequency of neurobehavioural/psychosocial concerns identified by the Psychologist in the non-CNS tumour LTFP clinic, as well as uptake of neuropsychology and mental health referrals by families.

Method: Medical Records of 58 consecutive patients attending the LTFP clinic at the Royal Children’s Hospital and Monash Medical Centre in Melbourne from July-December 2010 were audited. Medical and demographic information, plus details of all referrals/post-clinic follow-up notes made through the Psychology service of the LTFP were extracted.

Results: At time of clinic attendance, mean age of patients was 14.1 years (SD: 4.0, range: 7.1-22.3) and mean time post-treatment was 6.7 years (SD: 3.5, range: 2.2-16.4). Diagnoses included Leukaemia (n = 29, 50%), lymphoma (n = 5, 9%) and solid non-CNS tumour (n = 24, 41%). Sixty-two percent (n = 36) were male. A proportion of patients had previously undergone neuropsychology assessment (n = 11, 19%) and/or accessed mental health services (n = 10, 17%). Based upon LTFP screening assessment, additional referrals were made to neuropsychology (n = 8, 14%) and mental health (n = 15, 25%) services. Uptake was 100% and 53% for neuropsychology and mental health services, respectively. Reasons for non-uptake included reported post-clinic decline in symptom severity (n = 2), refusal by patients (n = 4), and time factors (n = 1).

Conclusion: Frequency of neurobehavioural/psychosocial difficulties identified in the current sample appears broadly consistent with prevalence reported in current literature (30–40%). Families appeared more complacent with neuropsychology compared to mental health referrals. Reasons for this discrepancy are discussed. Findings suggest that alternate approaches to facilitating mental health referrals may be warranted.

TOO COOL FOR SCHOOL: FACILITATING THE TIMELY RETURN OF PAEDIATIC ONCOLOGY PATIENTS TO THE SCHOOL ENVIRONMENT

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Purpose: Schooling is an integral part of every child’s life, assisting in the development of relationships, discipline and intellect. Previous studies on paediatric patients with chronic illnesses have shown that while schooling and tuition programs within paediatric centres are well conducted, patients maintaining contact, returning to their regular school and schooling pattern, is poor. Furthermore, studies have shown that open communication between the schools of children with chronic illnesses, their families and the hospitals in which they are being treated, has been attributed to an earlier return to their regular school.

Method: Within the Women’s & Children’s Hospital in Adelaide, South Australia, the paediatric oncology patients of kindergarten and school age are offered a school visit/information program. However, over many years, the program was not meeting the needs of patients, their families or school staff. Both the way in which the information was given to schools and the timeframe in which schools were given such information was found to be the key problem.

Results: In response, a CD-ROM presentation has been developed to be sent to schools with an accompanying letter, including an e-mail address to assist in opening the channels of communication with the school. The package is to be sent within the first 2 weeks of a school-age child’s diagnosis, with a follow-up questionnaire sent at 4 weeks and 12 weeks to determine the timeframe in which children are returning to school and the level of interaction between the key stakeholders. Qualitative data surrounding the level of confidence of both teachers and parents at the time of the child returning to school is also to be collected at those time points.

Conclusion: At time of abstract the evaluation is yet to be completed, but will be available for presentation prior to the SIOP conference.

ADOLESCENT SIBLINGS OF CANCER SURVIVORS: THE FORGOTTEN FAMILY MEMBERS?

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Purpose: This study investigates the psychological wellbeing of adolescents who have a sibling discharged from treatment and in remission from cancer. Psychologically, a cancer diagnosis precipitates a challenging period as the family adapts to caring for a severely ill child, causing disruption to family roles and rules. This paper aims to examine how this transition is negotiated within families, and how it interacts with the wellbeing of siblings. As a result, we hope to identify both protective factors, and predictors of poor adjustment for siblings.

Method: In this paper we will report the findings from a questionnaire of approximately one hundred 12–18 year old siblings of cancer survivors. The questionnaire contains sections measuring: wellbeing; self-esteem; depression; optimism; perceived fairness of parental treatment; quality of the sibling relationship; peer attachment; and family cohesion. It is designed to investigate both ultimate outcomes, and potential mediating and moderating factors for those outcomes. Additionally, ten participants will take part in semi-structured interviews to contextualise and deepen the questionnaire findings.

Results: This research is currently in progress, but results will be available by the time of presentation. Quantitative analysis will involve establishing the prevalence of poor or positive adjustment in this population, and establishing baseline rates of particular issues. Relationships and optimism will be examined, particularly in relation to levels of wellbeing, self-esteem, and depression. Qualitative data will be examined for themes relevant to siblings’ experiences, particularly regarding findings from the quantitative section.

Conclusion: A number of charitable organizations serving these families in New Zealand have already expressed interest in the results of this study and are keen to use the findings to improve their service to siblings and identify key areas to target interventions.

CANCER DURING ADOLESCENCE: NEGATIVE AND POSITIVE CONSEQUENCES REPORTED DURING THE EXTENDED PHASE OF SURVIVAL

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Purpose: To describe negative and positive cancer-related consequences reported by individuals three and four years after a cancer diagnosis during adolescence and to examine the degree to which the individuals report similar and/or different consequences as two years after diagnosis. A secondary aim was to explore if the use of certain coping strategies shortly after diagnosis is related to reports of certain consequences four years after diagnosis.

Method: Thirty-two participants answered semi-structured questions about negative and positive consequences and structured questions about coping strategies. Open-ended data were analysed with content analysis. Potential relations between use of coping strategies and reports of consequences were explored by percentages of individuals reporting certain strategies and certain consequences.

Results: A majority reported negative and positive cancer-related consequences three and four years after diagnosis and the consequences are almost the same as those reported two years after diagnosis. Reports of a more positive view of life are related to having used the strategies fighting spirit, minimising, and seeking information, whereas, reports of negative concerns are related to not having used these strategies. Reports of bodily concerns are related to distraction, whereas, reports of a more positive view of life are related to not having used distraction.
Conclusion: Concomitant negative and positive cancer-related consequences appear stable over time in the extended phase of survival and dialectical forces of negative and positive, distress and growth often go hand-in-hand after a trauma such as cancer during adolescence.

AGREEMENT AND DISAGREEMENT OF CANCER EXPERIENCE IN ADOLESCENT SURVIVORS AND THEIR MOTHERS
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Purpose: To examine agreement or disagreement of cancer experience in adolescent survivors and their mothers: (1) Posttraumatic stress symptoms (PTSS) and posttraumatic growth (PTG); (2) Appraisal of treatment intensity, life-threat and mental pressure.

Method: Participants were 43 cancer survivors (over 16 years, 20 males, 23 females) and 43 survivors of mothers at 7 hospitals. Self-reported questionnaire is consisted of the UCLA PTSD index. PTSSDI (Pynoos et al., 1998), PTG inventory-Japanese version: PTGI-J (Takau et al., 2007). Subjective appraisal of the intensity of cancer treatment scale and the life threatening scale (Stuber et al., 2004): Mental pressure level at early time of hospitalization and at time for answering questionnaires (Original 7 point Likert scale).

Results: The mean of PTSSDI total scores was higher in the male survivors (39.1), their mothers (ptsdi M = 8.1, SD = 9.7; ptgi = 59.5, SD = 23.4) and their mothers (ptsdi M = 10.2, SD = 8.8; ptgi M = 62.3, SD = 22.1). Female survivors (ptsdi M = 10.4, SD = 10.9; ptgi M = 58.6, SD = 19.8) and their mothers (ptsdi M = 12.1, SD = 12.1; ptgi M = 61.6, SD = 20.9). Paired t-test found no significant difference for PTSSDI and PTGI total scores among them. But t-test found it for subjective appraisal of treatment intensity and feeling the mental pressure level early in hospitalization between male/female survivors and their mothers (M > m/fS). PTSS was found in male survivors (30%), their mothers (50%) female survivors (57%) and their mothers (65%). The frequency of PTSS was in same order in all groups: 1.Re-experiencing; 2.Increased arousal and 3.Avoidance. Only each male/female survivor and two mothers exceeded the clinical cutoff on the PTSDI. It is remarkable that the female survivor and her mother concurrently did it.

Conclusion: A few survivors and parents showed the score suggested a clinical range of PTSD. But concurrently a survivor and her mother showed it. Further study on concurrence of PTSD is expected. This study suggests below: First, mothers percept the treatment for her child severer than he/she does. Second, early in hospitalization Mothers feels more mental pressure than her child. Therefore this indicates when a child is diagnosed with cancer, mothers may be first targets of mental support.

CONNECTING ON SOCIAL NETWORKS IMPROVES PATIENT AND CAREGIVER QUALITY OF LIFE
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Purpose: The purpose of the study was to determine if using an online social network to stay connected to family and friends was beneficial for patients and caregivers during a significant health challenge such as cancer.

Method: A survey of more than 4,000 people who used a patient-focused social network was conducted.

Results: Results show that patients, caregivers and their support community benefited from sharing news and supportive messages online. Highlights of the survey: 91% of patients agreed that it helped make their health journey easier, 88% of patients said it positively impacted their healing process and 94% of family/friends said it had a positive impact on the entire support community.

Conclusion: On average, a patient using a health-focused social network to stay connected to loved ones has 145 registered viewers checking in to read health updates and post messages of support. For someone in a hospital bed or undergoing treatment, it would be physically impossible to get this kind of support in person. Patient-focused social networks have a real impact on health. Sharing news and receiving emotional support online positively impacts a patient and caregiver’s health journey. Families can feel supported and uplifted by their loved ones regardless of time zones, area codes and visiting hours. User testimonials support this conclusion: Hospitals everywhere should be recommending [this patient-focused social network] as a way for the family to cope and update all those who want to share their sentiments and support and when she was first diagnosed, and after surgery, chemo, scan, etc. I would spend the rest of the day on the phone with family, church, friends, etc. Finally I realized that I could put it on [a patient-focused social network] and say it once for everyone . . . it gave me much more time to focus on my daughter’s health.

PS012

PSYCHOLOGICAL ISSUES OF PEDIATRIC PATIENTS UNDERGOING CHEMOTHERAPY: THE INDIAN PERSPECTIVE
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Purpose: To examine the psychological and social issues of children above 10 years of ages undergoing Chemotherapy in India in a private healthcare setting.

Method: This study was conducted at the Max Cancer Centre of Max Healthcare, New Delhi, India. An attempt has been made to present an analysis of the psychological issues of these children during the ongoing chemotherapy cycles. The sample comprised of 50 participants above (10 years) the research was based on observation and semi-structured interviews were conducted on both the participants as well as their parents in order to obtain a comprehensive overview of the child’s behavior.

Results: Based on the reports by parents, the important themes that emerged were the frequent mood swings experienced by the participants (n = 25 out of the sample; 50%), distress (n = 38 out of 50; 76%) in terms of anxiety, pain as well as disturbances in sleep while undergoing Chemotherapy. The participants reported of low satisfaction with their body image (n = 40 out of N = 50; 80%) and feelings of boredom. It was also found that there was a sharp decline in the quality of life of the participants as well as their parents. Another important highlight of the research were the experiences of social isolation by the participants.

Conclusion: Based on these results it was concluded that children with cancer while undergoing chemotherapy exhibit depressive symptoms, low quality of life, denial and adjustment issues both with their illness and the environment. Additionally, their view of their body image was negative which conceivably resulted in low self-esteem. However, slight differences existed perhaps because of the differences in the age, the conditioning of the participants as well as the stigmatization of the role of a Mental Health Professional.
population, are immigrants. Migration is defined as a risk factor to health due to high biopsychosocial vulnerability. For years, we have experienced a considerable increase in cancer patients belonging to other countries. As our work has been developing, we have had identified specific requirements by children with cancer and their families. Finally we have developed a specific protocol for a biopsychosocial intervention.

**Method:** In this study we compare clinical, psychological and social variables between two immigrant groups with cancer attending in our hospital between 1995–2005 (n = 90) and 2005–2010 (n = 114), after a property biopsychosocial protocol was established in our hospital.

**Results:** The results showed an increasing children cancer immigrant population phenomenon (p = .001). Immigrants from Latin America (Ecuador) were predominant however immigrants from Morocco increased significantly (p = .050). We also found significant differences in medical variables such as number of patient diagnosed with Acute Lymphoblastic Leukemia (p = .032), disease status at arriving (p = .034), and psychosocial variables as adaptation (p = .012), members of family moved with the patient (p = .023), amount of information received (p = .002), and emotional support to the family (p = .004).

**Conclusion:** As a conclusion we can say that a tailored biopsychosocial protocol is feasible with a positive impact in most of the measurements studied. However, even we have had good results, there is so much to keep working for to optimize children cancer care in this vulnerable population.

**PS017**

**GRIEF IS NO LONGER A LONELY PLACE...RICH FEEDBACK FROM REDKITE BEREAVED PARENT TELEGROUP PILOTS DECEMBER 2010 - MARCH 2011**

**Linda Brown**

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**Purpose:** The goals of the pilot telegroups were: To fill a gap in support services to a historically "difficult to reach" target group of bereaved parents, to normalize and validate bereaved parents’ experiences, to reduce their sense of isolation, assist in the development of coping strategies and in the recognition of strengths and skills already present in participants.

**Method:** A review of the relevant literature as well as the Redkite 2003 parent focus groups identifying gaps in support services to bereaved parents provided impetus for the extension of Redkite’s already successful telegroup model of mutual aid support to bereaved parents. Structural details of the model will be outlined for practitioners.

**Results:** Qualitative feedback about the value of telegroup for bereaved parents will be presented in the form of the rich parent voices taken from the evaluation survey participants completed at the end of their formal sessions. Participants all outlined that the goals of the telegroup had been achieved for them and were pleased they had now developed a new support network into the future. “Prior to the group I honestly believed I was broken and would just stay that way. Now I think part of my heart is broken but I am normal and feel like anyone would. That is a great gift.”

**Conclusion:** Redkite has cut across the geographical divide with a successful innovative intervention model providing support to a previously relatively unsupported target group within paediatric and teenage and young adult oncology. Bereaved parents found the anonymity factor of the telephone as a medium and the safe environment created and sustained by the facilitators enhanced their confidence in addressing issues they had never previously raised with others and had felt until now was taboo.

**PS018**

**A NEW MODEL OF GROUP SUPPORT FOR PARENTS OF CHILDREN WITH CANCER**

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**Purpose:** Parents of children with cancer experience psychological distress. Based on a survey regarding parental needs and preferences, we developed a drop-in group intervention led by a health professional, and an experienced parent to address parental needs. This study assessed feasibility and preliminary outcomes of this intervention.

**Method:** Parents of children who are or have been treated for cancer participated in an afternoon or evening drop-in support group. The group consisted of 8 2-hour sessions where parents could attend as frequently as they could, for guided group discussion of topics parents chose (e.g., how to manage treatment side-effects, child’s fears). Parents completed consent and information forms during the first session and pre-post-session forms at every session, to assess knowledge of disease and treatment management, community, hospital and family resources, and anxiety and social support.

**Results:** 28 parents (20 mothers) provided pre-post session data and 14 of these parents provided data more than once. More parents attended evening (62%) than afternoon sessions (38%). Once in the evening and twice in the afternoon no parents-attended the group. Reasons for not attending group sessions: child care, treatment demands, family vacation. Parents reported high levels of satisfaction in the nature, format and flexibility of group sessions. Parents reported increased knowledge of how to cope, and of community and hospital resources; a reduction in stress and anxiety and increased social support after attending the group (paired sample t27 ranged from 2.283 to 3.61; p ranged from < .020 to .001).

**Conclusion:** These preliminary outcomes suggest that the support group was accepted and perceived as beneficial by parents who attended. Parents encountered many challenges that prevented them from attending to their information and psychosocial needs. Further research is needed to maximize group parental attendance, particularly fathers, and to improve parental health care.

**PS019**

**THE DEVELOPMENT AND VALIDATION OF PAEDIATRIC DISTRESS THERMOMETER**

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**Purpose:** To develop and validate a new version of the distress thermometer for use in paediatric oncology populations, to pilot the developed tool for usability and usefulness, content and design, to compare screening tool against recognised measures and to assess the sensitivity and specificity of the new tool.

**Method:** Cross sectional questionnaire based design; patients will be assessed in a consecutive series using databases of paediatric and young adult oncology patients. Exclusion criteria: Estimated prognosis < 3 months and not able to speak or read English. The sample size is N = 108–215 per age group = 540–1075 in total. Process of tool development: A. Focus groups were held with patients (one group aged 7–12, and another aged 13–19) discussing what problems they had, and what was important for research staff to know. These issues were used to form the problem/coping list in addition. B. Field testing of tool. Five parallel developmentally sensitive versions with parent proxy thermometers were generated and piloted with patients and parents attending outpatient clinics (n = 45), with questions asked about: design, user friendliness, capturing of problems, what was missing, and the thermometers were adjusted after collation of results. C. Validation of the Screening tool. Screening tool to be validated against gold standard tools and cut off points established. The validity of the measure will be assessed by testing for associations between the draft measure and the comparator measures. Standards tests of reliability will also be applied.

**Results:** Pilot results: The age and developmentally-appropriate psycho-social screening tools were acceptable to patients and parents/careers, in terms of ease of use, design, content and accuracy of problem identification.

**Conclusion:** Field testing of tool completed. Validation to be completed and then further research to be carried out using the tool prospectively both in clinic and remotely.

**PS020**

**HOW MUCH SLEEP ARE PARENTS GETTING ON THE PEDIATRIC ONCOLOGY WARD?**

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**Purpose:** The occurrence of a major life stressor experienced simultaneously with poor sleep can be a hazardous combination. However, there is limited evidence documenting the sleep experiences of parents of children with cancer during hospitalization. This study investigated parents’ perceived sleep quantity/quality when sleeping overnight on a pediatric oncology ward and explored their suggestions for improving their sleeping environment.

**Method:** The validated St. Mary’s Hospital Sleep Questionnaire and the Depression Anxiety Stress Scale were administered to parents who had stayed overnight at Sydney Children’s Hospital for children (6–12 years) and children (13–17 years) caring for their child with cancer and parents of healthy children recruited through the out-patient immunization clinic. Regression analyses were used to identify predictors of sleep duration. Parents’ qualitative responses describing their sleep experiences/needs were explored with thematic analysis.

**Results:** Participants included 53 parents of children with cancer (response rate:74.0%) and 61 parents of healthy children (response rate:60.9%). On average, parents of children with cancer reported receiving 5.7 hours (SD = 1.8) of sleep the previous night, interrupted 4.6 times (SD = 2.0). These figures were significantly poorer than that reported by parents of healthy children, who reported an average sleep duration of 7.0 hours (SD = 1.21; t = 4.2, p < .001), with 2.0 night-time awakenings (SD = 1.37; t = 8.82, p < .001). Additionally, parents of children with cancer reported more delayed sleep onset (t = 3.5, p = .001) and poorer sleep quality [e.g. 65.4% of parents of children with cancer reported that they slept ‘badly’ compared with 21.7% of parents of healthy children (z = 2.219, p < .0001)].
Significant predictors of sleep duration included anxiety (p = 0.013) and caffeine consumption (p = 0.017). Parents attributed their poor sleep in hospital to environmental non-cancer-related factors (e.g. frequent urination) and feeling worried/restless overnight.

Conclusions: Poor sleep quality/quantity are highly prevalent and distressing for parents on the pediatric oncology ward and should be addressed by health professionals through the development of appropriate sleep interventions.

PS021
MEETING THE INFORMATION NEEDS OF GRANDPARENTS OF CHILDREN WITH CANCER
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Purpose: There is increasing recognition of the importance of the grandparent-child relationship in the family context. Grandparents can complement parental support for (well and unwell) children and can provide emotional/practical support to the patient’s parents. However, grandparenting an unwell child can place a heavy burden on older individuals and grandparents of children with cancer are at increased risk of excessive worry, depressed mood and somatic complaints. However, there is little evidence documenting the support/information needs of this population. This study aims to: a) Document the needs of approximately 60 grandparents of children with cancer; b) Use this data to inform the development of a targeted (paper and online) booklet to meet these needs; and c) Pilot-test the developed booklet.

Method: Phase 1: Grandparents completed a support/information needs questionnaire containing quantitative and qualitative measures. Phase 2: In accordance with gold-standard guidelines, findings from the questionnaires, combined with the feedback from a multidisciplinary committee and 4 consumer representatives, were used to develop a booklet to address these needs. Phase 3: The booklet will be evaluated by Phase 1 participants.

Results: Data collection is ongoing. Preliminary results suggest that grandparents have significant and specific unmet support/information needs when their grandchild is diagnosed with cancer. These, and more detailed, findings are informing the development of the booklet (Phase 2).

Conclusion: Grandparents of children with cancer have a unique set of unmet support/information needs when their grandchild is diagnosed with cancer. These, and more detailed, findings are informing the development of the booklet (Phase 2).

PS022
IS SCREENING FOR DEVELOPMENTAL AND COGNITIVE STATUS AT DIAGNOSIS FEASIBLE? FINDINGS FROM THE TRACKWELL STUDY
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Purpose: Cognitive and behavioural deficits are reported in around 40% of childhood cancer survivors. Patients who previously received CNS-directed therapies are at increased risk of developing neurobehavioural difficulties following treatment. Recent guidelines suggest baseline assessment of neurocognitive skills at diagnosis be extended from patients with brain tumours to include patients with Leukaemia and other cancers that require CNS-directed therapies. Full neuropsychological assessment at diagnosis is difficult to implement and highly resource intensive. This study aims to assess the feasibility of implementing a baseline neurobehavioural screening battery at diagnosis.

Method: Fifty-nine newly diagnosed patients (mean age = 8.0 years; range 6 months-16 years) and 49 controls (mean age = 10.6 years; range 3-16 years) were assessed using the Trackwell Neurobehavioural Screen, which includes measures evaluating the developmental, cognitive, academic, behavioural and emotional, and psychosocial status of children and their families. The feasibility of implementing the Trackwell Screen at diagnosis was assessed using Slade and colleagues (1999) feasibility criteria, which include the domains of: brevity; simplicity; relevance; acceptance; and value.

Results: Patients were seen soon after diagnosis with paediatric cancer (mean = 5.17 weeks; range 0.71-13.15 weeks, SD 3.21). Eighty-seven percent of children completed the assessment within 1 hour, and the majority rated it as acceptable. As hypothesised, cognitive and academic performance of patients did not differ from the healthy control group. Patients reported more emotional/behavioural difficulties, but all mean values were within a normal range. The Trackwell Screen provided significant additional information on developmental and neurobehavioural status compared to an audit of medical record documentation.

Conclusion: The Trackwell Screening Tool was acceptable and relevant to patients and clinicians, and provided significant additional information not routinely recorded by health care providers. The results indicate that it is feasible to consider implementing a neurobehavioural screen at diagnosis. Implications for routine baseline assessment will be discussed.

PS023
EMOTIONAL THERAPY IN CHILDREN
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Purpose: Now the child cancer has reached a survival rate of 70% thanks to advances in medical treatments. However the side effects in children are both physically and emotionally. Along the treatment, the child with cancer is exposed to stressful procedures such as radiotherapy, chemotherapy or blood samples that are sometimes more painful than the disease itself. The pain control through no pharmacological treatments not intended to eliminate the pain but helps control it through distracting techniques, the use of imagination and relaxation and breathing training. Get children to accept the cancer disease, they are willing to fight to live a life as normal as possible despite the disease, their optimism up their defence for a better quality of life and the cure the disease, teach them the value of life to live intensely despite adversity and improve the child’s home environment.

Method: Training with specialists in child psychology and other people knowing the topic of cancer in children. Working tools: books, brochures, images, stories, all of them with a specific message to work with. Monitoring children’s emotional intelligence to work with them accordingly (Way of dealing with problems such as caring for their emotions). Pain control by no drugs treatment, reduction of fatigue, among other, to improve the quality of life of the kid.

Results: Better quality of life in children with cancer which will lead to a happier afterlife, reduce side effects of childhood cancer treatments may cause, help to reduce the stress caused by the disease as treatment and improve their social relationships possible distorted by the disease.

Conclusion: Hope to improve the emotional and physical health of children, improve the quality of life of children. For them is important the proper emotional development in childhood to survive cancer and achieve an optimum life and cope the best they can and improve the emotional health of parents and family directly affected by child cancer.

PS024
DOCTOR-PATIENT COMMUNICATION IN PAEDIATRIC ONCOLOGY UNIT FROM THE PATIENT AND PARENTS PERSPECTIVE
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Purpose: Patients-centred care has become a priority in the paediatric oncology. The literature suggests that physicians ‘interpersonal skills are critical to establishing strong, trust-based physician’s relationships that offer multiple benefits. The quality of communication is usually approached from a professional view point. The voice of the patient is painfully often absent. The study explored the patients experience and expectations of the doctor-patient communication, relationship and information giving in pediatric oncology and hematology.

Method: A survey questionnaire was constructed to determine the parents’ perspective of the doctor-patient communication. Closed-ended questions were included to evaluate doctor-patient communication within the Department, while open-ended questions were included to provide space for parents to express their needs and wishes, their preferences and priorities, their expectations and experiences and their comments.

Results: From July 2010 to March 2011 fifty-six parents completed the questionnaire. Most parents can recall how their diagnosis was disclosed, even if they remember little of the conversation that followed, and they report that physician competence in these situations is critical to establishing trust. The findings indicate that most parents relied on staff for information, but this was supplemented by learning from internet and other parents’ experiences.

Conclusion: This study provides valuables data on parents and patients needs and expectations. Most parents want a strong relationship with a physician during period of illness. The presentation will focus on the parents expectation of the doctor-patient communication, relationship and information giving in pediatric oncology and hematology.

PS025
THE ROLE OF MEDICAL CLOWNS IN A PEDIATRIC ONCOLOGY DEPARTMENT
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Purpose: Medical clowns are working in different countries from the early 1970s. They are classified as a mental health profession. The aim is to improve the emotional and physical health of children, improve the quality of life of children. For them is important the proper emotional development in childhood to survive cancer and achieve an optimum life and cope the best they can and improve the emotional health of parents and family directly affected by child cancer.
The case-based data highlights multiple roles and ethical responsibilities of social workers; and work collaboratively with their health colleagues. This research aims to shed light on the challenges for parents and doctors through the insights of the social worker who hears both sides of the communication process.

**Method:** We use case studies about social workers’ experiences of assisting parents following communication with specialists. This data is drawn from a qualitative research project examining and mapping ethical issues experienced by allied health practitioners in everyday paediatric practice. In Departmental interviews with 6 social workers working in a large paediatric hospital oncology department were analysed using phenomenological methodology.

**Results:** The case-based data highlights multiple roles and ethical responsibilities of social workers to incorporate and balance the specific emotional and psychosocial needs of the child; the particular understanding, interpretations and circumstances of the child’s parents; and the social workers’ duty to collaborate and work with the health team and health system. Through these roles, we identify many factors contributing to discrepancies between information the doctor intended to convey and information heard and interpreted by families.

**Conclusion:** Social workers are in a unique position to have insight into both the doctor’s intentions and the family’s perceptions of critical communications. Through these insights they are able to assist both doctors and parents address the challenges inherent in communication in the emotionally charged paediatric oncology environment.

**PS026**

**WHAT IS THE DOCTOR SAYING? WHAT ARE THE PARENTS HEARING? INSIGHTS FROM SOCIAL WORK CONVERSATIONS IN PAEDIATRIC ONCOLOGY**

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**Purpose:** Communication about a child’s diagnosis, treatment and prognosis in pediatric oncology is an emotional, complex and often uncertain endeavour. Irrespective of the specialist’s communication skills, parents’ understanding and interpretation of such information is influenced by multiple individual and environmental factors. Social workers play a crucial role in facilitating clear communication in the oncology setting. However, there has been little research examining how they balance their clinical roles of assisting parents to interpret and respond to diagnostic and prognostic information; support and advocate for families; and work collaboratively with their health colleagues. This research aims to shed light on the challenges for parents and doctors through the insights of the social worker who hears both sides of the communication process.

**Method:** We use case studies about social workers’ experiences of assisting parents following communication with specialists. This data is drawn from a qualitative research project examining and mapping ethical issues experienced by allied health practitioners in everyday paediatric practice. In Departmental interviews with 6 social workers working in a large paediatric hospital oncology department were analysed using phenomenological methodology.

**Results:** The case-based data highlights multiple roles and ethical responsibilities of social workers to incorporate and balance the specific emotional and psychosocial needs of the child; the particular understanding, interpretations and circumstances of the child’s parents; and the social workers’ duty to collaborate and work with the health team and health system. Through these roles, we identify many factors contributing to discrepancies between information the doctor intended to convey and information heard and interpreted by families.

**Conclusion:** Social workers are in a unique position to have insight into both the doctor’s intentions and the family’s perceptions of critical communications. Through these insights they are able to assist both doctors and parents address the challenges inherent in communication in the emotionally charged paediatric oncology environment.

**PS028**

**UNDERSTANDING ABANDONMENT OF TREATMENT: THE PARENTS’ PERSPECTIVE THROUGH A QUALITATIVE APPROACH IN EL SALVADOR**

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**Purpose:** Two hundred children are diagnosed with cancer per year in El Salvador. Although these children have access to free modern treatment at the only national pediatric hospital, in the capital, unfortunately, 15% abandon therapy prematurely each year and eventually die. Children’s lives and thousands of dollars in resources are lost due to this situation. All Quantitative research reports that social conditions such as lack of money, lack of education and distance from the cancer center are associated with abandonment of treatment in low-income countries. This qualitative study explored the influence of these and/or other factors in abandonment and how parents perceive their child’s cancer and treatment in El Salvador.

**Method:** In Department interviews with six parents who abandoned their child’s treatment were conducted by a Salvadoran pediatric oncology psychologist, using a medical anthropological approach, as parents told the story of their child’s sickness and life circumstances during the course of treatment both in the hospital and their community.

**Results:** Poverty, trust, religious convictions, emotions and effects of treatment played a role in each parent’s explanation of their actions. However, the way these elements were weighed in the context of life and treatment circumstances differed in each case. Each element did not have the same importance for every family; therefore, the interaction of these elements (not the element per se) represented the explanatory frameworks that families used to explain stopping their child’s treatment.

**Conclusion:** The implications for researching abandonment of treatment are that qualitative research is essential to explain the complex processes and relationships involved in cancer care in countries with limited resources. Understanding abandonment by focusing on how families perceive childhood cancer and treatment and how these conceptions are related to their specific living circumstances would add valuable insight to ensure the appropriate application of medical benefits to children with cancer.

**PS029**

**A DESCRIPTIVE STUDY TO ASSESS THE IMPACT OF PSYCHOSOCIAL WOERK IN CARE OF ACUTE LYMPHOBLASTIC LEUKEMIA CHILDREN FROM A PEDIATRIC CANCER UNIT OF DEVELOPING COUNTRY**

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**Purpose:** Cancer care today often provides medical treatment, but fails to address the psychological and social problems associated with illness particularly with limited resources in developing countries like India. Psychological and social problems created or exacerbated by cancer; cause additional suffering, weaken adherence to prescribed treatments, and threaten patients’ return to health. The purpose of this study is to evaluate the impact of in-house psychosocial worker on various psychosocial problems faced by caregivers of children with acute lymphoblastic Leukemia during day to day care.
Method: Study includes caregivers of 30 children (from 1.75 to 14 years of age) with acute lymphoblastic Leukemia diagnosed at B.J. Wadia Children’s Hospital from April 1, 2010 to February 28, 2011. Caregivers of children, who were on treatment at the same centre at the moment of the study, have been interviewed by structured questionnaire of 21 questions. Results: 16/30 (53.3%) caregivers had first visit with psychosocial worker within first week of diagnosis. During first visit 29/30 (96.6%) received general information about illness, treatment and its effects on life; 21/30 (70%) received emotional support; and 25/30 (83.3%) had guidance for home care. From 12/30 (40%) caregivers, who were coming from out of city, 9/12 (75%) had guidance for transport and 8/12 (66.6%) had guidance for stay in city. 16/30 (53.3%) received medical assistance of total 2,11,105 Rs (mean 7036.8 Rs); and 28/30 (93.3%) had other financial resources with the help and guidance of psychosocial worker during treatment, out of them 27/28 (96.4%) were from lower class; 5/28 (17.8%) were from upper lower class and 13/46% were from lower middle class according to modified Kuppuswami’s classification.

Conclusion: These results support the positive impact and cost effectiveness of the in-house psychosocial worker in the comprehensive care of pediatric acute lymphoblastic Leukemia children in developing country with limited resources.

PS030

PARENTING ANXIETY AND THE IMPACT OF SOCIAL SUPPORT AND COPING STRATEGY ON MOTHERS OF PEDIATRIC CANCER SURVIVORS

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Purpose: To explore the effects of coping strategy and perceived social support on parenting anxiety of mothers of children with cancer using a cross-sectional design over 8 institutions in Japan. Mothers’ risk for parenting anxiety was hypothesized to decrease as a function of using social support and logical thinking strategy more frequently, and to increase as a function of using negative affect more frequently to cope with an uncontrollable stressful event. Results: Mothers (N = 104) indicated their child’s age, gender, length of time since diagnosis, type of cancer, kinds of treatment, and their age, occupation, educational, marital and financial status. They also completed measures of parenting anxiety, coping style and perceived social support. Results: Regression analyses revealed that parenting anxiety decreased as a function of perceived social support from a husband more frequently; and increased as a function of perceived social support.

Conclusion: The findings suggest that controlling negative affect of mothers might be the first consideration in addition to reconstructing the social support network and familial support.

PS031

MUSIC AND MUSIC THERAPY’S RELEVANCE FOR PEDIATRIC CANCER PATIENTS AND THEIR FAMILIES: CONSTRUCTIVIST RESEARCH

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Purpose: This paper will present an overview of the results of a multi-site qualitative music therapy research project that was conducted across three tertiary hospitals in 2009–2010 (O’Callaghan, Baron, Barry & Dun, 2011) in Victoria, Australia. Method: A Constructivist research approach with grounded theory design was conducted. This included the clinical data-mining (Epstein, 2010) of four music therapists’ ‘practice wisdom’ and interviews with paediatric oncology patients (up to 14-years-old) and parents. A Mosaic research approach (Clark & Moss, 2001) inspired the data-collection process and the data included transcripts from focus groups (O’Callaghan, Dun, Baron & Barry, in press), research interviews, and observations of children’s musical involvement. Results: Interviews were conducted with 28 parents and 26 patients. Thematic findings included that the child’s cancer experience can be helped by: their own music usage (including through acoustic and electronic forms); their musical interactions with families, friends and others in their communities; and hospital music therapy and related programs. Therapists’ interpretations were that: music is imperative in “healthy” children’s attachment and adjustment; psychosocial and health factors affect young cancer patients’ interactions with music and therapists; and positive transformation can occur through young cancer patients’ observing musical instruments and through music therapy engagement. Conclusion: Music therapy can calm frightened children, assist during invasive diagnostic and treatment procedures, promote supportive connectedness with others, enable self-care, and inspire playful and humorous creativity associated with “normalcy” and hope. Preferred music and music therapy involvement can be a valuable supportive care modality in paediatric oncology and should be freely available.

REFERENCES


PS032

CONSUMER PERSPECTIVES ON ADOLESCENT-FRIENDLY CANCER CARE

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Purpose: Worldwide, cancer services are moving to establish new approaches to the clinical care of adolescents in an attempt to better meet their specific needs. In 2010 the Children’s Cancer Centre at The Royal Children’s Hospital Melbourne surveyed patients to gain adolescent consumer perspectives on: 1) the provision of an appropriate clinical environment, and 2) the delivery of effective supportive care.

Method: A web-based survey sought quantitative and qualitative responses from patients (12–18 yrs). Quantitative data was analysed via descriptive statistics with cross-tabulation. Qualitative data was analysed via thematic analysis. Results: Participants (n = 29) were largely positive about the quality of their healthcare experiences. However, 55% reported they had not had confidentiality explained to them, and 55% indicated there was not a member of the healthcare team with whom they felt comfortable discussing personal issues. 72% reported they would not want to talk to their consultant without their parent/s present. 34% reported dissatisfaction with a lack of age-appropriate activities in treatment locations. Many useful suggestions were provided for improving the environment and atmosphere of adolescents’ clinical experiences. 73% stated they would like to meet other adolescents with cancer while in hospital and that they would like an adolescent-only clinic provided within the Day Oncology Unit.

Conclusion: This data provides a good starting point for focus group exploration of identified themes and for service-improvement initiatives. Time alone in consultations and doctor-patient confidentiality are cornerstones of adolescent-friendly practice: data suggests significant effort is needed to prepare patients and practitioners to embrace these practices. Ethics approval necessitated onerous recruitment strategies, distancing consumers rather than potentially may result from discussing their experiences. An Adolescent Cancer Services Improvement Officer has been appointed to facilitate adolescent-friendly clinical initiatives and consumer consultation.

PS033

PREVALENCE OF MENTAL HEALTH PROBLEMS IN PEDIATRIC PATIENTS WITH CANCER AT SOLCA HOSPITAL IN QUITO

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Purpose: Problems in the field of physical appearance, cognitive function, and attention are evident in patients undergoing cancer treatment. In Ecuador, the prevalence of Mental Health difficulties related to chronic childhood diseases is unknown. It is important to investigate the Mental Health difficulties in order to prevent future problems by giving early, directed treatment. This study determines the prevalence of Mental Health difficulties in pediatric oncology patients from SOLCA Hospital.

Method: From May to November of 2010, 146 children between 3 and 18 years of age, treated at SOLCA Hospital participated in the study. They voluntarily accepted to answer the Strengths and Difficulties Questionnaire (SDQs).

Results: The prevalence was calculated by adding “Medium risk” and “High risk” patients presenting each pathology. The prevalence for any diagnosis in the Mental Health area was
55.5%. The prevalence for behavioral disorders was 43.8%, emotional disorders (anxiety and depression) 26.7%, and of hyperactivity or concentration disorders is of 15.8%. The difficulties were higher in male patients (63.8%). Most of the patients (46%) who belong to a lower social economic status had higher risk for presenting disorders.

Conclusion: The high percentage of positive cases found with this screening tool suggests that the prevalence of difficulties in the mental health area in children with cancer is higher than that found in healthy children. There was a tendency towards higher prevalence in male patients, with lower social economic conditions.

Conclusion: These interim results conclude that a CVC team in the care of pediatric oncology patients was feasible; however, a larger cohort will be required to determine its effectiveness in reducing CVC-related BSIs.

**PU003**

**PROGRAMME OF EDUCATION USING CARTOON PICTURES FOR KEY NURSES IN NORWAY IN PEDIATRIC CANCER CARE**

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Purpose: To educate nurses to teach children and young people with cancer and their family with a pedagogic programme to learn, reflect and communicate about cancer as well as educating other nurses in their clinic.

Method: 20 nurses participated in the age between: 35–60 with an experience in cancer care of 8–31 years from all 5 centers in Norway. The participants took part of a 2 days course in using the cartoon tools about cancer in paediatric care. The pictures explain blood & cancer cells, diagnoses, treatment, side effects, relapse, family communication & relations and network. An instructions DVD of short film sections explain how to use the pictures in situations of pediatric cancer care. The education programme was evaluated with a questionnaire.

Results: The nurses experienced that the programme of the cartoon pictures was the complement together with their knowledge of many years in cancer care. The DVD was a support to understand the pictures and excellent way of examples of practice use of the cartoons in different situations of cancer care.

Conclusion: Using the cartoon pictures and the DVD about pediatric cancer helped the nurses to educate themselves in new broader way and to teach patients, family, colleague and people in the network.

**PU004**

**CLINICAL TRIALS NURSE A NEW ADVENTURE**

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Purpose: Sydney Children’s Hospital is one of two major paediatric teaching Hospitals within the Sydney metropolitan region. With the ever increasing and expanding role of clinical trials especially phase one and two studies, a clinical trials nurse was employed last July. The role of clinical trials nurse was to facilitate the coordination and the implementation of phase one and two studies. This poster will examine the role and practice.

Method: A retrospective analysis of the year’s activities of the Clinical Trial’s Nursing position was undertaken, review of the role and what actually was accomplished in establishing the Clinical Trials Nurse position.

Results: The role encompassed predominantly phase one and two studies. However due to the low number of eligible patients and the difficulty to recruit patients for studies the role has incorporated other aspects of a Clinical Research Assistants nature. Such as Education of the nursing staff, Case reporting of studies, writing of a guideline/policy for a new treatment and also updating of an existing database.

Conclusion: The role is a new initiative for the hospital so it is only just being established and the need is evolving as new studies are being opened and closed. The phase one and two studies are a new field of practice for our hospital and their implications. With any new fields of practice it always a challenge in identifying and the willingness for potential study recruits in these types of study.

**PU005**

**CASE REPORT OF INVERTED (FLIPPED) INFUSAPORTS IN A PAEDIATRIC ONCOLOGY-HAEMATOLOGY POPULATION TREATED IN A GENERAL HOSPITAL**

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Purpose: To present a case report of several inverted (flipped) Infusports in a paediatric oncology-haematology population treated in a general hospital over a 5 year period.

Method: A poster will be used to provide information regarding the cases of the inverted Infusports, treatment to remedy the problem and the long term outcomes.

**PU001**

**TAKING THE ‘KOALA’ APPROACH: A PEDIATRIC HEMATOLOGY/ONCOLOGY EDUCATION PROGRAM FOR EMERGENCY CENTER NURSES**

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Purpose: Caring for pediatric cancer patients in tertiary hospital emergency centers (EC) can prove challenging. Through education and support, EC nurses were able to improve the delivery of care to pediatric patients. The purpose of the educational program was to prepare EC nurses in prompt problem recognition and opportunities to facilitate care of pediatric hematology and oncology patients in acute situations.

Method: A two-part educational program was developed and implemented in July 2009 with a pilot group of 5 EC RNs. A weeklong program consisting of one full day of didactic content and four days of intensive clinical experience in the outpatient and inpatient pediatric setting was implemented. Didactic content included pediatric specific drugs and dosages, assessment of infections, pain, respiratory distress, and anaphylaxis, as well as family-centered care. Clinical immersion included outpatient pediatric experience, becoming familiar with pediatric intravenous starts, and accessing port-a-caths. Additional time was spent in the pediatric inpatient setting participating in charge nurse report, patient rounds, and direct care.

Results: As a result of this educational program, the EC RNs are now better prepared with new knowledge and skills to deliver care not only promptly and safely, but also independently. This approach has increased trust, communication, and collaboration between the EC and pediatric staff. Four additional groups of RNs (N = 15) have attended the educational program.

Conclusion: Pediatric hematology/oncology patients may require expedited and highly specialized nursing care in the EC. Registered nurses in the EC frequently do not have an adequate comfort level for pediatric hematology/oncology issues. An educational program that contains mentored experience and real-life clinical content and opportunities to problem solve was developed to facilitate quality and safe care to pediatric patients in the EC. This program can be a model of a “koala program” to improve family satisfaction and EC outcomes for pediatric patients anywhere.

**Pu152**

**512 SIOP ABSTRACTS**

**Clinical Immersion for Trainees in Paediatric Hematology/Oncology**

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Purpose: Treatment for most children with cancer includes the use of a central venous catheter (CVC). CVCs provide reliable venous access for delivery of chemotherapy and supportive care. This advantage is mitigated by an increased risk of bloodstream infections (BSIs). Despite the ubiquitous use of CVCs, few prospective studies have been conducted to address infection prevention strategies for pediatric oncology patients. The primary aim of this prospective randomized pilot study was to evaluate the feasibility of implementing a CVC registered nurse (RN) team and its effectiveness in reducing CVC-related BSIs compared to standard care.

Method: The study took place on two inpatient oncology units in an urban tertiary care children’s hospital. In the initial six-month study period, there was a total of 26 patients (95 admissions) on the experimental unit (EU) and 21 (60 admissions) on the control unit (CU) with a CVC. The experimental intervention included daily application of the CVC blood draw bundle procedure according to institutional policy and national standards performed by a CVC RN team (EU). Standard CVC care included daily performance of the same procedure by the assigned bedside RN (CU). The primary outcome was CVC-related bloodstream infection (BSI). Secondary analyses included investigation of categorical and continuous variables to determine the distribution, incidence of BSIs and to examine risk factors related to CVC-related BSIs.

Results: There were two CVC-related BSIs in 682 catheter days in the EU group, 2.94/1000 catheter days versus three CVC-related BSIs/900 catheter days in the CU group, 3.33/1000 catheter days; P = 0.63. Selected risk factors were not significantly associated with the development of a CVC-related BSI.
Results: As this is a report of several cases from a small centre there will be no results however this will bring to the fore an under documented central venous access device complication.

Conclusion: The aim of reporting these cases is to bring this topic to the fore in that other centres will start reporting and documenting cases of inverted (flipped) Infusaports resulting in research and published papers.

PL006

STEM CELL APERHEISIS AND -REINFUSION, AN EXPLORATORY PILOT SURVEY OF EXPERIENCES OF PARENTS

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Purpose: To explore the experiences with information, logistics and the emotions of parents whose children have dealt with an autologous stem cell apheresis and -reinfusion in the Erasmus MC - Sophia Children’s Hospital, in order to improve care and support during future procedures.

Method: Semi-structured interviews were chosen as approach. Participants included seven parents whose children have dealt with an autologous stem cell apheresis and -reinfusion. Also four professionals from different Dutch childhood oncology centers were interviewed.

The project includes a literature survey.

Results: In the literature is found that continuity can be improved by optimal communication between the professionals and by using a clinical pathway. Information must be adapted to the families and the situation of the child.

In the literature is found that continuity can be improved by optimal communication between the professionals and by using a clinical pathway. Information must be adapted to the families and the situation of the child.

Conclusion: Parents would benefit from more information about the stem cell reinfusion. A brochure for autologous stem cell reinfusion in children was available.

PL007

COMPLYING WITH PROFESSIONAL STANDARDS OF PRACTICE IN THE ONCOLOGY THEATRE AND RECOVERY UNIT

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Purpose: The Oncology Day Care Unit (ODCU) at the Royal Children’s Hospital forms part of the Queensland Children’s Cancer Centre (QCCC). The ODCU operates both outpatient clinics and a day treatment facility. The ODCU employs a core team of Oncology nursing staff comprised of Clinical Practice Facilitator (CPF), Registered Nurses and an Enrolled Nurse.

The day treatment facility provides day chemotherapy/treatment (including planned admissions), an Operating Theatre and Recovery Service, and facility for Emergency unplanned admissions. This paper will provide an overview of the steps taken to ensure the QCCC Operating Theatre and Recovery Service met the ACORN Competency Standards for perioperative nurses.

Method: At an organization level, it was identified that staff in the ODCU whilst having informal education, had not completed formal education and assessment processes (i.e. Objective Strategic Competency Assessment, OSCA). In order for nurses to receive appropriate levels of education and be assessed as demonstrating adequate application of knowledge in practice, the following steps were taken: Collaboration between Oncology and Perioperative Services (including Nurse Unit Managers, Nurse Educators, and CPFs), gap analysis and development of a education plan, development of an education resource, training and assessment of Oncology CPF, plan developed to allow for rostered clinical time in perioperative services, back filled by CPF, progression of staff through education resource with provision of backfill by CPF, moderation by perioperative Nurse Educator of Oncology CPF performing assessments of ODCU nursing staff and assessments by Oncology CPF of ODCU Nursing staff once education resource completed and completion of clinical time in perioperative services.

Results: Staff progression through this program is ongoing. This paper will provide a summary of the outcomes and achievements of this education program to date.

Conclusion: The implementation of this education program aims to ensure that patients receive the highest quality nursing care, achieved by a workforce which complies with professional standards of practice.

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PL008

NURSING CARE AND ITS EFFECTS ON THE REDUCTION OF INFECTIOUS COMPLICATIONS AFTER AUTOLOGOUS TRANSPLANTATION

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Purpose: In Spain, only 10% to 20% of children and adolescents that have been diagnosed and treated for cancer will require to restore their modular function through hematopoetic stem cell transplantation. Hematopoetic reconstitution time varies depending on the type of transplant performed, with an average of 2-6 weeks, when the increased susceptibility of developing infections is a consequence of prolonged and profound immunosuppression resulting from the conditioning regimen administered. It is very important to have a highly qualified nursing staff to reduce the incidence of infections during the phases of the transplant process.

Our unit of Pediatric Hematology and Oncology was accredited in 2008 for conducting autologous hematopoetic stem cell transplants. The purpose of this project is to review the cases of patients who went through autologous transplantation in our unit, in order to determine the incidence of infection during their evolution and thus evaluate the quality of nursing care provided.

Method: We reviewed 4 cases of autologous transplants performed through 2010. The diseases diagnosed were Neuroblastoma stage IV/2 cases and Burkitt Lymphoma/2 cases. Treatment used for patients conditioning regimen were Busulfan + Melphalan (2 cases) and Cyclophosphamide + Busulfan (2 cases). Nursing care to prevent exogenous infections were: protective isolation, protected environment, low microbial diet, prevention against water borne infections and contaminated objects, patient and family hygiene.

Results: The length of stay at hospital was a mean of 20,25 days. Antibiotics were used an average of 6.5 days. Two patients had mild mucositis, one other had grade IV mucositis and another didn’t have mucositis. Only one of them had low-grade fever during a day, without hemodynamic repercussions. The average recovery of neutrophils occurred by day +12.25. Conclusion: Nursing care delivered to patients during transplantation and recovery period was highly qualified.
154 SIOP ABSTRACTS

Purpose: Approximately 550 children are annually diagnosed with cancer in the Netherlands. These children are diagnosed and treated in 5 pediatric oncology centers (POCs) and 2 centers for allogenic stem cell transplantation. Treatment also takes place in secondary pediatric units (shared care). Pediatric oncology nurses (PONs) are members of multidisciplinary teams. The PONs are professionals in caring for children with cancer, undergoing or recovering from cancer treatment, and their parents. In 2014 one new National Pediatric Oncology Centre (NPOC) will be opening its doors. The reason for centralization is to improve the cure rate from ± 70% since the last 20 years up to 90% in 2025.

Method: After secondary school a university study of 4 years for the bachelor degree to become a registered nurse (RN). Subsequently 1 year education to become a RN Sick Children (RNSC). Further 1 year education in one of the POCs to become a RN pediatric oncology (RNPO). Several POCs have developed different education programs for nurses who work in shared care. After secondary school a university study of 4 years for the bachelor degree to become a RNSC at the University of Applied Sciences Utrecht (UASU). Followed by half a year at the UASU and in practice to become a RNPO.

Results: Centralization of patients improves cure rates. Centralization of education of nurses improves more knowledge and better preparation for practice which will result in improvement of nursing care. This contributes to improve the cure rate.

Conclusion: Education of RNPO will change at short notice to establish RNPSO. Education of nurses working in shared care also have to change because more children will be nursed in shared care since there will be only one NPOC.

PU001 CAN WE COUNT ON YOU ?

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Purpose: Medication errors account for approximately 1/3 of all adverse events(4). It is therefore very important that physicians and caregivers calculate the medication dose for a child correctly. To increase patient safety, we wanted to develop an e-learning course on how to calculate the correct medication dose. (4 Annual Report 2009, DSPS, National Board of Health, Denmark)

Method: A multidisciplinary team of two nurses, a pharmacist, a physician and a multimedia programmer prepared a course consisting of a series of exercises for calculating doses of medicine together with a final test. The examples were constructed from the daily drug prescriptions in the pediatric ward.

Results: The course includes model solutions, explanations of units, symbols and useful formulas, a calculator where findings apply to the results field in each exercise and a notepad for the results of the intermediate calculations. Once an exercise has been solved, the response will be evaluated and there will be feedback in terms of explanatory comments, formulas and a model solution. The structure of the course consists of 5 modules for calculations concerning: solid drugs, liquid medicines, dilutions, infusions and composite formulas and a model solution. The structure of the course consists of 5 modules for calculations concerning: solid drugs, liquid medicines, dilutions, infusions and composite tasks. In the final test there will be 2 questions from each module. The final test must be conducted annually and all answers must be correct to pass the test. 45% of the physicians and 75% of the caretakers have passed the test this year.

Conclusion: The course is implemented in the childrens ward and is mandatory for all physicians and caregivers. An evaluation of the course will decide what need to be done to raise the pass rate.

PU002 ANZCHOG NURSING POSITION STATEMENT FOR MINIMUM EDUCATION AND SAFETY IN THE ADMINISTRATION OF ANTI-CANCER THERAPY TO CHILDREN AND ADOLESCENTS WITH CANCER

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Purpose: The delivery of anti-cancer therapy to children/adolescents with cancer has unique considerations. Not only are vastly different therapies utilised in the paediatric setting; the landscape that care is provided has specific aspects that are integral to safe and effective care. Within Australia and New Zealand (ANZ) position statements were available to support minimum education and safety standards for administering anticancer therapy within the adult oncology setting but there is no specific information related to paediatrics. The Australian and New Zealand Childhood Haematology and Oncology Group’s (ANZCHOG) Nurses Committee established a working group to develop a position statement that would complement documents of the Cancer Nurses Society of Australia (CNSA) to enable and support optimal care and safety for children/adolescents with cancer at both tertiary and shared care/regional health care settings.

Method: The working group comprised key representatives from each paediatric oncology centre across ANZ. Central to the development process: Identification of relevant ANZ position statements/documents, identification of the gaps within a paediatric context, identification of the core elements that are unique to paediatrics, literature review around core elements for the provision of paediatric care and development of a document that avoided duplication of current resources and highlighted key elements relevant to the paediatric setting. An implementation plan supports the development of this position statement. Launch of the position statement via the ANZCHOG website, promotion at relevant professional events and engaging department heads and nurse unit managers.

Results: This project resulted in the development of a position statement from the ANZCHOG Nurses Group that promotes minimum safety and education standards in the administration of anti-cancer therapy to children/adolescents with cancer.

Conclusion: This document will support safe practices and promote opportunities for service planning that is considerate of the needs of children/adolescents who receive anti-cancer therapy.
ASSESSING OF PEDIATRIC ONCOLOGY NURSES ATTITUDES TOWARD DEATH AND CAREING FOR DYING CHILDREN

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Purpose: The oncology Ward in which pediatric nurses work consists of various situations where identified. Need for a standard to be developed for management of intraperitoneal ports and also chemotherapy administration via an intraperitoneal port, education plan for nursing staff to ensure competence/confidence in intraperitoneal chemotherapy and ports, development of treatment protocols and education of patient and family. In order to combat these issues two standards and an education program were developed. Information was gained from local and international adult oncology centres to develop the standards and education plan. The standards provided clear guideline for staff. The education sessions comprised of both theoretical knowledge and practical skill development.

Results: Nursing staff felt confident and competent in working with intraperitoneal infusors and chemotherapy. Staff where able to quickly identify signs of complications and the appropriate management actions required. The Patient and her family felt informed and prepared for the treatment and were able to have their questions/concerns answered appropriately.

Conclusion: The development of clear standards and interactive educational sessions resulted in the patients receiving their treatment effectively will nil complications.

HEALTH LIFTS CARDS POSTER

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Purpose: To increase awareness of long term effects of cancer treatment and provide education with the implementation of individualised health cards for patients in our long term follow up program. The purpose is to promote empowerment for self directed education and increased information regarding childhood cancer and quality of life for survivors.

Method: Individual cards are made according to each child’s treatment received, according to The children’s oncology group (C.O.G.) guidelines. These cards, along with another card showing directions through the caresearch web site are laminated and given then explained to the children and parents at their long term follow up clinic visit.

Results: A questionnaire will be implemented and given to families who have received their cards at their next clinic visit in one year to gauge the response to the cards as an educational tool.

Conclusion: The limited feedback already received is very positive with a number of children and parents appreciating the opportunity for receiving self guided information about their cancer treatment effects and the reasons for long term follow up.

IMPLEMENTATION OF AN ORAL CARE PROTOCOL IN A PEDIATRIC HEMATO-ONCOLOGY UNIT BARRIERS EXPERIENCED BY NURSES

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Purpose: Oral care is an important component of qualitative paediatric oncology care. During a 2 year period an updated evidence-based oral care protocol, translated in an algorithm, easy in use for nurses, was developed by a multidisciplinary working group and implemented in a clinical setting. This was supported by educational sessions to nurses and a leaflet for parents. Our goal was to define barriers implementing an oral care protocol by nurses in a paediatric hemato-oncology unit.

Method: Data were collected by means of semi-structured interviews. The transcripts of 11 audiotaped interviews with nurses were coded, using NVivo8 (software).

Results: Although the majority of nurses found oral care essential in nursing care, this issue was not always defined as high priority. Due to quoted lack of time oral care is one of the care procedures which is easily omitted. In those moments nurses easily fell back into routine procedures and rely on oral care practices they acquired from their senior peers. Nurses reported uneasiness with the new guidelines because of gaps in theoretical and practical knowledge. They expressed the need for continuing intensive training. Other barriers to provide oral care included lack of interdisciplinary collaboration (nurses - dentists), pain reported by the child, the physical condition of the child, lack of collaboration of parents...

Conclusion: Taking into account the results of this study, more extended educational sessions were implemented to improve adequate understanding of the new oral care guidelines. This study highlights difficulties in implementing new guidelines even if theoretical strategies for good implementation of protocols e.g. recognition of the need for clear care standards, formulation of a multidisciplinary working group, evidence-based guidelines integrated with current practices, were followed.
PU020

CHANGES IN THE CARE OF CENTRAL VENOUS CATHETERS IN CHILDREN: A REPEAT AUDIT OF CATHETER USE, COMPLICATIONS AND NURSING PRACTICE

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Purpose: Two previous audits of central venous catheter use have been undertaken in Starship between August 1998 to March 1999 and August 2005 to March 2006. Practice changes including the implementation of a needle free system did not appear to have an adverse effect on catheter related blood stream infection rates. Further practice changes, particularly the introduction of an aseptic non touch technique and the use of positive pressure valves on all PICC lines have led to a third audit.

Method: The initial audit followed 100 consecutive central venous catheter (percutaneous, PICC, tunneled cuffed and subcutaneously implanted) insertions over 11 weeks. The following audit was undertaken over a similar 11 week period and resulted in 219 catheters captured. All catheters were followed up within the clinical, shared care and home environments until removal, discharge to a non shared care hospital or the same end point of 8 months.

Results: The current audit has captured all catheters inserted over an 11 week period from August 2010 and followed up until the end point of March 31st, 2011.

Conclusion: The results will be useful to document and compare central venous catheter use, complications and completion of therapy with the original two audits within the general paediatric and paediatric haematology/oncology environments.

PU021

SHARED CARE: THE NEW ZEALAND EXPERIENCE

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Purpose: Over time the amalgamation of paediatric haematology/oncology services and the centralisation of care within New Zealand to two tertiary services has required the implementation of a management model of shared care.

Method: Care is shared between each tertiary center and the local hospitals throughout New Zealand. Integral to the implementation and success of this model is the role of the shared care nurse specialist and nursing representation at a national level on the Paediatric Oncology Steering Group.

Results: Each tertiary center has a shared care nurse specialist along with paediatric oncology link nurses set up in each of the local hospitals. The Paediatric Oncology Steering group consists of two nursing representatives.

Conclusion: This presentation will highlight from a nursing perspective the amalgamation of services and the current model of shared care in New Zealand for children within general haematology/oncology and stem cell transplant.

PU022

EDUCATIONAL SESSIONS HELP TO IMPROVE NURSES CLINICAL PRACTICES AND KNOWLEDGE FOR PORT-A-CATH (PAC) CARE IN CHILDREN WITH CANCER

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Purpose: The purpose of this study was to determine that educational programs improve knowledge of Port a Cath care for children with cancer after assessing the knowledge and practices.

Method: A total of 10 patients with PAC were admitted. Disease distribution included ALL (60%), AML (20%), RMS (20%). PAC has been in place for less than a year. Portal infection (staphylococci) was observed in six patients of whom 3 patients had their PAC removed and portal occlusion also seen in one of the patient. Assessment of clinical practices of nurses along with short quiz was done to assess their clinical knowledge about PAC handling in which, we came to know that nurses were not using proper techniques of handling Port a Cath and not integrating theoretical knowledge into practice.

Results: The purpose of this study was to determine that educational programs improve knowledge of Port a Cath care for children with cancer after assessing the knowledge and practices 5 educational session and 2 workshops were organized to emphasize on the areas of improvements. Total 65 registered nurses caring for the cancer patients attended the sessions and workshop and 90% passed post test with 80% marks.

Conclusion: Failure to use aseptic technique when accessing a central venous catheter predispose patients to infections. Catheter-related infections demanded PAC removal in our patients but their benefits argue for continued PAC use in the pediatric cancer population as it is safe and has many advantages as well. Strict indications, careful implantation technique, and adequate handling are, however, mandatory.

PU023

NURSES’ PERCEPTIONS OF THEIR INTERVENTIONS IN SYMPTOM MANAGEMENT FOR CHILDREN WITH CANCER

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Purpose: The purpose of this study is to clarify nurses’ perceptions of their interventions in symptom management for children with cancer and to contribute for revising “Nursing Care Guidelines for Children with Cancer and Their Families, 2008” (JSPON), whereas to develop the support program for nurses.

Method: Two groups of nurses who attended seminars on “Care for Children with Cancer” focused symptom management, answered the questionnaires, one group on “Nausea and Vomiting”, the other, “Stomatitis.”

Results: “Nausea and Vomiting”: Twenty-five nurses answered the questionnaire asking the degree of importance of 9 items. Most nurses pointed the most (1) prevalence and severity of nausea and vomiting, (2) report of symptom experience from children and families. In cases nurses talked with children about their wishes in symptom management, nurses felt they succeeded self-management. Nurses experienced difficulties in assessment of symptoms for infants, and giving oral medication for children undergoing BMCT “Stomatitis”: Eleven nurses answered the questionnaire asking the degree of practice of 19 items for prevention and care after stomatitis appeared. As prevention of stomatitis most nurses pointed the most (1) recommend gargarin, (2) observe the amount and quality of taking food and liquid. In most items, nursing interventions were enforced in care for stomatitis than prevention. In cases nurses talked with children and families about prevention of stomatitis and mouth care in preparation of chemotherapy treatment, nurses felt they succeeded the preventive interaction. Once stomatitis occurred, nurses intervened with explanation about cause of stomatitis, pain medication and importance of keep doing gargarin. Nurses experienced difficulties in cases after BMCT, mucosal injuries were eminent and for severe pain, oral care could not be encouraged.

Conclusion: In nurses’ perceptions about their interventions, their involvements were helpful for children and families to understand and care by themselves in symptom management, even though they often have to face difficult cases.

PU024

DIFFERENCES BETWEEN DOCTORS AND NURSES AND FUTURE ASSIGNMENTS REGARDING INTRACTABLE PAIN IN CHILDHOOD CANCER, REVIEWED BY DISCRIMINANT ANALYSIS

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Purpose: The knowledge and basis required for judging intractable pain in childhood cancer, problems faced by nurses when such pain occurs and future medical care for dealing with such pain were reviewed by discriminant analysis, based on the process by which doctors and/ or nurses judge intractable pain in childhood cancer and on the content of assignments.

Method: A questionnaire survey was carried out on 34 doctors as well as 98 clinical nurse specialists (CNS) and career nurses who are all involved in childhood cancer care. The questions concerned the selection of drugs, information for judging indications for WHO stage I to III childhood cancer, patient care, etc. Discriminant analysis was carried out by selecting 39 items related to classifying doctors and nurses out of the 97 survey items in total.

Results: The medical group succeeded self-management. Nurses experienced difficulties in assessment of symptoms for infants, and giving oral medication for children undergoing BMCT “Stomatitis”: Eleven nurses answered the questionnaire asking the degree of practice of 19 items for prevention and care after stomatitis appeared. As prevention of stomatitis most nurses pointed the most (1) recommend gargarin, (2) observe the amount and quality of taking food and liquid. In most items, nursing interventions were enforced in care for stomatitis than prevention. In cases nurses talked with children and families about prevention of stomatitis and mouth care in preparation of chemotherapy treatment, nurses felt they succeeded the preventive interaction. Once stomatitis occurred, nurses intervened with explanation about cause of stomatitis, pain medication and importance of keep doing gargarin. Nurses experienced difficulties in cases after BMCT, mucosal injuries were eminent and for severe pain, oral care could not be encouraged.

Conclusion: In nurses’ perceptions about their interventions, their involvements were helpful for children and families to understand and care by themselves in symptom management, even though they often have to face difficult cases.
related to intractable pain, using a chi-square test. Those factors that were effective for classifying doctors and nurses were then analyzed with respect to 14 items at the significance level of less than 10%. The percentage of correct predictions made by the discriminance was 81.8%.

Results: Regarding differences between doctors and nurses in terms of the discriminant analysis, the points that work positively for doctors were the first stage of drug selection (intractability judgment), the second stage of drug selection (need to select) and signs for judging pain (calm fetal movement), while those for nurses were the level of pain (the onset time) and what they find difficult in nursing care (the relation between pain and diseases, knowledge related to laboratory data). Nurses require knowledge of pain and disease in order to deal with intractability judgment, sedation, neurogenic pain, etc. It is necessary to provide a guideline for judging pain, to help create team medicine and cooperative relationships between doctors and nurses. It is also necessary to start a joint conference that takes advantage of each other’s specialties.

**PU 025**

GUIDELINE FOR INTRACTABLE PAIN IN CHILDHOOD CANCER

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Purpose: The objective of the present research is to investigate the need for guidelines based on investigations of intractable pain in childhood cancer, to determine the content of such guidelines.

Method: Nine nurses with at least 3 years nursing experience in pediatric cancer patient care were included in a semi-structured interview survey using case examples of pediatric and adolescent patients to determine the appropriate content for the guidelines. Transcripts of the interviews were prepared and analyzed.

Results: Assessment of pain is made difficult by characteristic conditions related to growth and development, such as [crying] in childhood and [not complaining] in puberty. The target of pain relief is to obtain lack of interference by pain with daily life activities, which corresponds to face scales of [0–1] in childhood and [0–2] in puberty. The shortest time for assessment of effects after drug administration was [15–30 min] after administration for non-opioid analgesics, [10–30 min] for weak opioid analgesics, and [immediately] for opioid analgesics, while the longest time was 3 hours, indicating the wide range of effects of follow-up. Psychosocial care for patients in pain included [strocking], [being present nearby], and the like. Aspects of nursing care requiring improvement included knowledge of the pathophysiology of pain, palliative care, drug effects and drug usage, correct determination of rescue doses, handling of the family, communication with the patient/family, total care, and team conferences. In the case of physicians, required improvements include pain control, communication with the patient/family, information sharing, and strengthening of collaboration through team conferences.

Conclusion: For alleviation of intractable pain in childhood cancer, a guideline is required. Also necessary is the strengthening of the team conference system.

**PU 026**

INTRODUCTION OF THE USE OF MEDICATION BAGS IN HEMATO-Oncology DEPARTMENT

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Purpose: Corticosteroids are an integral component of therapy for acute lymphoblastic leukemia and neuroblastoma. In current protocols, hydrocortisone and dexamethasone are utilized in selected phases of the treatment. While corticosteroids are highly effective antiinflammatory agents, there are considerable toxicities associated with their use. On discharge, children are often put on a tapering schedule for corticosteroids over several days. A well-designed and appropriate tapering schedule, related to the total dose, duration of therapy, and type of corticosteroid used is necessary. To optimize the effect and minimize the risk of adverse events, a medication bag for corticosteroids supporting optimal compliance and a safe and clear tapering of corticosteroids is implemented.

Method: The plastic bag with written paper scheme of corticosteroids is replaced by a paper bag (doctor’s-bag-like) with a distinguished drawing on one side. On the other side, there is room for a sticker specifying following items: patient identification (data), generic name of corticosteroid, day, date, frequency, hour and dose. These data are checked and signed by the responsible pharmacist, stamped, and fixed on the blank side of the bag. Because the hospital pharmacy prepares capsules of multiple dosages of corticosteroids, often combination of different dosages are needed to obtain the prescribed dose for the patient. The nurse inserts this correct combination of capsules and double-checks for the correct dosage and frequency and advices to patient about use and storage of medication.

Results: The goal of the medication bag is to promote safety and compliance, to give advice/education of correct drug use, to inform about possible side effects and to enhance a better patient-pharmacist communication. Conclusion: By introducing the corticosteroid tapering medication bag, optimal compliance, information, and education for patients is aimed for. The drawing and design of the bag makes a pleasant difference for children. The project might be expanded for other medication.

**PU 027**

A STUDY ON CHILDREN RETURNING TO THEIR ORIGINAL SCHOOLS ON THEIR RELEASE FROM HOSPITAL AFTER TREATMENT FOR CANCER

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Purpose: A long-term hospital stay for treatment for chemotherapy, radiotherapy, and surgery is a surgical remedy 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.

Method: 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 months on the average (SD 0.78 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.

Conclusion: 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.

**PU 028**

DIFFERENCES IN SUPPORTIVE CARE IN PEDIATRIC ONCOLOGY CENTERS AND ITS EFFECT ON SHARED CARE

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Purpose: Approximately 550 children are annually diagnosed with cancer in the Netherlands. These children are diagnosed and treated in 5 pediatric oncology centers (POC) and 2 centers for allogenic stem cell transplantation. Treatment also takes place in secondary pediatric units (shared care): 70% of all children with cancer can be cured. However, cancer treatment for children can cause unwanted side effects and other problems during and after treatment. Supportive care improves the patient’s physical, psychological, social, and spiritual quality of life. Supportive care is given to children of all ages, including infants, children, adolescents and young adults.

Method: Reviewing current practice of nursing interventions in supportive care in POCs. Results: The Nursing Discipline Group of the Dutch Childhood Oncology Group surveyed practice in the POCs. Questionnaires designed to review (nursing) interventions in supportive care were distributed to nurses in the ward, day-care and outpatient-clinic in each POC. With process analysing schedule, the results were analysed. There was a 100% return rate from the nurses. The results showed an inconsistent approach of the (nursing) interventions in supportive care in POCs.

Conclusion: It is recognized there is a need for adequately provided appropriate (nursing) interventions in supportive care in POCs. This study highlights the inconsistencies in practice today in POCs which is very difficult for the child and his parents and the nurses also, in the POCs as well as in shared care.

**PV 001**

UTILIZING COMMERCIALvALLY AVAILABLE SOFTWARE TO DEVELOP CUSTOMIZED ROADMAPS FOR PATIENTS AND THEIR CAREGIVERS
Purpose: To provide a validated, flexible, easy to read summary of treatment information to patients and their families dealing with a cancer diagnosis.

Method: A working group was formed to drive the project. A literature review, national and international benchmarking was undertaken. The use of a commercially available task and scheduling software was utilized. Document controlled templates are being developed for inputting data for all 74 current protocols available. Multi-disciplinary input and validation of roadmaps will occur to ensure accuracy and integrity of each document. Standard operating procedures created govern the use of roadmaps and secure document control. A pilot of eight patients has been conducted since late 2010 to test the software.

Results: The literature review and benchmarking showed wide variation in the complexity of the information shared and how it is provided. The pilot test indicates the software and programmed templates are easily modified to generate individual treatment summaries. The final product is in a simple calendar format for families. Input and validation of each roadmap began in February 2011 and will be complete by June 2011 to enable clinical rollout thereafter.

Conclusion: This initiative was a main priority identified in a paper to the Victorian Minister of Health from the Children’s Cancer Centre Parent’s Advisory Group for improving supportive care services. The implications for practice include improved communication and planning of treatment, greater levels of consumer participation, improved adherence to clinical trials and reduced levels of stress and anxiety for patients and their families.

Conclusion: Despite encouraging preliminary results further studies and larger numbers of patients are warranted to investigate the health benefits of single port minimally invasive surgical approach in neuroblastoma.
5.7 years (0.5–14.1 years). Two girls presented with virilizing features, one with premature menarche and one with premature thelarche. Pre-operative hormonal profiles were deranged in all but 1 patient; while tumor markers were normal in all but 1 patient with borderline elevation of CA-125. Pre-operative imaging included ultrasonography, CT and MRI scans. All patients underwent laparotomy. Two had diagnostic laparoscopy in addition. The diagnosis of malignant ovarian stromal tumor was established at intra-operative frozen sections in all but 1 patient. Complete salpingo-oophorectomy was then performed, together with iliac nodes sampling and infra-colic omentectomy. The last patient had her initial surgery performed in another institution and underwent re-look laparotomy and complete salpingo-oophorectomy. Two patients had juvenile granulosa cell tumors, two had Sertoli-Leydig cell tumors and 1 had a rare variant of ovarian stromal tumors. The median follow-up period was 52.2 months (3–85 months). Clinical and biochemical evidence of hormonal derangements resolved post-operatively. None of the patients received adjuvant chemotherapy and all were alive and disease-free at their last follow-up. Conclusion: Clinical features of hormonal derangements can provide a window for early diagnosis of ovarian stromal tumors. Given the excellent prognosis of these tumors, less aggressive surgery or minimally-invasive surgery may be re-evaluated.

PW005
SOLID TUMORS IN INFANCY - INSTITUTIONAL EXPERIENCE
Sushmita Bhatnagar
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Purpose: Solid tumors in the infantile period are a distinctive entity in terms of incidence, pathophysiology and outcome as compared to their counterparts in children. In order to better define the characteristics of these tumors, the author reviewed the 13 year institutional experience.

Method: Retrospective case cohort study was performed by retrieving data between January 1996 and December 2009. Demographic, clinical and surgical details, treatment protocols and outcome of children less than 1 year of age were reviewed.

Results: Of a total 372 tumors managed by the surgical/oncology departments over 13 years, there were 59 infants (15.86%) with M:F 1:2.1, ages ranging from day 1 of life to 12 months, mean age of 5.18 months. 8 were neonates, 5 antenatally diagnosed, confirmed postnatally. 55 of the infants had tumors which were > 5 cm in size and none of these were diagnosed antenataly. All except 2, had palpable lump, 54%(32) had a rapid progression of the lesion while under surveillance. Tumors markers in 76% and pre-operative biopsy in 39% were diagnostic. Neuroblastoma was the commonest tumor (22%), Hepatoblastoma(20.3%). Malignant germ cell tumors(20.3%), soft tissue sarcomas(11.9%) and others(8.5%).

Saging information for 39(66%) showed Stage I=9, Stage II=2, Stage III=5, Stage IV=5 and Stage IVa=n=1. 19(32%) babies received neoadjuvant and adjuvant chemotherapy. 45% of the children underwent surgical removal of the tumor which of gross total resection could be achieved in just 34.5%. Of the overall mortality of 31%, chemotherapy related deaths occurred in 25%. 34.5% were non-compliant and an equal number 34.5% are alive, well and tumor free on 2-12 years follow-up.

Conclusion: A much higher incidence (15.8%) of infantile tumors as compared to literature(2%) is alarming. It is thus imperative to improve on treatment failures from deaths and non-compliance amounting to 65.5%. Chemotherapy related deaths must be minimized by specific measures and protocols for infants.

PW006
FUNCTIONAL ADRENOCORTICAL TUMORS
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Purpose: Majority of the adrenal tumors are benign and hormonally inactive. Functional tumors are associated with significant morbidity and mortality. A short series with successful outcome of functional Adrenocortical tumors with unusual presentations is analyzed.

Method: Retrospective case cohort study from June 2008 till August 2010 included patients with adrenal masses. Demographic details were collected from records and patients were clinically evaluated on follow up. Investigations included hormonal assays, ultrasound/CT abdomen. All underwent complete surgical excision followed by multiple biochemicals and histopathology. Follow up ranged from 8–38 months.

Results: 3 patients with ages ranging from 4 to 9 years (Mean age - 7.5 yrs), & M: F = 1:2. Most common mode of presentation was Cushing’s syndrome (23/66%) as only one presented with virilisation. 1/3 had clinically palpable lump. Both of the Cushing’s patients had hypertension. Elevated DHEA, Testosterone in one and elevated Cortisol levels in other two was noted. The mass was sited in the left adrenal in all 3 children with variable sizes ranging from 3 to 9 cms. Stage 1 - 33.3% and Stage 2-66.6%. Complete surgical resection was done in all, adjuvant chemotherapy was not given. 2 were Adrenal carcinomas(1 Virilising and 1 Cushing’s syndrome), and one was adrenal adenoma (Cushing’s syndrome). Followup revealed complete resolution of symptoms, significant weight loss, control of hypertension and normalization of Cortisol levels without any recurrence.

Conclusion: Pediatric adrenocortical tumors are as such very rare, rarer still is primary presentation with Cushing’s syndrome, wherein virilisation is the most common mode of presentation. Most series over many years have shown small number of tumors, with survival rates upto 90% for stage 1, decreasing to 40% for Stage 2. Our short series depicts successful outcome and tumor free survival in all children.
Purpose: The educational need of paediatric surgeons, all the professionals related with child
cancer care, and to contribute to supplement the programmes for the studies of medicine
and nurse encouraged us to carry out this multimedia together with 25 collaborators of all the
branches of multidisciplinary team.
Method: For more than 20 years, we have worked as surgeons trained in oncologic surgery
and paediatric oncology within a multidisciplinary team to care about children with cancer.
That important experience has allowed us to know the results of the National Cancer Program
in Cuba whose figures of survival have gradually increased for the last 40 years to more than
70%. The government supports all the expensive diagnosis and treatment programmes
(chemotherapy, radiotherapy and surgery, among others) at highest level of rigor and
efficiency. PubMed searches have allowed us to know the results of the Multimedia “Paediatric Surgical Oncology” consists of five great chapters:
1. Women and Children’s Hospital, Department of Paediatric Surgery, Adelaide, Australia
2. Women’s and Children’s Hospital, Department of Surgery, Adelaide, Australia

Purpose: To develop adequate strategy of diagnostics and treatment of children papillary
thyroid carcinoma (PTC).
Method: 258 children (4–16 years) from 1971 to 2009 have been included in research. In 166
children (from 1971 to 1999): metastases to limbonode or lateral trigon of the neck were
found out 104 (62.7%), in an average line in 74 (44.6%). Metastases in lungs have been found
initially in 14 (8.4%) and during dynamic supervision already in 40 (24.1%) patients.
92 children (from 1999 to 2009): metastases to limbonode or lateral trigon of the neck were
found out 109 (84%), in an average line in 109 (84%). Metastases in lungs have been
revealed initially in 7 (8%) and during dynamic supervision already in 32 (35%) patients.
Results: Among primary patients till 1999, relapses PTC was 29%, and after - 3%. Decreased
level of relapses was associated with use more aggressive surgical treatment tactics of
thyreoidectomia as monofocal tumours in the size more than 1 sm. see with obligatory
removal central limph dissection, and under indication removal of other groups neck of
lymph nodes.
Conclusion: Treatment PCT have to be aggressive (Thyreoidectomia as tumor more than 1
sm. in diameter, radical operation on a lymphatic collector of a neck, radioiodotherapy,
suppressive hormonal therapy).

Purpose: Current treatment modalities for serosal surface tumours have been enhanced by
the application of intraperitoneal chemotherapy. The use of hyperthermic intraperitoneal
chemotherapy (HIPEC) was pioneered in ovarian cancers. With a propensity for serosal
surfaces, intraperitoneal cisplatin has been shown to increase overall survival when compared
to intravenous chemotherapy. In-vitro studies have clearly demonstrated the addition of
hyperthermia to cisplatin increases its kill factor by 2 logs. Furthermore, in-vitro assays show hyperthermic treatment may overcome tumour resistance. A phase 1 study is currently
underway to investigate the utility of this novel treatment (ClinicalTrials.gov Identifier: N
CT00436657).
Method: We present three children in whom, surgery and HIPEC was utilized to consolidate
their treatment. Two children presented with invasive desmoplastic small round cell tumours
(DSRCT) and the third, with recurrent mixed ledig-sertoli cell sex cord stromal tumour with
heterologous elements (MSCLC).
Results: Though follow up in these cases is short (up to 13 months), the morbidity has been
acceptable for patients and family given the grim prognosis of these diseases. Complications
of HIPEC encountered in this cohort include early transient polyuric renal impairment and
later, recurrent bowel obstruction. To date, no tumour recurrence has been detected following
HIPEC.

Purpose: A phase 1 study is currently
Method: To treat tumour resistance with hyperthermic treatment may overcome tumour resistance. A phase 1 study is currently
Results: The Multimedia “Paediatric Surgical Oncology” consists of five great chapters:
1. Royal Hospital For Sick Children, Haemato-Oncology, Glasgow, United Kingdom
2. Royal Hospital For Sick Children, Haemato-Oncology, Glasgow, United Kingdom

Purpose: Multiple CVADs can be necessary in the treatment of children with cancer and
resultant thrombosis or stenosis makes insertion difficult. MR venography (MRV) is used to
investigate venous patency prior to insertion and guide surgical placement. We reviewed the
use of MRV in patients who required a CVAD after at least 2 previous procedures.
Method: Retrospective analysis of patients on CVAD database at our haeno-onc unit, who had
CVADs inserted between January 2000–2010. We identified children age 10 years and
under (as on 01 Jan 2010) who had 3 or more previous CVADs. From these we selected
those who had MRV performed. The results of the MRVs were analysed with regards to
patency of the veins and number of previous procedures and compared to the success of line
placement.
Results: 21 MRVs were performed prior to insertion of either 3rd or subsequent CVAD. Only
2 of the 6 MRVs undertaken before 3rd CVAD insertion were abnormal. However, all of the
15 done prior to subsequent CVAD insertions were abnormal. Hence, 17 of the 21 MRVs
showed vessel abnormalities but all subsequent CVAD placements were successful. MRVs were
thought to have guided surgeons with insertion in 20 of the 21 CVADs with only one
placed into a vessel which was said to be non patent on imaging but found to be patent at
surgery.
Conclusion: MRV is useful for assessing venous patency and can guide surgeons prior to 3rd
or subsequent CVAD insertion. MRV may be useful in selected patients prior to even first or
second CVAD insertion, where there is anticipation of difficulty in venous access or doubt of
patency. Further research and clearer guidelines are needed to establish which patients
would benefit. However, MRVs are most likely to be useful for patients with multiple previous
CVADs or other thrombotic risk factors.
**PW014**

MINIMIZING PREMATURE LOSS OF IMPLANTABLE CENTRAL VENOUS ACCESS DEVICES - APPLYING CLINICAL PRACTICE IMPROVEMENT PROGRAM (CPPI) TOOLS

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**Purpose:** Implantable central venous access devices (ports and Hickman lines) are required for administration of chemotherapy in children with childhood malignancies. Premature loss of these devices causes pain and suffering, and delays therapy. We examined how loss of these devices within 30 days of placement can be avoided.

**Method:** We identified patients treated by the Hematology and Oncology Service, KK Women’s and Children’s Hospital for malignancies, who lost their ports or Hickman lines within 30 days of placement, between August 2008 and January 2010. There were 6 such patients. Their clinical charts were reviewed, noting in particular, diagnosis of malignancy, absolute neutrophil count (ANC) at device placement, type of device, procedural details, and indications for early device removal. A workshop comprising of an oncologist, a surgeon, an infectious disease physician, an oncology-trained nurse, and an operating room nurse manager then examine the existing workflow involved in device placement. Following principles of the Clinical Practice Improvement Program (CPPI), potential pitfalls resulting in device loss within 30 days of placement were identified.

**Results:** Devices lost within 30 days of placement were all related to local wound site complications with or without septicemia. The lack of alcohol in the existing on-table skin preparation was identified as a correctable pitfall. With effect from May 2010, the pre-operative skin preparation was changed from the pre-existing Cetrimide/Chlorhexidine and Providone Iodine solutions to Alcohol-impregnated 2% Chlorhexidine solutions. We had not lost any device within 30 days of placement since (May 2010-March 2011).

**Conclusion:** CPPI tools provide a systemic approach to examine and improve existing clinical practices. Our experience with 2% Chlorhexidine-70% Alcohol skin preparation solutions in reduction of implantable central venous access device-related infections mirrors the evidence in current literature.

**PW015**

INFLAMMATORY PSEUDOTUMOR OF THE LUNG - CASE REPORT

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**Purpose:** Inflammatory pseudotumor is a rare condition of uncertain etiology and highly variable biologic potential. We report a case of a young patient surgically treated for pulmonary inflammatory pseudotumor.

**Method:** A 10-year-old boy with two-day history of chest pain and palpitations was admitted to the University Children’s Hospital Rijeka, Croatia. His physical finding was normal. Laboratory tests were within normal ranges. Chest X-ray revealed a solitary, well-defined, homogenous, peripheral left-sided mass measuring 5 × 4.5 cm. Computed tomography (CT) of the chest confirmed this finding, with heterogeneous attenuation and enhancement. There was no associated hilar or mediastinal lymphadenopathy.

**Results:** The radiologic finding was inconclusive. CT-guided biopsy was performed. Histology showed abundant spindle cells arranged among the fibromyxoid matrix, without definite diagnosis. Exploratory thoracotomy was indicated, and, during the procedure, the surgeon opted to perform left lower lobectomy having an impression of malignancy. Histopathologic examination was reported as inflammatory pseudotumor. Postoperative course was uneventful. On three months follow-up, the patient is in a good condition without evidence of the disease.

**Conclusion:** Inflammatory pseudotumor of the lung is rare quasineoplastic lesion. Clinical and radiological appearance is variable and non-specific. Complete surgical resection is the mainstay of the treatment and leads to excellent outcome. Taking into account possible local recurrence and very rare distant metastases, a long term follow-up of our patient is mandatory.

**PX001**

DAILY SETUP UNCERTAINTY ANALYSIS FOR CRANIAL-SPINAL IRRADIATION USING HELICAL TOMOTHERAPY

Pediatr Blood Cancer DOI 10.1002/pbc
SIOP ABSTRACTS

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Purpose: Fertility preservation in children undergoing cancer therapy requires careful planning. Oncologists focus on curing children while minimizing long term morbidity. Ovarian function has not been widely addressed in this population. Cranial spinal radiation may cause ovarian failure, however objective data is absent. We recommend ovarian transposition to protect ovaries from radiation exposure, but we are unsure of the impact of multimodality therapy on ovarian function/fertility preservation. We examine ovarian failure related to CSI.

Method: We reviewed charts of 13 surviving female children < 18 years old who had CSI between 1973–2003. Age range at time of RT was 2–14 years. Features addressed were type of malignancy, treatment regimen, menarche, menstrual cycle pattern, endocrine deficits, hormone replacement, and pregnancies.

Results: Twelve patients had medulloblastoma, one suprasellar germinoma. 5/13 had chemotherapy. CSI was given to all 13 patients. Dose range to the whole brain was 18 Gy – 40 Gy and the spinal axis 18 Gy to 35 Gy. Total tumor dose was 35 Gy to 55.6 Gy. 13/16 developed spontaneous menarche and 1/13 with primary ovarian failure had menarche induced. This patient did not have ovarian transposition. Two patients reached menarche prior to RT. One had temporary interruption in her cycle, where as the other did not resume her menses. One patient has not reached menarche but is showing early signs of pubertal development. This patient had ovarian transposition prior to RT. 4/13 are lost to follow up. Two patients had 2 pregnancies each, one 7 and 8 years post treatment and the other 17 and 20 years after treatment.

Conclusion: Although CSI has been implicated in causing ovarian failure, we did not observe this universally in our population. It is necessary to consider all ovarian preservation approaches with patients treated with CSI. We recommend ovarian transposition for fertility/ovarian function preservation in female children undergoing craniospinal radiation.

PX005

SAFE GENERAL ANESTHESIA FOR CHILDREN UNDERGOING RADIOTHERAPY

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Purpose: To examine the utility of PET-CT in conjunction with conventional imaging (CI) before, during and after chemotherapy but prior to RT for pediatric HL.

Method: 68 patients < 21 years with HL were seen for involved field RT. All had initial FDG PET-CT scan and CI (CT scan of neck, chest, abdomen, pelvis +/- bone scan prior to treatment). Treatment consisted of 2–6 cycles of chemotherapy prior to RT. Interim PET-CT scans were performed after the 1st or 2nd cycle of chemotherapy. After all chemotherapy, 41 (60.5%) had a PET-CT prior to RT. 169 PET-CT scans were reviewed in conjunction with CI; the average number of PET-CT scan per patient was 2.49

Results: Initial PET-CT: Discordant sites of involvement between PET-CT and CI were seen in 25 (36.8%). PET-CT led to a change in RT fields in 13 (19.1%). Interim PET-CT. After the 1st or 2nd cycle of chemotherapy, PET-CT response was complete or near complete in 62 (91.2%) patients. PET-CT and CI were concordant regarding tumor response in all cases. PET-CT After Chemotherapy and Prior to RT: Five (12.2%) had PET-CT progression when compared to the interim PET-CT. In 1 patient, progression was also seen with CI, but in the other 4, PET-CT progression was not concordant with CI. In these 4 patients, PET-CT progression occurred in the mediastinum: 3 of the 4 had undergone biopsy of the FDG avid nodal sites which were consistent with infection without neoplastic involvement.

Conclusion: The use of PET-CT resulted in a change in RT field in 19% of patients. A complete or near complete response by PET-CT was achieved in 91% at the end of the 1st or 2nd cycle of chemotherapy. PET-CT, when done in conjunction with CI, at the end of chemotherapy was not found to be useful in this study.

PX006

WHOLE-BODY MRI IN PEDIATRIC ONCOLOGICAL PRACTICE

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Purpose: an estimation of the prevalence of pathological process, the definition of surgical treatment tactics.

Method: from November 2010 to February 2011 whole-body MRI 15 patients (8 females and 7 males age range from 9 month to 16 years) was performed in Cancer Research Center. Primary tumors comprised soft tissue sarcomas (n = 6), Ewing sarcoma (n = 4), neuroblastoma (n = 2), testicular germ cell tumors (n = 1), osteosarcoma (n = 1), Hodgkins lymphoma (n = 1). All cases were confirmed by biopsy.

Results: 3 patients had only primary lesions, 12 patients - multiple foci in bone marrow, lymph nodes, pleural cavities, lungs, spleen. The most frequent changes were localized in bone structures. We identified 4 variants of bone lesions: destruction with soft tissue component (n = 6), round multiple foci (n = 4), coalescing irregularly shaped foci in the medullary space (n = 3), the total abnormality of the medullary canal (n = 5). Soft tissue lesions were detected in 4 children with soft tissue sarcomas: lower extremities (n = 2), pelvis (n = 1), parameningial region (n = 1). Among 6 patients with soft tissue sarcomas primary focus wasn’t determined in two children (one - after surgery, one - with plural metastases from undiagnosed primary tumor). Lung tissue lesions identified in two patients (0.5–2.5 cm in diameter), liquid in the pleural cavity - in one. Conglomerates of lymph nodes were identified in 4 patients, multiple enlarged - in 9. In patients with retroperitoneal neuroblastoma (n = 2) and LN whole-body MRI allowed to evaluate connection with the vessels, internal organs and the spinal canal without contrast media.

Conclusion: Whole-body MRI in children reveals a pathological process, evaluating the local and distant spread. Only MRI registered bone marrow lesions (CT and ECT - were negative), that required the correction of resection level or withdrawal the artroplastics.
solid heterogeneous structure with a thin capsule, oval form, with clear contours, low echogenicity, with calcifications.

**Conclusion:** The typical signs of benign neurogenic mediastinal tumors are posterior mediastinum location (93.7%), these tumors have oval form (77.1%), mostly medium size (42.4%), clarity contours (72.9%), low echogenicity (100%), soft tissue density (100%), and the capsule (68.7%).

**PX008**

**USING IMRT AND RADIOSURGERY FOR THE TREATMENT OF CANCER IN CHILDREN AND ADOLESCENTS: ASSESSMENT OF EARLY TOXICITY**

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**Purpose:** IMRT (intensity-modulated radiotherapy) inverse Planned and SRT (Stereotactic Radiotherapy) are widely used in cancer treatment for adult patients but in the pediatric population is treated in the same way, although 50% of children with cancer should be treated with radiotherapy. This study evaluates the acute toxicity using IMRT and SRT in children and adolescents treated at our institution.

**Method:** Between January 2008 and January 2011 ten pts, 6 men and 4 women, mean age 11 years (4-20) were treated with IMRT and/or SRT, using opticex Siemens Primus linear accelerator, planned with Konrad and SRT collimator with BrainLAB stereotactic and iPlan planner v 4.12. Were divided into 7 central nervous system, 2 cervical and 1 pt. with Ewing tumor in the sacral area. Acute toxicity was evaluated according to CTCAE Guide 4.02: nausea, vomiting, rash, mucositis, terostomia, headache, alopecia.

**Results:** All pts were covered with 95% of the target volume with 95% of the prescribed dose, was 58 Gy (45-66 Gy) for CNS, 21 Gy and 54 Gy in cervical region and 60 Gy to the tumor sacrum. The organs at risk are restricted at maximum dose (MD) of tolerance: DM brainstem 54 Gy, 48 Gy to the optic way DM, DM spinal cord 44 Gy, median dose 14 Gy cochlea, salivary gland mean dose 13 Gy, small bowel DM 45 Gy. The average follow up of 29 weeks (4-116), there was moderate or severe acute toxicity. G1 toxicity was observed in 6 pts: 3 erythema, dyshypia in 1 and 2 alopecia with less than 50% hair loss. There were no treatment interruptions.

**Conclusion:** Despite the fewer number of patients IMRT and SRT can deliver an adequate dose to target volume with minimal acute toxicity in children and adolescents.

**PX009**

**TOTAL BODY IRRADIATION: EVALUATION OF TECHNIQUE AND EARLY TOXICITY IN CHILDREN AND ADOLESCENTS**

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**Purpose:** Total body irradiation (TBI) in association with chemotherapy is indicated for bone marrow transplant (BMT) conditioning. The evaluation of acute complications and dosimetric study have contributed to the evolution of technology and thus reduce the toxicity. The aim of this study was to evaluate the patients treated at our institution with TBI, describing the technique and acute toxicity.

**Method:** Between January 2005 and January 2010, 5 girls and 5 boys, median age 13 years old (3-20) were treated with TBI: 9 Leukemias and 1 non-Hodgkin lymphoma. All patients were treated with Linear Accelerator and received daily bifracionated TBI to a total dose of 12 Gy in 6 fractions, dose rate 4Gy/h over 3 days. Each session should have an interval of at least 6 hours. The positioning was dorsal decubitus in 6 patients and lateral decubitus in 4 patients. 4D CT was placed to limit the lung dose to 9 Gy. We performed in vivo dosimetry with termoluminscense dosimetry (TLD) in all patients to verify the dose received at each session. In two children aged 3 and 5 years of age used general anesthesia for treatment. We evaluated the TBI-related acute toxicity of the International Classification CTCAE v4.03.

**Results:** TBI related toxicity was seen in 9 pts: G1, 4 patients: 1 headaches, 2 nausea and 1 vomiting; and G2: 1 nausea and 1 headache. All these symptoms were resolved during the treatment. No treatment were interrupting or delayed and was technically reproducible for all the patients. The BMT was made in the 10 patients. The results of the TLD was consistent with the prescribed dose of 12 Gy.

**Conclusion:** The TBI is well tolerated during treatment and low rate of acute toxicity with this technique. It is technically feasible and safe to perform with equipment and trained specialists.

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**PX010**

**INITIAL EXPERIENCE WITH INTEGRATION OF RESPIRATORY-CORRECTED MULTISLICE CT IN A PEDIATRIC RADIATION ONCOLOGY DEPARTMENT**

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**Purpose:** With the availability of PET/CT scanner with respiratory-corrected multislice CT (4D CT) capability, further means to reduce radiation delivered to surrounding normal tissue in pediatric patients has become available. We review the issues and challenges associated with the utilization of 4D CT in pediatric age group.

**Method:** Since 2009, we have utilized Philips Gemini PET/CT scanner for radiation therapy simulation. We performed 4D CT scans with the respiratory air bellows belt and Mayo respiratory feedback system. The simulations were performed by 2 radiation therapists, 1 medical physicist, and 1 radiation oncologist. Intravenous contrast was often utilized. Around one-third of the scans were performed under sedation. Simulation scans were transferred to the Varian Eclipse treatment planning workstation. Our indications for 4D CT scans include lower thoracic and upper abdominal tumors such as Hodgkin lymphoma with pericardial involvement, selected right adrenal neuroblastomas and bilateral Wilm tumors, which require IMRT for normal tissue sparing and/or dose escalation.

**Results:** 4D CT scanning reduced motion artifact and reveals the range of motion of the tumor and normal organs. In some cases, margins were significantly refined based on the 4D CT scan. Unlike in adults, the impact of 4D CT scan is reduced in children who require sedation, as their diaphragmatic motion is decreased. In addition, in many of the younger patients, the respiratory bellows was too large, preventing us from performing a 4D CT. Breath coaching young children with the Mayo system was not possible. We are exploring the possibility of using the respiratory trace from a Philips Intellivue patient monitor or a real-time 3D surface imaging system rather than the bellows system. In addition, CT dose with 4D CT must be monitored for patient safety.

**Conclusion:** Adaptations have to be made for pediatric patients before wider application of 4D CT in this age group.

**PX011**

**PET-CT, INTENSITY-MODULATED RADIATION THERAPY AND IMAGE GUIDED RADIATION THERAPY INCORPORATION TO THE RADIATION THERAPY TREATMENTS PLANNING IN PEDIATRIC TUMORS**

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**Purpose:** The recent advances in Radiation Oncology have been largely due to the incorporation of imaging techniques (CT, PET-CT), in order to identify improve tumor measurement, dosimetry (conformational radiotherapy 3D and intensity-modulated radiotherapy (IMRT) and treatment verification (image guided radiotherapy (IGRT)). The objective of this abstract is to describe how we incorporate these advances to the treatment of childhood tumors.

**Method:** Radiation treatment planning and administration in pediatric brain tumors is described. Treatment planning is carried out with 18-FDG PET-CT with an individualized immobilization system. The tumor contours, and critical organs and the dosimetry were made with the XiO or iPlan planners. Patients were treated in an Oncor accelerator with verification system through IGRT (Conbeam) or in a Novilus accelerator with IGRT (ExacTrac system).

**Results:** Since November 2007 until March 2011, we have used PET-CT for RT planning 7 children (range: 3–16 years). Diagnosis were: Burkitt lymphoma with bone metastases, osteosarcoma with bone metastases, nephroblastoma pulmonary recurrence, intrathoracic persistence Hodgkins lymphoma, bladder embryonal rhabdomyosarcoma and two neuroblastomas. The doses administered were between 21 and 36 Gy, with 1.5–3Gy/day fractionation. In five patients conformal radiotherapy 3D was performed and in two IMRT “step and shoot” (nephroblastoma pulmonary recurrence and retroperitoneal neuroblastoma). In two patients (neuroblastoma, and bladder rhabdomyosarcoma) an internal marker (Visirol)® was placed intraoperatively, to improve treatment accuracy, through IGRT in the Novilus). In the remaining five patients, treatment verification was conducted through IGRT with Conebeam in an Oncor accelerator. The treatment tolerance was good in all patients.

**Conclusion:** The better tumor contouring definition by the PET-CT planning, as well as the better dosimetry precision with IGRT, result in safer radiation treatment in pediatric patients.
IMPROVING THE QUALITY OF THE EXPERIENCE: 3D PHOTOGRAPHY IN THE PRODUCTION OF HEAD & NECK STABILISATION DEVICES FOR PAEDIATRIC RADIATION ONCOLOGY PATIENTS

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Purpose: The production of radiation therapy (RT) stabilisation devices can be extremely confronting for children, particularly when head immobilisation is required. At the Peter MacCallum Cancer Centre either thermoplastic or PETG masks are used. The processes involved in the manufacture of a stabilisation device occur on the child’s first visit to the RT centre and may be challenging and frightening. Thus, a number of children often require general anaesthesia to undergo these processes. In 2009, a multidisciplinary team commenced trials utilising 3D photography linked to computorised prosthetid technology to produce a ‘no touch’ method of producing stabilisation masks for children. This poster presents our ongoing research into improving the use of this technology.

Method: A 3D handheld digital photography system is used to acquire a three-dimensional image of the child’s head, neck and upper torso. An Omega™ computer aided design prosthetic carver uses the 3D photographic dataset to produce a foam bust of the child. The mask is constructed on the bust prior to the child’s appointment for CT simulation and the mask fit is assessed during planning and treatment procedures.

Results: At time of abstract, seven children (aged 4 to 8) have had stabilisation masks produced using this method. None have required GA for simulation or treatment, negating 160 GA procedures. Verification imaging indicates that masks produced by this method are equivalent to traditional masks. Two masks have required considerable modification at simulation to improve patient comfort.

Conclusion: The technique allows RT mask moulding without contact between the child and construction materials. Alterations in our mask manufacture techniques have lead to a reduction in the use of general anaesthesia and concomitant savings in time and expense, increased efficiency and an improved quality of experience for the children.

TREATMENT OF CHILDREN WITH PRIMARY METASTATIC RHABDOMYOSARCOMA

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Purpose: to improve the results of the treatment of primary metastatic rhabdomyosarcoma (RMS) for children and adolescents.

Methods: 38 children and adolescents, at the mean age of 8.4±3.8 years (20 males, 18 females) with rhabdomyosarcoma were treated between 1990 and 2007 years. Histologically, 9 patients had the undifferentiated RMS, 12 had the embryonal rhabdomyosarcoma and 17 - alveolar rhabdomyosarcoma. The most often affected area was the area of the lower extremity -15 cases. According to the staging systems adopted, the size >5 cm (22B) was reported in 33 cases. Eleven patients had regional nodal involvement, and 27 had distant metastases. The analyzable group of patients was disintegrated to the group of historical (HCG) (23 patients) and the investigation group (IG) (15 patients). The general scheme of the treatment for patients of IG included: 8 courses of chemotherapy (used ifosfamide or cyclophosphamide, etoposide, carboplatin); the harvesting and preservation of the stem cells after the stimulation of the haemopoiesis by G-CSF; the stage of the local control of the tumor consisting of the surgical ablation of the primary lesion and the radiotherapy of the initial tumor and metastasis left after the induction. Patients, who were included in HCG, received standard CT.

Results: the partial effect was registered by most of the patients of IG - 80.0%, vs HCG - 26.1%. We observed progression of the disease during inductive CT in 21.7% of cases in HCG. In our research we have analyzed the 3 year disease free survival (DFS). Thus, 3-year DFS was 21.8±11.1% in IG, vs 49±4.8% in HCG.

Conclusion: less than 20% of STS patients will survive 5 years. Complete resection, RT and aggressive systemic chemotherapy are the most predictive factors for prolonged survival.

DETECTING CHROMOSOMAL ANOMALIES THROUGH M-FISH IN ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose: relatively little is known about the severity of physical functioning deficits in pediatric recipients following HSCT; therefore, the objective of this study was to compare physical functioning between those children who received reduced-toxicity conditioning (RTC) versus myeloablative conditioning (MAC) regimens prior to HSCT.

Method: Based on hierarchical linear modeling, trends in the PedQL 4.0 physical functioning sub-scale and select individual items were explored in 80 children (9±4 years old. Functioning was assessed once pre-HSCT and on days 100, 180, 365, and 730, post-HSCT.

Results: Mean age: 12.62 years. RTC/MAC 54%/46%. A significant change from baseline in overall physical functioning was estimated for RTC (M = 66.84) compared to MAC (M = 68.05) with RTC improving by 0.48 points per month (ppm) (t = 2.34; p = 0.02) and MAC improving by 0.04ppm. Baseline impairments in lifting something heavy was evidenced for RTC (M = 55.55) and MAC (M = 56.06). However, the RTC group rapidly improved by 7.12ppm (t = 2.07; p = 0.03) with no lifting problems estimated by 6-months post-HSCT. MAC improved by 1.23ppm, with some lifting difficulties predicted throughout the follow-up period. Greater improvements in fatigue scores were predicted for RTC (M = 60.11; 3.39 ppm) compared with MAC (M = 65.19; 2.46 ppm) (p = 0.05) with no fatigue estimated by 1-year post-HSCT for both groups. RTC pain scores improved from baseline by 2.82 ppm (M = 66.02) and 5.35 ppm for MAC (M = 66.95). No difficulties with pain were estimated by 1-year for RTC and by 6-months for MAC.

Conclusion: Deficits in physical functioning appear transient with most perturbations expressed in the acute post-HSCT period. It is unknown why RTC experienced more pain compared to MAC. However, for pediatric HSCT recipients, RTC had fewer deficits and faster recovery in overall physical functioning, strength, and fatigue versus MAC.
The purpose of this study is to identify the presence and frequency of complex chromosomal anomalies and criptical chromosomal rearrangements which are not visible in conventional cytogenetic methods (CCM), through the use of Multicolor Fluorescence In Situ Hybridization (m-FISH) method in the samples of bone marrow aspiration of the children with acute lymphoblastic leukemia (ALL). 

Method: Out of 20 cases with ALL diagnosis, m-FISH method has been applied to children with acute lymphoblastic leukemia (ALL). Situ Hybridization (m-FISH) method in the samples of bone marrow aspiration of the cases which were identified to have metaphasis obtained by directly or applying 24-hour cell culture in bone marrow aspiration material and analyzed with GTG banding method routinely and at least 5 metaphasis have been tested in each case under fluorescent microscope.

Results: Abnormal karyotype has been observed in 10 of 20 cases in total in which chromosomes were obtained. At the end of m-FISH application, no structural anomaly which are not observed with conventional methods, has been observed in cases with normal karyotype. Hyperdiploidy in one case, additional structural changes other than anomalies identified with CCM in two cases and the origins of derivative chromosomes in 4 cases have been detected. Chromosomal changes in 2 cases have been verified with m-FISH, as well. Conclusion: It has been possible through the use of m-FISH method, to solve complex karyotypes which have not been defined through CCM, to reveal hidden chromosomal abnormalities. So it is suggested that m-FISH application should be used not only in leukemia cases with complex karyotypes but also in the cases defined as one anomaly cytogenetically.

Pub005

PRIMARY MEDIALASTINAL B-CELL LYMPHOMA IN CHILDHOOD LYMPHOMA

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Purpose: To evaluate the clinical characteristics, treatment regimens, and outcome of the patients with primary mediastinal B-cell lymphoma (PMBCL).

Method: 1110 patients who were eligible from 1546 newly patients diagnosed with non-Hodgkins lymphoma between 1971 and 2008 were retrospectively evaluated. All patients were classified according to Murphy’s staging system. All patients were treated with chemotherapy and/or radiotherapy. Chemotherapeutic regimens included LMB and LS-A2L2.

Results: 12% of the patients with non-Hodgkins lymphoma (133 patients) was mediastinal lymphomas, while PMBCL consists of only 5.2% (7 patients) of mediastinal lymphomas. There were 1 female and 6 male patients. The median age was 7.5 years (2-14 years). All patients had stage 3 clinical characteristics. LMB chemotherapy protocol was used in 4 patients and 3 patients were in LS-A2L2 protocol. Five patients received radiotherapy while 2 patients did not. Two patients relapsed and died while the other 5 patients were on disease-free follow-up. The 10-year event-free survival (EFS) and overall survival (OS) rates for PMBCL were similar and 66.7%. However, the 10-year EFS and OS rates for mediastinal T-cell cases (126 patients, 11.3%) were 36.5% and 50.7%, respectively. Abdomen was the primary site of involvement with 591 patients (52%). The 10-year OS rate for abdominal B-cell lymphomas was 48.1%.

Conclusion: PMBCL was rare in mediastinal localization. Outcome of these patients treated with B lymphoma protocols were better than the other mediastinal T cell lymphoma and abdominal B cell lymphoma.

Pub006

ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL) IN MALAWI, PROGRESS IN THE FIRST MALAWI ALL PROTOCOL.

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Purpose: In Malawi, one of the world’s poorest countries, children with ALL have until now not been treated, many have not been diagnosed, and those who have invariably presented late and died rapidly. The team initiated the first Malawi ALL therapy in 2010. This basic protocol has enabled treatment with parental consent within the capacity of the current medical infrastructure.

Method: 13 patients with morphologically confirmed ALL were treated with a 3 drug induction of Prednisolone, weekly vincristine, cyclophosphamide and intrathecal (IT) methotrexate. Post induction patients received 5 four weekly cycles of vincristine (day 1), prednisolone (5 days), daily 6 mercaptopurine and IT methotrexate. All patients were aged between 1 and 16 years, none had life threatening infection. All patients received dietary supplementation and families assistance with transport to and from the hospital. Bone marrow has been collected for retrospective molecular cytogenetic analysis.

Results: There were 7 males and 6 females. Median age at diagnosis was 5 years (1.5-12) and median white cell count 27.5 (1-150). 5 children remain alive (15-318 days from start of treatment) (median 275). Of the 8 children that died, 1 died before treatment, 3 during therapy with prednisolone as a prephase, one with Kwashiorkor and 3 others during induction all apparently from disease. Median initial WBC was 17 for those alive and 86 for those who died.

Conclusion: ALL treatment remains a challenge in very low income countries with poverty, malnutrition, co-morbidities especially infection and delays in diagnosis compounding the challenges. As shown in this original small cohort the patient’s general condition and a high initial white count adversely influence the outcome. The use of a 7 day prednisolone prephase for all is now being considered and development of optimal supportive care within the context of the Malawian setting. To date no family has stopped the therapy prior to its completion.

Pub007

THE TREATMENT OF CHILDREN WITH LOW AND INTERMEDIATE RISK NEUROBLASTOMA

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Purpose: The evaluation of treatment of children with low and intermediate risk neuroblastoma.

Method: From 2007 to 2011 years we had been observing 72 patients with morphologically confirmed neuroblastoma at the mean age of 2.6 years (from 1 month till 15 years). There were 20 patients with stage I, 16 patients with stage IIA, 17 patients - IIA, 15 patients with stage III, and 4 patients with IVS stage of the disease. All patients received therapy according COG 9641, A3961 protocols after thoroughly evaluation (imaging, MBG, bone marrow morphology, molecular studies, immunohistochemistry). Surgery treatment was performed before chemotherapy. Stage by INSS and group of the risk were established after histological examination. The general scheme of the treatment included chemotherapy (used doxorubicin, cyclophosphamide, etoposide, carboplatin) and RT.

Results: 71 (98.6%) patients (from 72) were alive without disease with a follow-up of 5 to 38 months. One patient at the age of 1 month with multiple liver metastases died from toxicity of chemotherapy.

Conclusion: Our data confirm the overall good prognosis of localized NBs. Chemotherapy allows surgical excision and excellent outcome in children with localised and resectable NB. Less intensive chemotherapy should be investigated in such patients.

Pub008

PEDIATRIC PALLIATIVE CARE SERVICES IN KUWAIT: A UNIQUE EXPERIENCE FROM MIDDLE EAST COUNTRIES

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Purpose: Pediatric palliative care (PPC) is being recognized as an important aspect of holistic care for children with cancer. PPC can offer a wide range of services including symptom management of dying child, support for the parents, spiritual services, home care, bereavement services etc.

Method: Kuwait Association of Care of Children in Hospital (KACCH) is a NGO, which provides support to hospitalized children through Child Life Specialists (CLSs). In November 2005, this NGO started PPC in Kuwait and made a PPC team, which consist of pediatric oncoligist, pain management specialist, CLSs, nurses, and physiotherapist. One CLS is assigned for each child. CLSs are key contact person with child and family. The first contact between CLS and family is made in the hospital. Subsequently home visits are made by CLS to establish better rapport with child and family. The home services include pain medications, blood sampling, blood transfusion, dressing, care of Hickman’s line, physiotherapy, oxygen inhalation etc. The children are also taken out for outdoor activities. The emphasis is on keeping the child at home as long as possible. The family members are encouraged to contact CLS at any hour of the day.

Results: Till date 58 children have been registered for palliative care. They suffered from various malignancies including brain tumors, bone tumors, neuroblastomas, adenocortical carcinoma etc. Out of these 58 children, 50 have died of their disease. They were under care of palliative care team ranging from few weeks to more than 18 months. Majority of the
children died in the hospital, but few died at home also. In our assessment and feedback, the patients and their families got tremendous benefit from palliative care services in terms of pain control, social support, and bereavement services.

Conclusion: Hospital and home based PPC services make a tremendous impact at “end of life care”.

Pub009

PROFILE OF PEDIATRIC NON HODGKINS LYMPHOMAS IN KUWAIT: A 10 YEAR ANALYSIS FROM KUWAIT CANCER CONTROL CENTRE, KUWAIT

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Purpose: Pediatric Non Hodgkins Lymphomas (NHLs) are aggressive tumors but with high care rates. The survival for these tumors have considerably improved over the last 3 decades mainly due to different strategies of treating each subtype as well as better supportive care.

We analyzed the epidemiology and outcome of all the patients of pediatric NHLs, who received treatment between January 2001 and December 2010.

Method: During the study period 40 children were registered with diagnosis of NHL. All were subjected to standard investigations for staging workup. They were staged according to the Murphy’s classification. Majoritiy of the patients were treated on BFM protocols.

Results: Out of the 40 children who were registered during the study period, there were 29 males (72%) and 11 females (28%). The median age was 6.5 years. Majority of the children had stage III disease (70%). Seventy percent had B - NHL. T- NHL was seen in 35% while ALCCL was seen in only 5% of cases. All children with T - NHL, had their disease in mediastinum, while children with B - NHL had disease located at various places, like neck, nasopharynx, tonsils, chest wall, and abdomen. Majority of children were started on treatment with chemotherapy, while three had primary surgery. BFM 95 protocol was used in 67.5%, while alternative protocol was used in others. At the end of chemotherapy, 80% of the children achieved CR status. Two more achieved CR after surgery. There were three documented deaths, all due to progressive disease. One was lost to follow-up. Two relapsed and are under salvage therapy, and 36 children are alive (90%). The median survival of whole group is 41 months (range - 6 - 120 months).

Conclusion: Modern protocols for treating childhood NHL have very good results with acceptable toxicity, but should be treated in tertiary care centers.

Pub010

RETNONBLASTOMA: TEN YEARS OF EXPERIENCE AT KANTI CHILDREN’S HOSPITAL, KATHMANDU, NEPAL

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Purpose: To describe the clinical characteristics and survival of children with retinoblastoma at Kanti Children’s Hospital over a 10 year period.

Method: A retrospective hospital based study was conducted from March 1998 to February 2008 on post-operative patients with retinoblastoma. Information on gender, age, clinical presentation, pathology, treatment, follow-up, and outcome was collected.

Results: A total of 42 post-operative children with retinoblastoma (85.7% unilateral, 14.3% bilateral) were studied. Twenty-one out of 42 (52%) had optic nerve involvement. The most common presenting signs were extraocular (28.6%), proptosis (23.8%), leukoria (23.8%), ptosis (16.7%), strabismus (7.1%). Age at presentation ranged from 6-120 months, with mean age of 46.6 months. Two-thirds presented between 2-5 years, followed by 23.8% presenting at 12-24 months, and 9% after 5 years of age. The male to female ratio was 1.11. The majority had poorly differentiated retinoblastoma (62%), followed by well differentiated (28.6%), and moderately differentiated (9.5%). CEB based protocol was used to treat, and the overall 10 year survival was 23.8%. Death occurred in 19% of cases, and 57.2% of patients were lost to follow-up or left against medical advice.

Conclusion: Despite severe resource limitations, the pediatric oncology unit at Kanti Children’s Hospital in Kathmandu, Nepal, has been successfully treating retinoblastoma with the success rate of 23.8%.

Pub011

GENE EXPRESSION OF THE HYPOXIA-RELATED GENES VEGF, SLC2A1 AND HIF1A: LACK OF IMPACT IN TREATMENT RESPONSE AND PROGNOSIS IN CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA

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Purpose: Hypoxia represents an important indicator of prognosis in solid tumors and has been associated with aggressive behavior and poor response to treatment. Few studies have been conducted in childhood ALL and its effect in the treatment response and survival is unknown. The aim of the present study was to evaluate the expression levels of the hypoxia-related genes VEGF, SLC2A1 and HIF1A in childhood ALL samples and to analyze its association with treatment response and prognosis.

Method: We analyzed 82 consecutive childhood ALL samples (73 B-lineage ALL and 9 T-ALL) classified and treated according to the GIMLI-ALL 99 protocol. Gene expression profile was evaluated by real-time quantitative PCR using the 2-DDCT method. The expression levels of the genes and the clinical and biological variables were analyzed by Mann-Whitney test and event-free survival by Kaplan-Meier and log-rank test. Values of gene expression higher than median were considered as overexpressed. Correlation between the genes was evaluated by Spearman correlation test.

Results: We observed a significant correlation among all analyzed genes (P < 0.01) by Spearman test. No significant association was observed between the gene expression values and clinical/biological characteristics at diagnosis (age, WBC count, immunophenotype and risk group), treatment response criteria (WBC count at day 7, bone marrow morphological status and minimal residual disease at days 14 and 28) and prognosis in the overall group of patients, neither in the B-lineage CD10 positive patients.

Conclusion: Our results suggest a common activation pathway of the hypoxia-related genes VEGF, SLC2A1 and HIF1A in childhood ALL. The expression levels of these genes although, appear not related with treatment response and prognosis.

Pub012

APPLICATION OF EIGHT COMMON MUTATIONS INTERPHASE-FISH PROBES TO DETECT GENETIC ALTERATIONS IN PEDIATRIC B-CELL PRECURSOR ACUTE LYMPHOCYTIC LEUKEMIA

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Purpose: Alterations in genes involved in B-cell development and cell cycle control contribute to pathogenesis of B-cell precursor acute lymphoblastic leukemia (B-precursor ALL). Particular chromosomal abnormalities determined prognostic significance of ALL. Cytogenetics and fluorescence in situ hybridization (FISH) techniques led to more understanding of genetics role in leukemogenesis. However, conventional cytogenetics (CC) of ALL is problematical due to low mitotic index and difficult metaphase preparation from bone marrow culture. Eight common gene translocations and rearrangements of B-precursor ALL were tested in this study by dual color interphase-FISH in addition to CC.

Method: Thirty-two children with B-precursor ALL were investigated for chromosomal abnormalities using FISH. Eight common gene mutations consisted of TEL/AML1, TCF3/ PBX1, BCR/ABL, ETV6, TCF3, MLL, IGH, and PAHX were tested with dual color DNA probes.

Results: TEL/AML1 was a most frequent translocation detected in 11 children (34.4%) Two patients with BCR/ABL (6.3%) and one with TCF3/PBX1 (3.1%) were also observed. For break apart rearrangements, 11 children (34.4%) revealed positive FISH for ETV6 followed by one each patient with MLL (3.1%), PAHX (3.1%), and 2 cases with IGH (6.3%). Notably, most of every single patient with TEL/AML1 fusion translocation revealed split rearrangement in ETV6 gene. In addition, other abnormalities including extra copies and deletion of genes were obtained in a range of 3.1%–34.4%. Conventional cytogenetics (CC) exhibited only one each case of BCR/ABL fusion, and MLL and IGH translocation (each of 3.1%). Remarkably, none of cases with FISH-positive TEL/AML1 fusion and ETV6 split apart was detected by CC. Likewise, one each case with TCF3/PBX1 fusion and PAHX split signal captured by FISH was not recognized by CC.

Conclusion: In comparison of CC and using 8 common mutations FISH probes by number and percentage of positive cases, interphase-FISH technique was more sensitive to uncover chromosome aberrations in children with B-cell precursor ALL.

Pub013

CLOFARABINE AS A SINGLE AGENT BEFORE HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR RELAPSED AND REFRACTORY LEUKEMIA IN CHILDREN: THE REPORT OF 4 CASES IN A SINGLE MEXICAN INSTITUTION

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PEDIATRIC NELITIS: AN OVERVIEW

Purpose: Acute Lymphoblastic Leukemia (ALL) treatments for relapsed disease are sometimes unable to achieve complete remissions in order to proceed to a hematopoietic stem cell transplantation (HSCT). Clofarabine is a nucleoside analog and its effect is dependent on intracellular phosphorylation by kinases 9 and 10 that inhibit DNA polymerase alpha, interfering with DNA elongation. HSCF is currently being used as an induction therapy in children with relapsed or refractory leukemia before HSCT. We described our experiences with Clofarabine as a monotherapy in pediatric patients with relapsed or refractory disease.

Method: During March 2006 to December 2007 four pediatric patients were enrolled, two on their first ALL relapse, one in his second relapse and one with a T cell relapsed/refractory ALL. All of them received 5 cycles of chemotherapy (etoposide, ifosfamide, carboplatin). Two years later, other patient received 4 cycles of chemotherapy (vincristine, dactinomycin, cyclophosphamide, etoposide, ifosfamide, cisplatin, doxorubicin). Two patients were treated with 5 cycles of chemotherapy (etoposide, ifosfamide, carboplatin). One patient died 13 months after HSCT regarding to relapse, three of them are alive; only one with a GVHD.

Conclusion: Clofarabine has been used in combination with other cytotoxic agents, nevertheless the toxicity has been increased; we conclude that clofarabine could be an active single drug for relapsed and refractory pediatric ALL before HSCT.

PUB014
SOCIAL NETWORKING AND THE IMPACT ON THE ONCOLOGY COMMUNITY

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Purpose: This quantitative study is seeking to explore the ethics of social networking and the oncology community. The Pediatric Oncology setting is often referred to as a community with unique challenges, where boundaries are frequently obscured. Long term relationships, acuity, and the general anxiety invoked by a cancer diagnosis contribute to this close relationship where the interdisciplinary team and the patient/family unit become enmeshed. The concept of family centered care takes on a life of its own. The advent of social media presents further complications to this relationship. Connections are made through global networks where people can connect on yet another level and the computer becomes the vehicle for communication. Boundaries are blurred and confidentiality and privacy compromised. Despite having an institutional policy regarding the use of social media, it continues to be a practice among staff to allow patients and their families to become friends on Facebook and other public blogs.

Method: An anonymous questionnaire using survey monkey is being used and sent to all the staff in the pediatric oncology department. The data is collected over a 30 day period, allowing for shift changes and vacation/sick leave. Analysis will be descriptive in nature using descriptive statistics.

Results: Results will be communicated to all staff and consultation and recommendations will be compiled by all the stakeholders.

Conclusion: The study will endeavour to raise awareness of the ethical implications associated with social media in the oncology community. Based on the results compiled the data will be used to develop guidelines and teaching models to educate and support both the staff and the patient/family unit.

PUB015
FOLLICULAR THYROID CARCINOMA AFTER PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN A CHILD WITH PLEUROPULMONARY BLASTOMA

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Purpose: Periopulmonary blastoma (PPB) is a rare and aggressive intrathoracic neoplasm and the prognosis is poor. The role of high-dose chemotherapy (HDC) with autologous hematopoietic stem cell rescue (AHSCR) is not established so far.

Method: A 23-month-old female was found to have mass shadow on chest X-ray during treatment of pneumonia. The mass grew rapidly in a month and whole left thorax was occupied by the mass. The mass was removed surgically with lingular segmentectomy and the prognosis is poor. The role of high-dose chemotherapy (HDC) with autologous hematopoietic stem cell rescue (AHSCR) is not established so far.

Conclusion: HSCF is currently being used as an induction therapy in children with relapsed or refractory leukemia before HSCT. We described our experiences with Clofarabine as a monotherapy in pediatric patients with relapsed or refractory disease.

PUB016
GUIDELINE FOR PEDIATRIC PALLIATIVE CARE: MULTIDISCIPLINARY APPROACH IN PEDIATRIC ONCOLOGY

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Purpose: Improved survival rate of childhood cancer in recent years means lesser number of children die of childhood cancer. The development of programs such as cares for terminally ill children, smooth transition from therapy to palliative care and community supports systems have become relatively stagnant. Though many guidelines on pediatric palliative care exist, most of them are written from medical professional’s views. Therefore, publication of a guideline useful for families and caregivers is much in needs.

Method: To formulate the guideline, Children’s Cancer Association of Japan, a leading parent organization, has taken initiatives so that it should reflect families perspectives. A special committee consists of medical professionals, educators as well as parents and a sibling made a discussion in manners not to be caught up in too professional opinions.

Results: After 14 meetings in four years and several discussions in open symposium, the committee concluded the final draft with the following four principles: 1. Since prevailing condition should change over time, clear references should be given for the sources of information, 2. Since no right answer to the subject exists, the guideline should be a true guide of enabling families to reach and chose appropriate information in needs, 3. Topics on bereavement should be included, and 4. The booklet should be the size easy to handled.

Conclusion: Since launch in last December, 5,000 copies have been distributed to childhood cancer centers, relevant institutions and families. The needs are so high that additional 4,000 copies have been printed. Furthermore, issuance of newsletters through which latest experiences of families could be shared is planned.

PUB017
ACUTE NEUROLOGICAL COMPLICATIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose: ALL is the commonest childhood malignancy with high cure rates. The disease per se and the prophylactic therapy for the CNS predisposes the child to varied complications, like cerebrovascular events, infections, drug toxicities. etc. The purpose of this study is to document the types of complications and highlight the imaging features that help in prompt recognition and early treatment.

Method: A retrospective analysis of CT/ MRIs done for patients with leukemia presenting with acute symptoms has been done. The study period spans from January 2007 to December 2009. The CT/ MRI were read from PACS while the clinical details were obtained from the relevant institutions. The complications were infection (13), posterior reversible encephalopathy syndrome (9), dural sinus thrombosis (4), drug induced leukoencephalopathy(4), Arterial infarcts (2), Plain haemorrhage (1), chemical meningitis (1). Acute Disseminated Encephalomyelitis (ADEM) (1), secondary in the CNS (2), secondary CNS infiltration (2). We did not have any patient with primary CNS disease.

Results: A total of 70 patients underwent neuro-imaging, of which 39 were found to have abnormalities on imaging studies. Patients with normal scans and extra-cranial findings like sinusitis were excluded. The complications were infection (13), posterior reversible encephalopathy syndrome (9), dural sinus thrombosis (4), drug induced leukoencephalopathy(4), Arterial infarcts (2), Plain haemorrhage (1), chemical meningitis (1). Acute Disseminated Encephalomyelitis (ADEM) (1), secondary in the CNS (2), secondary CNS infiltration (2). We did not have any patient with primary CNS disease. The commonest presenting symptom was seizure (19), visual disturbances (4), aphasia (2).
headache (5), altered sensorium (1), choreo-athetoid movements (1) and gaze palsy (1). 22 patients were in induction phase, 13 patients on consolidation phase and 4 were in maintenance phase when the event occurred.

Conclusion: The various acute neurological complications have common presenting symptoms and varying imaging abnormalities. Reading these scans in the light of clinical inputs very often helps us reach an appropriate diagnosis and accelerate treatment.

Pub018

GROWTH IN CHILDREN TREATED FOR ACUTE LYMPHOBlastic LEUKAEMIA

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Purpose: Cancer survivors are at risk of impaired growth attributable to chemotherapy and radiation. The clinical impact, predictability & reversibility of this adverse outcome needs to be determined. The purpose of this study was to research the pattern of distance and velocity growth in children treated for acute lymphoblastic leukemia [ALL].

Method: 85 children [60 boys & 25 girls] treated for ALL & off drugs for at least 2 years were analysed. Mean age at diagnosis was 5.52±12] years. 73 received cranial radiation (1800 cGy). All children were measured for body weight & height using standardised techniques at diagnosis and at every visit thereafter. Z scores were calculated to assess catch up growth. Student’s t test & ANOVA was applied for comparison.

Results: Height z scores decreased during initial intensive therapy [–1.01]. They continued to decrease in girls till the end of treatment [–1.42] as compared to boys [–0.99]. Catch up after completion was better in boys [–0.88 vs. –1.32]. Weight z scores decreased in the first 6 months [–1.26]. Subsequent catch up was better in boys as compared to girls [–0.88 vs. –1.32]. Children who received cranial radiation had greater reduction of height. The BMI increased throughout treatment, being higher after completion of therapy. Peak growth velocity of height and weight occurred at 13 years for girls and 14 years for boys.

Conclusion: Weight and height decreased during the initial intensive treatment with subsequent catch up at the end of therapy. Height catch up was less and continued to be reduced even after completion of therapy. Growth was impaired more in children receiving radiation. The BMI increased during treatment. However, no child was overweight. This is possibly because of greater impact of therapy on height. Final adult height remains to be evaluated.

Pub019

ACUTE RENAL FAILURE AS AN INITIAL MANIFESTATION OF ACUTE LYMPHOBLASTIC LEUKAEMIA: A CASE SERIES WITH REVIEW OF LITERATURE

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Purpose: Acute renal failure is a known complication of acute lymphoblastic leukemia (ALL). But serious renal failure as the primary manifestation of ALL is rare. Here we report two such cases.

Method: Two cases of renal failure in children treated for acute lymphoblastic leukemia (ALL) and one case of acute renal failure as the primary manifestation of ALL were reported.

Results: In one child, renal failure required dialysis. The other two children had renal failure due to tumor lysis syndrome. The child with dialysis had acute renal failure due to urate nephropathy. The child with tumor lysis syndrome had acute renal failure due to tumor lysis syndrome.

Conclusion: Acute renal failure is a known complication of acute lymphoblastic leukemia. But serious renal failure as the primary manifestation of ALL is rare. Here we report two such cases.

Pub020

ATYPICAL RELAPSED OF ACUTE MYELOID LEUKAEMIA FAB MT AS A GRANULOCYTIC SARCOMA

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Purpose: Granulocytic sarcomas are rare, extramedullary tumor masses that consist of immature granulocytic cells. These tumors can arise de novo or can be associated with other myeloid disorders. Presentation can occur prior to, in association with the underlying myeloid disorder, or upon relapse. It occurs most commonly in bone, perosteum, soft tissue, lymph nodes, and skin, although it can occur anywhere throughout the body.

Method: We report an unusual case of granulocytic sarcoma involving the temporal bone.

Results: We present the case of a 3 years old boy diagnosed of AML in January 2009. He presented treatment with high doses of 6-mercaptopurine, L-asparaginase, Lidentine and Mitoxantrone, in another institution. He remained in remission for a period of 1 year and 3 months and was referred to us after developing a solid mass at his right temporal region. The mass involved the temporal bone and protruded into the brain causing mass effect. His complete blood count showed no alteration. A biopsy was performed and a granulocytic sarcoma with the same characteristics of those in bone marrow. The AML M7 relapsed diagnosed was performed and the child received re-induction with Citarabine plus fludarabine with no response.

Conclusion: Recognition of this rare entity is important, because early aggressive chemotherapy can cause response of the tumor, as in our case, and thus improve patient survival.

Pub021

GOOD SURVIVAL OF PEDIATRIC OSTEOSARCOMA IN HUNGARY

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Purpose: Osteosarcoma is the most common primary bone tumor in childhood. There are 8–10 new patients per year in Hungary. We analysed our data between 1988 and 2006 at the 2nd Department of Pediatrics in Budapest.

Method: Data of 122 children with osteosarcoma (65 male/57 female, mean age 13.8±3.6 years) treated with COSS 86 or 96 protocol were processed. Overall survival (OS) and event-free survival (EFS) were analysed. Mean age at diagnosis, gender, localization, date of diagnosis, histologic patterns, type of surgery, histological response to chemotherapy.

Results: 3.6 year OS was 68%, 5-year EFS was 62%. OS of patients without metastasis was 80% while metastatic patients’ OS was 17%. 30 patients had amputation, 82 patients underwent preserving surgery. There was no difference in survival between the two surgical procedures while every patient without radical surgery has died. Date of diagnosis, gender and histological classification had no prognostic significance. Patients with tumor on the upper or on the lower extremity had almost the same survival (p=0.7), while patients with tumors of axial skeleton had worse survival (p=0.0133). Poor responders to the chemotherapy had worse survival than good responders (p=0.0182). EFS was better in patients under 14 years than in patients over 14 years (p=0.0085).

Conclusion: In our centre, 68% of children with osteosarcoma are curable with intensive chemotherapy and surgery. limb-salvage surgery is not associated with an increased risk of unfavorable outcome. Patients with metastatic disease or local relapses have bad prognosis. Nonmetastatic cases, tumours of extremities and patients under 14 years have a better survival (80%).

Pub022

THE COMPLEX PSYCHOLOGICAL SUPPORT FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Purpose: Acute lymphoblastic leukemia is one of the most common malignancies in children. It is characterized by the development of leukemic cells, which can be found in different tissues and organs. The therapy of acute lymphoblastic leukemia is based on chemotherapy and sometimes high-dose therapy with hematopoietic stem cell transplantation. The main goal of therapy is to eliminate the leukemic cells and to prevent relapse. However, the therapy of acute lymphoblastic leukemia is associated with significant physical and psychological burden for children and their families. The complex psychological support for children with acute lymphoblastic leukemia is very important.

Method: The complex psychological support for children with acute lymphoblastic leukemia includes individual and group psychotherapy, family therapy, education about the disease and treatment, and support for siblings. The main goal of psychotherapy is to help children and their families to cope with the diagnosis of leukemia, to manage the physical and psychological effects of the therapy, and to prevent relapse.

Results: The complex psychological support for children with acute lymphoblastic leukemia is effective in managing the physical and psychological burden of the disease. It helps children and their families to cope with the diagnosis of leukemia, to manage the physical and psychological effects of the therapy, and to prevent relapse.

Conclusion: The complex psychological support for children with acute lymphoblastic leukemia is very important. It helps children and their families to cope with the diagnosis of leukemia, to manage the physical and psychological effects of the therapy, and to prevent relapse.
Purpose: The modern tendency of increasing in evidential base of medicine requires objectifying the results of paraclinical support of the patients who receive polychemotherapy for acute lymphoblastic leukemia. Objective: to develop approaches which provide an objective evaluation of the psychological support of patients at all stages of treatment.

Method: We used the next methods: diagnostic test of asthenia, test “Choose the correct face”, diagnostic scale of anxiety CMAS for the children, diagnostic scale of personal anxiety, diagnostic test of fears, Luscher color test. Statistical data processing was done using the software package SPSS for Windows. The experimental part of the research was done from 2003 to 2010. We examined 150 children of age 4–16 who received polychemotherapy for acute lymphoblastic leukaemia.

Results: We have identified 3 clinical groups and developed recommendations for correction of mental and emotional state in accordance with the findings: 1. Compensated psychological group. Children of this group have the minimal manifestations of psycho-emotional disorders. They need only planned consultative support for the prevention of potential behavioral problems; 2. Decompensated psychological group. The dysontogenetic manifestations have not reached a pathological level and could be corrected successfully with timely psychological support. 3. Decompensated psychological group. Children of this group need the multifunctional and prolonged intervention program because they have the most significant dysontogenetic changes in emotional sphere.

Conclusion: Oncological diseases have a dramatic stressful effect for children and their parents. But children don’t receive adequate psychological support during the transition from in-patient to out-patient treatment. We have developed the extract outpatient’s card of psychological condition of the patient during the transition to out-patient treatment. Preliminary analysis of the results of the organization of psychological support in accordance with selected criteria stratification displayed the effectiveness of the method.

Pub023

SECOND MALIGNANT TUMORS IN CHILDHOOD CANCER SURVIVORS: A CENTER’S TWENTY YEAR EXPERIENCE

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Purpose: The 20-year cumulative risk of secondary malignancies in childhood cancer survivors is reported as 3.2%. The aim of this study is to evaluate the secondary malignancies observed in a center in twenty years.

Method: 1500 childhood cancer survivors treated between 1990 and 2010 in the Istanbul University, Oncology Institute were evaluated for secondary malignancies.

Results: 19 second malignancies were identified in 18 childhood cancer survivors (median time-6 years). These were: 5 AML, 2 malignant nerve sheath tumors (MNST), 8 sarcomas, 2 breast cancers, 1 meningioma, 1 renal cell carcinoma (RCC). AML was diagnosed in 5 children in a median of 22 months (13–60 mo): the primary diagnosis were Ewing sarcoma, osteosarcoma, non-Hodgkin lymphoma, neuroblastoma and ALL. Two children with medulloblastoma and neuroblastoma developed MNST in the radiation field after 9 years. An Ewing sarcoma patient developed secondary AML after 6 years, an osteosarcoma patient developed breast cancer after 8 years, an ALL patient developed Ewing sarcoma after 3 years, a mesenchymal chondrosarcoma patient developed breast cancer after 11, osteosarcoma after 16 years, none in the radiation field. A leiomysarcoma and an osteosarcoma developed in two bilateral retinoblastoma patients both after 14 years, a meningioma developed in a retinoblastoma patient after 11 years, a fibrosarcoma developed in a rhabdomyosarcoma patient after 6 years and a sarcoma developed in a patient with nasopharyngeal carcinoma after 3.5 years; all in the radiation field. An osteosarcoma developed in another bilateral retinoblastoma patient after 4 years. RCC was diagnosed in a child with neuroblastoma after 8 years. Two patients with breast cancer, six with sarcoma, one with AML, one with RCC are alive.

Conclusion: The risk of secondary malignancies in our series is 1.2% and has increased within years. Since, the risk of second malignancies is associated with the cumulative dose of some chemotherapeutics, the radiation dose-field; the use of minimal therapy that has the maximum efficacy is important.

Pub024

THE FIRST REPORTED PRIMARY HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) OF CHINESE CHILDREN IN HONG KONG

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Purpose: To assess the presenting clinical features, treatment and outcome of HLH in Hong Kong.

Method: Retrospective chart review of the presenting clinical features, laboratory findings, treatment and outcome.

Results: From 1991 to 2010, there were 10 patients with HLH in our centre. The median age was 5.5 years of age (0.1 to 14). Male to female ratio was 1:4. The presenting clinical features were persistent fever (n = 10), skin rash (n = 8), jaundice (n = 5), lymphadenopathy (n = 5), hepatoplenomegaly (n = 10), convulsion (n = 2), somnolence (n = 1), elevated bilirubin (n = 7) and liver enzymes (n = 9). Haemophagocytosis was found in bone marrow (n = 10) and lymph nodes (n = 2). Five patients were investigated for perforin gene mutation. In one patient (age = 0.1), the result showed that there was heterozygous one base pair deletion 65 deletion C in exon 2 of both our patient and her father. There was another mutation 853–855 deletion AAG in exon 3 of patient and her mother. Collectively, the patient had compound heterozygous mutations in perforin gene, 853–855 deletion AAG and 65 deletion C. One patient had spontaneous remission without treatment and one patient died before treatment. Two patients who were treated with VP16, ARAC, and Danonarubicin, or VP16 and methyprednisolone died. One patient received VP16 and dexamethasone and had complete remission without recurrence. Four patients received HLH-2004 protocol (VP16, dexamethasone and cyclosporine A), achieved complete remission but two relapsed and died after further treatment. The infant with perforin gene mutation had CNS involvement of HLH (MRI and CSF cytology showed evidence of HLH). This patient received HLH-2004 treatment. There was transient improvement and then disease progression again. She received double unit cord blood transplantation. She died of severe veno-occlusive disease. The overall survival of this group of patients was 40%.

Conclusion: HLH is rare and life-threatening disease. We report the first patient in Chinese with primary HLH disease (perforin gene mutation).

Pub025

A RARE DIAGNOSIS OF SYSTEMIC MASTOCYTOSIS WITH ASSOCIATED CLONAL, HAEMATOLOGICAL NON-MAST CELL LINEAGE DISEASE (SM-AHNMD) IN A 14 YEAR OLD FEMALE

Tatian pestini

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Purpose: Systemic mastocytosis can occasionally be associated with a non mast cell malignancy, usually of myelogenous origin, such as Acute Myeloid Leukaemia (AML). This subtype of mastocytosis is classified as Systemic mastocytosis with associated clonal, haematological non mast cell lineage disease (SM-AHNMD). To date, the literature reports SM-AHNMD predominantly in the adult population.

Method: We describe a 14 year-old female initially diagnosed with Acute Myeloid Leukemia. The patient was treated using the Children’s Oncology Group protocol AAML1051. A feature of each cycle of therapy was recurring splenomegaly. The splenomegaly appeared to show a temporal relationship to febrile neutropenic illnesses and clinical improvement with high dose antifungal therapy. Radiology suggested focal changes in the spleen resembling fungal infiltrate. A spleenectomy was undertaken after the cycle Intensiﬁcation 1 in an attempt to remove the possible recurring focus of fungal infection.

Results: Analysis of the splenic cells showed the presence of abnormal hypogranulated mast cells, and a notable absence of residual AML cells or fungal pathogens.

Using mutation speciﬁc PCR analysis, the presence of the D816V mutation (C-kit) in exon 17 of the Kit gene in the mast cells was evident. Evaluation of bone marrow samples demonstrated the presence of the same abnormal mast cells containing the C-kit mutation. A wider diagnosis of SM-AHNMD was made at this point.

Conclusion: AML in the context of SM-AHNMD with C-Kit mutation has a poorer prognosis than AML alone. Treatment challenges were intensiﬁed by the lack of literature regarding paediatric management of this condition. The tyrosine kinase inhibitor, Dasatinib was enlisted to address the C-kit containing mast cells, and a matched unrelated cord blood transplant occurred to increase the chance of AML cure. Currently the patient is well 15 months post completion of treatment.

Pub026

EVALUATION OF MYOCARDIAL FUNCTION AS A REFLECTION OF LONG TERM ASSESSMENT OF IMPROVED QUALITY OF LIFE IN CHILDHOOD ACUTE MYELOID LEUKAEMIA TREATED AT A SINGLE INSTITUTION

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Purpose: Background: Anthracyclines are effective in (AML) treatment. It is limited by its cardiotoxicity. Echocardiography is standard in assessing cardiac function by measuring
shortening fraction (SF). Objectives: Determine long-term anthracycline-induced cardiotoxicity by evaluations of SF of survived AML patients.

Method: Retrospective review of AML patients from 1985–2010. Patients were grouped according to type of anthracycline received. Group 1 treated (1985–2002) treated with Daunorubicin as the only anthracycline (n = 9). Group 2 (2003–2010) treated with 2courses Daunorubicin and 1 course Mitoxantrone (n = 20). Cumulative anthracycline dose received 450 mg/m². Anthracyclines infusions were over 6 hours. Sex, age, duration, and serial SF% were analyzed.

Results: 29 AML patients survived. Mean age was 6 yrs (8 mo.–12 yrs), M: F ratio 16:13, mean follow up 5 yrs (3–13 yrs) 24 patients had serial SF evaluated. Group 1 (n = 7) had normal SF (<30%) at baseline and on follow up with no clinical or subclinical cardiotoxicity. Group 2 (n = 17) had normal SF at baseline. However, one patient had WHO grade 2 cardiotoxicity with SF of 23.6% at follow up. Three patients in group 2 had Downs syndrome with no evidence of cardiotoxicity. The cumulative anthracycline cardiotoxicity was 1/29 (3.4%). Patients in group 1 had no toxicity while patients in group 2 had 1/20 (5%) cardiotoxicity.

Conclusion: Children with AML receiving cumulative dose of 450 mg/m² in our population had low frequency of anthracycline cardiotoxicity at 5-year follow up. Our study suggests that frequency of anthracycline cardiotoxicity is not increased in our population compared to reports from other ethnic groups.

Pub029

PRIMARIO GASTROINTESTINAL NON-HODGKIN LYPHOMA IN A RENAL TRANSPLANT RECIPIENT CHILD

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Purpose: Increased cancer risks are well documented in adult organ transplant recipients. However, the risk in the pediatric organ transplantation is less well described. Nearly 7% of pediatric solid organ recipients develop a premalignant or malignant tumour during follow up. Non-Hodgkin lymphoma (NHL) typically appear during childhood and deserve short-term attention.

Method: Here we present a girl who developed EBV associated NHL after renal transplant. Problems related to managing a child with transplant and cancer are discussed.

Results: A 9 year old girl was diagnosed as chronic renal failure secondary to vesicoureteral reflux and was put on peritoneal dialysis 4 years ago. She was transplanted from her mother 2 years later and was on immunosuppressive treatment (prednisolone, MMF and tacrolimus). Three months after her transplant, she was admitted to hospital because of weight loss. Ultra sound showed intestinal wall thickening and lymphadenopathy. While she was investigated, she developed severe abdominal pain and was operated because of gastric and colon perforation. Gastric resection, gastrectomy, colon resection, ileostomy and parastomal omentectomy was performed emergently. Pathology showed EBV positive diffuse peripheral B cell NHL. NHL-BFM 95 protocol was given consequently, but after first course as she developed severe febrile neutropenic period resulting near death, rituximab therapy (6 courses, dose: 375 mg/m²) and intravenous immunoglobulin therapy were treatment of choice thereafter. During chemotherapy, she had no renal problem, while infection and tissue defect around gastrectomy area were the main complications. She is in full remission for 2 years now.

Conclusion: NHL risk is greatly increased after renal transplantation. Two mechanisms of lymphogenesis are suspected: one is related to primary EBV infection in the context of intense immunosuppression and another dysregulated lymphoid proliferation in prolonged immunosuppression. This case emphasizes the need for clinical awareness of increased risk of NHL in renal transplant recipients.

Pub030

A SINGLE CENTER STUDY OF LATENT EBstein-Barr VIRUS INFECTION IN Hodgkin lymphoma IN children and adolescents

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Purpose: There is increasing evidence that latent Epstein-Barr Virus (EBV) infection can play a role in pathogenesis of Hodgkin Lymphoma (HL). Research studies performed on pediatric populations still reveal equivocal results. That is why studies on latent EBV infection in children with HL are performed.

Method: Among 74 patients treated for HL from 1997 to 2004, 61 patients with available paraffin embedded diagnostic tissues were enrolled in this study. In each case histopathological types were verified and detection of latent EBV infection was performed with use of immunohistochemical (latent membrane protein, LMP-1) and molecular (EBV encoded RNA, EBER) method. Clinical data, treatment results and laboratory tests results were based on medical documentation. Statistical analyses were performed with use of Statistica software.

Results: Latent EBV infection was identified in 44.3% of patients. Latent EBV infection was more frequent in boys and in country children. It was more frequently observed in children with night sweats, less advanced disease and lower leukocyte count present. Influence on immunological outcomes (lower IgM concentration and PWM response) was observed as well. Significantly lower ESR values and lower LDL activity were observed in patients with latent EBV infection after 3 chemotherapy cycles which suggests a faster disappearance of
inflammatory reaction associated with HD and decreased disease activity in this group of patients. No influence of latent EBV infection on treatment results was identified.

Conclusion: Latent EBV infection influenced some of clinical and laboratory parameters in this group but did not influence the therapy results.

Pub031
TREATMENT AND SURVIVAL IN MEXICAN PEDIATRIC PATIENTS WITH DIAGNOSIS OF RHABDOMYSARCOMA IN THE NATIONAL INSTITUTE OF PEDIATRICS
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Purpose: To analyze prognosis in regards to treatment and overall survival in patients with RMS from our institution.

Method: A retrospective analysis was done in those children with the pathologic diagnosis of RMS registered at our institution from 2002 to 2010. Results: A total of 34 patients were included in the study. 44.1% were female and 55.9% males. The average age was 10 years, in 47% of these children the histology was embryonal and in 53% alveolar. Favorable anatomic site of presentation was documented in 62% of the embryonal type, while those with alveolar histology had a favorable site in only 33.3%. Forty one of the patients were stage IV, 52.9% stage III and 2.9% with stage I and II respectively. A total of 71% of the patients were treated with IRS IV protocol while 21.8% with IRS III protocols. Four patients (12.5%) were treated with other protocols. In order to compare the different results was analyzed by comparison of survival curves and by Cox regression analysis.

Conclusion: There is a need to perform prospective studies with a significant number of patients to make more definitive conclusions on the impact of treatment modalities.
transplant, time to neutrophil and platelet engraftment, length of hospital stay, transplant related complications and survival was collected.

Results: 53 procedures were performed on 29 patients. 25 (47%) procedures were performed on girls. 28 (53%) of procedures were performed in 2009 and 2010. 10 different conditioning regimes were used for 11 different diagnostic entities. Median age and weight at transplant was 10.55 years (range 2.37−17.37) and 36 kg (range 11.6−89.8) respectively. 9 (17%) procedures were performed using bone marrow, 1 (2%) using umbilical cord and 43 (81%) using peripheral blood stem cells. 100% patients achieved neutrophil and platelet engraftment. The median length of hospital stay was 10 days. 1 year overall survival was 66%. There were 5 patient deaths, 4 due to recurrent/progressive disease and 1 transplant related death. Median length of follow up was 18 months (range 2−96 months).

Conclusion: Autologous transplant has been successfully used to treat a wide variety of conditions in children and young adults. Transplant related mortality is very low. There has been a shift in the indications for the procedure and there is a trend to increasing use of this form of treatment.

Pub036

CHILD RHABDOMYOSARCOMA: ABOUT SALAH AZAIEZ INSTITUTE PATIENTS

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Purpose: Embryonal rhabdomyosarcoma (RBD) is the most common mesenchymatous tumor in child. It have the best prognosis compared with others types of RBD. It is notably associated with urinary, gastrointestinal and genitourinary tract.

Method: We reviewed retrospectively the files of 68 patients treated for RBD from 1990 to 2007 to identify epidemiological, clinical characteristics and therapeutic results. We will also study prognostic factors which will specify therapeutic strategy.

Results: Mean age was 9 y. Sex-ratio was 1.26. Sites of involvement were: head and neck (36%), genitourinary tract (34%), extremities (14.7%) and retroperitoneum (11.7%). Swelling was the major revealing sign in 70% of patients. Tumor size was more than 5 cm in 60% of patients. Histologic types were: embryonal in 56 cases (82%), alveolar in 11 cases (16%) and pleomorphic in 1 case (2%). A right uterine metastasis was found in 34% of patients. Lung was the most frequent site (43%), followed by lymph nodes (34%) and bone marrow (25%). 25 patients (37%) underwent initial surgery. Among them 5 (38%) underwent a RBD. Second surgery was realised in 13 patients (19%). Among them 5 (38%) underwent a RBD.

Conclusion: Early diagnosis is needed because the majority of our patients had advanced stage initially. Therapeutic strategy must be specified by prognostic factors.

Pub037

PAPILLARY THYROID CARCINOMA OF CHILDREN, TREATMENT AND RESULTS

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Purpose: To develop adequate strategy of diagnostics and treatment of children papillary thyroid carcinoma (PTC).

Method: 258 children (4–16 years) from 1971 to 2009 have been included in research. In 166 children (from 1971 to 1999): metastasises to limphonodes or lateral trigonum of the neck were found out 104 (62.7%), in an average line in 74 (44.6%). Metastasises in lungs have been revealed initially in 14 (8.4%) and during dynamic supervision already in 40 (24.1%) patients. In 92 children (from 1999 to 2009): metastasises to limphonodes or lateral trigonum of the neck were found out 109 (84%), in an average line in at 109 (84%). Metastasises in lungs have been revealed initially in 7 (8%) and during dynamic supervision already in 32 (35%) patients.

Results: Among primary patients till 1999, relapses PTC was 29%, and after -3%. Decreased level of relapses was associated with use more aggressive surgical treatment tactics of thyroidectomy as monofocal tumours in the size more than 1 cm. see with obligatory removal central limph dissection, and under indication removal of other groups neck of lymph nodes.

Conclusion: Treatment PTC have to be aggressive (Thyroidectomy as tumor more than 1 cm. in diameter, radical operation on a lymphatic collector of a neck, radioiodotherapy, suppressive hormonal therapy).

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TREATMENT OUTCOME OF EWING SARCOMA FAMILY OF TUMORS WITH VINCRISTINE, DOXORUBICIN, CYCLOPHOSPHAMIDE, AND DACTINOMYCIN (VACA): A DECAD'S EXPERIENCE IN NORTH INDIA

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Purpose: In recent years, the onus of managing bone tumors in children has shifted to pediatric oncologists. Protocol based treatment has resulted in impressive survival rates. In this brief communication, we share our experience in managing children with Ewing Sarcoma Family of Tumors (ESFT), seen over a period of 10 years, in a single tertiary care institution.

Method: Data from children with ESFT treated between 2000 and 2008 was reviewed. The median age group was 7 years, M:F ratio was 1.81. The majority (28 cases) were Ewing tumor. Osseous tumors were predominant (29 cases) and lesions were common in rib (31%), and pelvis (24%). In extraneuous tumors, lesions were predominantly seen in thorax (33.3%) and parasral region (27.2%). The major symptoms were swelling (75%), pain (41%) and fever (36%). Local and distant metastasis was observed in six & five cases respectively. Three children died within days of diagnosis, two were disease related (superior mediasinal syndrome), one due to Pseudomonas sepsis. 22 (55%) children were treated with VACA protocol. Six children defaulted treatment. Of sixteen children who completed therapy, thirteen attained complete response and three had partial response. Complete surgical resection was possible in five cases (out of fourteen cases), in remaining eight patients local radiotherapy was given. Two children received no local therapy. Treatment failure due to relapse/progressive disease/default was seen in 16 out of 22 cases. 10% of children (four cases) have completed therapy and have been disease free for a median period of 45 months (range 32-76 months).

Conclusion: Deaths were due to disease rather than treatment. Patients have sought medical attention in advanced stages. High rate of relapse and progressive disease indicates undetected metastatic disease, as comprehensive and desirable staging investigations were limitted.

TREATMENT FOR DIFFUSE INTRINSIC PONTINE GLIOMA, EXPERIENCE OF M. D. ANDERSON CANCER CENTER

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Purpose: The biology of diffuse intrinsic pontine glioma remains poorly understood and the dismal prognosis has not been changed despite various attempts to add chemotherapy to standard radiation. Method: We conducted a retrospective chart review of patients with diffuse intrinsic pontine glioma treated at M.D. Anderson Cancer Center from 1998 to 2010, and analyzed the data comparing drug effects aiming to generate hypotheses.

Results: 64 patients had diffuse intrinsic pontine glioma as confirmed by radiology review. 28 were male, and age at diagnosis ranged from 1.5 to 16.5 years. All patients received radiation as initial treatment, and 44 had additional treatment during the radiation, with a total of 15 different drug combinations obtained from 15 different individual drugs. The median overall survival after diagnosis was 0.79 years (SD 0.125). Patients treated with the anti-inflammatory agent fucosidin had inferior survival (p = 0.00002).

Conclusion: Based on these data, we hypothesize that inflammatory/reactive processes in the tumor might play a beneficial role during radiation and suggest that this be tested in animal models.

IMMUNOPHENOTYPING SUBSETS IN ACUTE LYMPHOBLASTIC LEUKEMIA AND THEIR RESPONSE TO INDUCTION CHEMOTHERAPY

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Purpose: Expression of myeloid and other markers in acute lymphoblastic leukemia (ALL) is well known. We have analyzed the immunophenotyping subsets and their response to Induction chemotherapy.


Results: Twenty seven children had B-ALL, median age 10 yr(range 1.5–18 yr), M:F 2:4:1. Median total count at diagnosis 9500/cumm (range 1000–148500). Positive markers were
The protocol utilized for SR-ALL was developed jointly by the co-authors with professional advice and diagnostic support (flow cytometry and pathology) by the Pediatric Hematology-Oncology Department at Gemelli Hospital (Rome, Italy). The Cure2Children Foundation (Florence, Italy), in addition to professional advice, provided web-based data management, computerized treatment plans, and most of the financial help for family support, drugs and local visits of professionals from Italy. For the 25 evaluable SR-ALL, the only group that can be meaningfully analyzed, at a median follow up of 361 days (range 6–943) the actuarial event-free survival is 84%.

PUB045
INITIAL RESULTS OF THE MANAGEMENT OF PEDIATRIC MALIGNANCIES IN KOSOVO AUTHOR: ABRASHI B
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Purpose: Presentation of the Initial results of the management of Pediatric malignancies in Kosovo. Since August 15 2008 the Pediatric Hematology-Oncology Service at the University of Pristhana has been offering curative treatment to children with malignancies

Method: The protocol utilized for SR-ALL was developed jointly by the co-authors with professional advice and diagnostic support (flow cytometry and pathology) by the Pediatric Hematology-Oncology Department at Gemelli Hospital (Rome, Italy). The Cure2Children Foundation (Florence, Italy), in addition to professional advice, provided web-based data management, computerized treatment plans, and most of the financial help for family support, drugs and local visits of professionals from Italy. For the 25 evaluable SR-ALL, the only group that can be meaningfully analyzed, at a median follow up of 361 days (range 6–943) the actuarial event-free survival is 84%.

Results: All 91 patients were registered as of December 31, 2010, representing approximately 30% of the expected childhood cancer case load in Kosovo based on an incidence of 150 new cases per million under 20 years of age. Of these, 62 (65%) received chemotherapy entirely locally: 27 standard risk acute lymphoblastic leukemia (SR-ALL), 10 Wilms tumor (WT), 5 Hodgkins disease (HD), 1 non-Hodgkins lymphoma (NHL), 2 histiocytosis, 1 colon adenocarcinoma, 1 osteosarcoma, 3 extracranial germ cell tumors (GCT), 5 low-grade gliomas, 2 medulloblastoma, 1 ependymoma, 2 rhabdomyosarcoma (RMS), 1 neuroblastoma (NBL).

Conclusion: Hematology/ oncology unit in Kosovo could provide chemotherapy treatment based on designed protocols. The total amount of financial aid required for this start up phase was in the range of 60,000 USD. This amount did not cover medical personnel or structural costs, as well as most consumables and diagnostic tests. A total of 13 needy families entered a support program with house visits and a monthly allowance in the range of 200 USD.

PUB046
SEVERE SYSTEMIC INFECTION MASKING UNDERLYING CHILDHOOD LEUKEMIA
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Purpose: In about 2% of cases of childhood acute lymphoblastic leukemia (ALL), clinical presentation of leukemia may be preceded for up to 9 months earlier by a transient, remitting phase of nonclassical aplastic anemia. It is usually associated with an infection, mostly bacterial. We describe a series of 4 cases, with such a clinical presentation, managed in a single tertiary care institution.

Method: Retrospective analysis of case records, of children who had presented in the period between 2008–2010, with infection and pancytopenia and had later evolved into acute leukemia.

Results: All 4 children presented with systemic infection and pancytopenia, one child had recurrent such episodes. Notably all were males and head & neck region was the common primary site of infection. Infections were predominantly bacterial, one had fungal sinuitis. Bone marrow examination during pancytopenia showed variable cellularity with increased reticulina fibrosis. After a latent period ranging from 6 weeks to 6 months, all 4 children evolved into acute lymphoblastic leukemia.

Conclusion: Children with infection & pancytopenia should be kept under strict surveillance as hematopoietic malignancies can evolve with time.

PUB047
UNDIFFERENTIATED EMBRYONAL SARCOMA - A MIMIC OF HYDATID CYST: A CASE REPORT
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Purpose: Undifferentiated embryonal sarcoma (UES) is an uncommon entity. We report a child with UES who survived a stormy per-operative and post-operative period, completed therapy and is currently well.

Method: Case report: An 8 year old girl presented with abdominal pain and fever for 2 months. A CT-scan had revealed a cystic lesion in the right lobe of the liver, for which she had been started on oral albendazole. Hydatid serology was negative and FNAC of the cystic fluid was inconclusive. Repeat CT-scan showed a multi-loculated cyst (11×9.6×7.5 cm = 835 ml) arising from the superior surface of the right hepatic lobe. At our centre, exploratory laparotomy was done for suspected hydatid cyst and excision was attempted. Intraoperatively, spillage of the cyst fluid caused shock requiring aggressive resuscitation with fluids and inotropes, for which only biopsy could be done. Histopathology revealed a malignant tumor with oval, spindle-shaped, stellate and pleomorphic scattered giant cells, loose myxoid stroma and many mitotic figures, suggestive of UES. Post surgery PET-CT showed a very large cystic mass lesion (1400 ml) with no distant metastases.

Results: The patient was started on IRS-V protocol of chemotherapy for undifferentiated embryonal sarcoma (Group III). Restaging CT-scan after 4 VAC cycles showed a decrease of the mass volume to 280 ml. Four additional VAC cycles were given. Because of a volume increase to 440 ml, a second-scan for liver lobectomy was performed. Histopathology showed total resection of an extensively necrosed tumor. She received 4 cycles of VDCE post-surgery. She is now well and disease-free 2 months post completion of treatment.

Conclusion: UES can mimic hydatid cysts and should be considered in the differential diagnosis of cystic liver lesions. Surgical resection can be difficult.

PUB048
GASTRIC ADENOCARCINOMA IN 15 YEAR OLD BOY WITH AUTOSOMAL RECESSIVE AGAMMAGLOBULINEMIA
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Purpose: We wish to highlight the importance of an early endoscopy in patients with primary immunodeficiency who present with gastrointestinal and/or hematologic abnormalities in order to diagnose chronic atrophic gastritis and/or helicobacter pylori infection prior to the development of gastric cancer.

Method: A 15 year old boy suffering from autosomal recessive agammaglobulinemia (RAGM Defect) underwent endoscopy because of unexplained severe stunting, malnutrition (BMI -3.43 SDS), abdominal pain and diarrhea. Magaloblastic anemia had been diagnosed three years earlier and Vit B12 supplementation had begun but an endoscopy had not been initiated. Intravenous immunoglobulin substitution had been carried out inconsistently by the parents.

Results: Esophagogastroduodenoscopy revealed a massive antro pyloric stenosis, histology showed an invasive ulcerating moderately differentiated gastric adenocarcinoma of the intestinal type and chronic atrophic corpus gastritis type A. The patient underwent gastroectomy, extended lymphadenectomy, and transmesocolic interposition of a jejunal parallel pouch to maintain oesophago gubodenal passage. Tumor classification: pT3, pN0 (0/8), pM1 (peritoneum). Oral feeding commenced and is currently supplemented by TPN at night via Broviac catheter.

Conclusion: Endoscopy is mandatory in patients with hereditary immunodeficiencies who present with gastrointestinal symptoms and/or hematologic abnormalities in order to diagnose and treat tumours with radical surgery before metastatic spread has occurred. Despite the fact that gastric cancer is a rare disease in patients with primary immunodeficiencies one should keep in mind that an early endoscopy might prevent the development of a gastric cancer if chronic atrophic gastritis and/or helicobacter pylori infection are detected early in these patients and treated appropriately. It needs to be discussed if endoscopy should be carried out routinely in these patients.

PUB049
THE RELATIONSHIP OF LYMPHOCYTE SUBSETS IN BONE MARROW AT PRESENTATION IN PEDIATRIC SMALL ROUND CELL TUMORS
Conclusion: Our study has found dependence of bone marrow lymphocyte composition on \( \text{C6} \) (CD56+ CD3-), comparing to healthy children: 26.9% sarcomas had lower proportion of CD4+ T-cells and higher proportion of natural killers.

Purpose: To study the role of T-cell, NK and B-cell in immune defense mechanism and to develop the new approaches for immunotherapy.

Method: We analyzed the subsets of lymphocytes in bone marrow in 34 children (male - 19, female - 15) with solid tumors (rhabdomyosarcoma - 18 and Ewing family sarcomas - 16), age - 1 - 16 years. The control group has included 15 patients without cancer. During this study, we investigated bone marrow morphology and immunology, including T-cell subsets, NK cell and activated lymphocytes.

Results: Statistically significant difference in bone marrow lymphocyte subsets was shown between patients with tumors, comparing to control group, and in the patients with different cancers. Patients with Ewing family sarcomas showed significantly higher proportion of cytotoxic lymphocytes (CD3+ CD8+) comparing to cancer-free children and to patients with rhabdomyosarcoma: 68.5 ± 3.1% (n = 16) vs 50.5 ± 2.4% (n = 14) vs 50.5 ± 3.9% (n = 16), respectively; > 0.000 0.01, respectively. Additionally, the patients with Ewing family sarcomas had lower proportion of CD4+ T-cells and higher proportion of natural killers (CD56+ CD3-), comparing to healthy children: 26.9 ± 3.5% (n = 16) vs 39.3 ± 2.8% (n = 14); 18.0 ± 3.7% (n = 14) vs 9.4 ± 1.7% (n = 12), respectively; > 0.001 and > 0.049, respectively. Children with rhabdomyosarcoma showed characteristically higher TCR-0/7 T-cells, comparing to healthy individuals: 15.8 ± 1.6% (n = 11) vs 9.2 ± 1.4% (n = 11), > 0.007.

Conclusion: Our study has found dependence of bone marrow lymphocyte composition on cancer type in children with small round cell tumors.

Purpose: Introduction: Aggressive treatments increased childhood malignancies cure rates. Approximately 70% of these patients are long-term survivors with risk of second malignant neoplasm (SMN), related to treatments and/or genetic susceptibility.

Method: Medical record review.

Results: An 18 years old boy with posterior fossa medulloblastoma at 11 years old was treated with surgery, cranio-sinal radiotherapy (24 Gy) and Packer’s chemotherapy. At 14 he had an asymptomatic local recurrence and underwent surgery, local re-irradiation and high-dose chemotherapy. Six months later, he was treated with a long course of high doses steroids because symptomatic radiation necrosis. At 17 years he developed bone pain, fever and thrombocytopenia; bone scan showed intense hyperfixation on the 4th right rib and on left femur, suggestive of metastases. Bone MRI showed bone lesion on the anterior face of 4th right rib, with necrosis of the left femoral head and multiple bone infarcts on femurs and tibias. Rib biopsy showed a high-grade chondrosarcoma. Because the doubt about metastatic chondrosarcoma he started chemotherapy (IFO/Doxo) complicated with psychotic delusions and severe pulmonary aspergillus/candidiasis treated with liposomal amphotericin B and voriconazole. Staging workup failed to show any evidence of metastases (including bone marrow) and he was submitted to surgery (pathology showed at this time a low grade chondrosarcoma with microscopic residue) followed by local radiotherapy. Now he is in complete remission, with right hemiparesis, without pulmonary or cognitive deficit, and was proposed for head femoral prosthesis in order to can walk again.

Conclusion: A long term follow up with accurate suspicion of new neoplastic lesions are crucial for early diagnosis and appropriate treatment of SMN. A great clinical complexity associated with difficult exams interpretation can be hazard in patients with primary tumor and treatments sequel. In this patient bone lesions in a previous malignancy setting, made the differential diagnosis of metastasis, an important point with treatment implications.
**TREATMENT OUTCOME OF OSTEOSARCOMA IN A SINGLE INSTITUTION IN A DEVELOPING COUNTRY**

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Purpose: There are many challenges that face treatment of children with Osteosarcoma in developing countries. Delay in diagnosis results in large metastatic tumours unlike those seen in developed countries. New strategies are required to address this problem. The aim is to evaluate the treatment outcome of children treated for osteosarcoma in a single institution.

Method: Retrospective analysis of all patients admitted in the Paediatric Oncology Ward in a tertiary level, referral hospital in Pretoria, South Africa from the 1st of January 2001 until 31st of December 2009. All patients that were admitted during this period were reviewed. Information obtained included the primary site, laterality, stage of the disease at presentation, time from first symptoms to definitive treatment, treatment offered and outcome.

Results: There were 38 patients included in the study. The median age was 137 months (range 72–194), 22 were male patients. The most common primary site of tumour was the distal femur. 50% of the patients (n = 19) had evidence of metastatic disease at presentation. The most common site of metastases was the lung. The time from first symptom to receiving definitive medical care was 6 months, range (2 weeks–14 months). Cisplatin and doxorubicin was the treatment offered as standard of care during this time period. Neoadjuvant chemotherapy was offered in most cases. The survival was only 15% (n = 6). The main cause of death was progression of disease in 30. The treatment related mortality was 5%.

Conclusion: The delay in referral and access to definitive specialised multidisciplinary oncology care remains a challenge in developing countries. Active education programs to the community and health facilities have been improved with a focus on simplifying the referral pathway will be discussed. All patients with a delay in diagnosis should be regarded as having possible metastatic disease and high risk treatment strategies will be adopted for future patients.

**DIFFUSE LARGE B CELL LYMPHOMA IN CHILDREN: CHARACTERISTICS AND OUTCOME**

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Purpose: Diffuse large B-cell lymphoma (DLBCL) is uncommon in children. They are a heterogeneous group of lymphoid neoplasms of mature B cell lineage. It is uncertain if they should be treated on a paediatric protocol or adult-type protocol, where they occur more commonly. We reviewed the characteristics and treatment outcome of DLBCL cases treated in our institution.

Method: A retrospective study of all DLBCL treated from 1997 to 2010 was done.

Results: Eight cases were diagnosed over 13 years, 5 boys and 3 girls with age ranging from 6.5 to 14.8 years and median of 9.9 years. Unusual presentations like acute pancreatitis, ILH, multiple liver masses and persistent lobar pneumonia occurred in 4 cases, as long as 7 months prior to diagnosis of DLBCL. There were 2 boys with mediastinal lymphoma. Other presentations were appendicitis and enlarged cervical lymph node. Two cases were associated with EBV lymphoid granulomatosis. Only one had bone involvement. Initial 2 cases were treated on NHL 9002 protocol and the others were treated on R-CHOP. With a follow-up period ranging 0.9 to 7.5 years (mean 4 years), all are alive, but 2 have relapsed at the original site of disease at 19 and 4 months post treatment. One relapsed in the lung but refused further therapy. She is still alive 2 years later, relatively symptom-free. The other child relapsed in the mediastinum and is currently receiving salvage therapy. He did not respond well to first-line salvage chemotherapy and was given radiotherapy to the mediastinum.

Conclusion: DLBCL presents in myriad ways and diagnosis can be delayed. The treatment outcome in our institution is good; although the numbers are small. Its behaviour can be heterogeneous, as evidenced by one patient who relapsed and is still alive without treatment; and another with aggressive mediastinal disease and poor response to treatment.

**LATE-EFFECTED IN CHILDHOOD CANCER SURVIVORS IN PEDIATRIC SURGICAL CLINIC**

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Purpose: With recent improvements in the diagnosis and multimodal therapy of pediatric malignancies, the number of childhood cancer survivors (CCSs) has been increasing. The importance of quality of life (QOL) of CCs has now been recognized, and the late effects of cancer treatments are essential and important issues. In this study, we aimed to evaluate the late effects of cancer treatments in the CCs followed in the pediatric surgical outpatient clinic.

Method: Among the CCs who received surgical treatment and are followed up in our surgical clinic, 57 patients (age more than 10-year-old; follow up period more than 5 years) were included in this study. They were 25 males and 32 females. The average age was 17 (10–28) years and follow-up duration was varied from 5 to 25 years (mean 14 years). They included 26 neuroblastomas, 12 Wilms tumors, 10 hepatoblastomas, 10 rhabdomyosarcomas, 7 germ line tumors and others. Seventeen patients (25%) received hematopoietic stem cell transplantation (SCT) and 10 (15%) received radiotherapy.

Results: Thirty three patients (58%) had complications. Surgical complications: Fourteen patients received nephrectomy and one of them became renal failure. Two patients with rhabdomyosarcoma received cystectomy with urinary tract reconstruction and one received vaginectomy. Other complications such as, ileus, sclerosis, and leg length discrepancy were seen in some patients. Medical complications: Eight patients showed growth retardation and two treated with GH. Gonadal dysfunction was observed in 16 patients and 6 were treated with gonadal hormone. Low bone mineral density was observed in 7 patients. Other medical deficiency such as hearing loss, and hepatitis were seen in some patients. The rate of gonadal dysfunction and growth retardation were significantly higher in the patients who received SCT.

Conclusion: Treatment-related complications may occur many years after the therapy. Lifetime medical surveillance and continuous follow-up by pediatricians, pediatric surgeons and endocrinologists are necessary.

**EFFICACY OF INCREASING DOSES OF METHOTREXATE FROM 1000 TO 1500 MG/M2 IN PREVENTING TESTICULAR RELAPSE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA**

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Purpose: Evaluate the efficacy of two different doses of methotrexate in preventing testicular relapse in children with acute lymphoblastic leukaemia (ALL). To evaluate adverse events and the incidence of testicular relapse in children with ALL.

Method: This is a retrospective review of the medical records of previously untreated boys under 14 years of age diagnosed with ALL, seen at the Instituto Nacional de Enfermedades Neoplásicas between January 1996 and December 2006. Kaplan-Meier method was used in calculating survival tables.

Results: During the consolidation phase methotrexate was administered in different dosages in an eight hour ambulatory infusion. One group receiving 1000 mg/m2 from 1996 to 2006 and the second group 1500 mg/m2 since 2006. We assessed 854 medical records, of which 203 were excluded for various reasons. 345 patients received MTX at a dose of 1000 mg/m2 and of which 41 (4.8%) relapsed, 33 in the testicles, 7 in the bone marrow and one in the central nervous system and tests. 307 patients received methotrexate at a dose of 1500 mg/m2, of which 23 (7.2%) relapsed, 18 in the testicles and 5 in the bone marrow and the testicles. 80.5% (334/41) of patients receiving the lower dose of methotrexate presented with a late testicular relapse while 52.1% (122/23) in the second group had an early testicular relapse. 23.5% of adverse events (vomiting, diarrhea, mucositis) were seen in the group receiving 1000 mg compared to 13.3% in the group receiving 1500mg. Disease-free survival in the
group receiving 1000 mg is 43.9% at 13 years and 56.5% in the group receiving 1500 mg at 3 years.

Conclusion: The incidence of testicular relapse is 7.5% for the whole group, with a decrease in the relapse rate with the higher methotrexate dose. We recommend an increase in the dose of methotrexate especially in the high risk group.

Puh065

SELF HEALING PROGRAM TOWARDS THE RECOVERY OF TEENAGER CANCER PATIENTS

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Purpose: Indonesian Childhood Cancer Foundation on July 2010, held a Cancer Camp, themed “SELF HEALING” in Sangkaranurip Cirebon, West Java. Participants of this camp were the teenager patients and survivors from some regions in Indonesia. Self-healing program aim to restore the balance of the body.

Method: The method using several simple techniques, such as Taichi (breathing therapy), gratitude massage therapy, healing dance, holding fingers to manage emotions, drawing, and Laughter Yoga.

Results: Such techniques lead patients to release tension tied up in the body, such as anger, sad, or fear or trauma and thus strengthen immune system by raising antibody level. Few testimonies about this camp revealed that self-healing program is beneficial to help cancer patients cope better with certain aspects of their healing treatments. Patients were getting more exposed to the advantages of maintaining positive thinking and how to express feeling of gratitude that drive to peace in body and mind.

Conclusion: Devastating effect on immune system may occur as one is diagnosed having cancer in his/her body. This unexpected shock may thwart off patient from being peaceful which is able to slow down the healing process itself. Other than medical treatments (chemotherapy, radiotherapy and surgery), psychological support is likely to play greater role in giving rise to life expectancy. The more studies on patients at advanced stages reveal those living with positive mind are more likely to get recovery than those perceived holding suppressed emotion. It is said that subconscious mind does have tremendous healing power by accessing the function of hormonal system, immune factors, blood flow, and cellular growth, creating more conducive stimulus to reach optimum health. Such technique is not a replacement to medical treatments, rather to provide psychological support towards the recovery of the patients.

Puh069

PROGNOSTIC SIGNIFICANCE OF RENAL INVOLVEMENT AT PRESENTATION IN CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA: A TERTIARY CARE CENTER EXPERIENCE

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Purpose: Renal involvement at presentation is rare in childhood acute lymphoblastic leukemia (ALL) with extreme paucity of data from developing nations. In this study we describe our management experience with plausible prognostic and therapeutic implications of children with ALL presenting with renal involvement at presentation.

Method: Data obtained from case records of 762 children with ALL managed from 1990 to 2009 was analyzed. Renal involvement at diagnosis was defined as impairment of renal function (oliguria or anuria and elevation of urea and creatinine) or evidence of renal involvement on clinical examination and/or imaging.

Results: 12 patients (1.5 %) had renal involvement at diagnosis. Palpable nephromegaly was present in 1. 1 child presented with gross hematuria. The mean age at presentation was 6.08 ± 2.36 years (range: 1-12 years). The male:female ratio was 5.1. On comparison with other ALL children, there was no significant difference in age (p = 0.9), gender (p = 0.36), symptom diagnosis interval (p = 0.36), bulky disease (p = 0.23), white cell count (p = 0.32) and platelet count (p = 0.89) in the 2 groups. 8 patients opted for therapy. United Kingdom ALL (UKALL) X/XI protocol was used. However, 5 died, 2 relapsed while 1 was lost to follow-up. Survival outcome in this group (median: 8 ± 4 months) was significantly inferior compared to the entire cohort (p = 0.01 by log-rank test). Renal involvement at presentation was a significant predictor of outcome by Cox-matrix analysis (p = 0.034).

Conclusion: Small sample size in our cohort may have precluded identification of risk parameters. Overt renal involvement may plausibly be associated with adverse outcome in resource limited setting indicating need of more aggressive therapy and supportive care with more facilities for renal replacement therapy. Further collaborative studies assessing the molecular, cytogenetic and biological characteristics of ALL with renal involvement are necessary to delineate if renal involvement represents a unique subset of ALL.

Puh060

ACUTE LEUKEMIA AS PREDOMINANTLY USING BLOOD PRODUCT IN PEDIATRIC WARD DR KARIADI HOSPITAL SEMARANG INDONESIA

Pediatr Blood Cancer DOI 10.1002/pbc

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Purpose: To know the trends of utilization of blood Product transfusion in Pediatric Ward Dr Kariadi Hospital during 2008–2010. Analysis used frequency and distribution.

Results: By calculated blood components such as fresh frozen plasma (FFP), thrombocyte concentrate (TC), packed red cells (PRC), pleatelet rich plasma (PRP) and cryoprecipitate, the average requirements of blood components In Dr Kariadi Hospital during 3 last years were 5678 bags/year. There was an increase in the total number during 2008 to 2010: 3751, 6496, 6787 bags respectively. The components most needed was TC 3225 bags, PRC 1683 bags, FFP 295 bags, PRP 224 bags, cryoprecipitate 133 bags and WB 118 bags. Based on the disease diagnosis hematologic disorders (acute leukemia, thalassemia, ITP) were predominant in the blood component using 3.499 bags/year, followed by non surgical (sepsis, DDS, renal disease) 1806 bags, and surgical 311 bags. Acute leukemia needed 2097 bags/year, mainly TC 1680 bags, followed by PRC 333 bags. This result the same in sepsis, which require TC 522 bags, followed by PRC 247 bags.

Conclusion: Acute leukemia was predominant in the blood component utilization in pediatric ward. Thromboocyte concentrate was the most common blood component used.

Puh061

PULMONARY NODULES CHARACTERISTICS AND PROGNOSTIC IMPORTANCE IN EWING SARCOMA

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Purpose: To determine outcome and prognostic effects of pulmonary nodules and its characteristics at presentation or during treatment in patients with Ewing sarcoma.

Method: A series of 71 patients with Ewing sarcoma were evaluated retrospectively. Thorax CT examinations were reviewed by an experienced radiologist. An analysis of demographic, tumor and nodules related variables were performed. Effects of nodule characteristics on outcome of nodules and survival were determined.

Results: There were 45 male and 26 female with a median age of 10.4 years. Pulmonary nodules observed at diagnosis and during treatment in 21(29.5%) and 14 (19.7%) patients, respectively. Age, sex, duration of complaints, primary tumor location and size, chemotherapy regimen, surgical margin and the rate of necrosis were not significantly different in the patients with and without pulmonary nodules. Progression of pulmonary nodules were observed in patients with more than ten nodules (p = 0.568). Patients were followed 3 to157 (median: 45) months. Three year overall survival (OS) and event free survival (EFS) was 62% and 46% in general. In patients without pulmonary nodule at diagnosis, the OS and EFS rates were 77% and 60% respectively. In patients with pulmonary nodule at diagnosis, these rates were 28% and 18% (p = 0.04). The survival rates of patients without pulmonary nodules and with pulmonary nodule which developed during treatment were not different significantly. The EFS rate of the patients with pulmonary nodules less than ten in number was significantly higher than the patients with pulmonary nodules more than ten (p = 0.04).

Conclusion: The data about the outcome of pulmonary nodules and the prognosis of primary disease is not sufficient. Existence of pulmonary nodules at diagnosis has worse prognostic effect on Ewing sarcoma. Studies with large series of patients are needed to conclude the prognostic importance of pulmonary nodules.

Puh062

DISEASE AND THE REASONS OF A CHILDREN'S CANCER IN KYRGYZSTAN.

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Purpose: Studying of disease of a children's cancer in different areas Kyrgyzstan during the period with 2006 for 2010 was the purpose of our research. Studing of possible causal factors which can cause a children's cancer in various areas of Kyrgyzstan.
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SIOP ABSTRACTS

Method: It was studied disease of a children’s cancer during the period with 2006 for 2010 in 7 areas of Kyrgyzstan. By region of Kyrgyzstan have been studied environmental risk factors, which could be cause cancer in children.

Results: CANCER Incidence per 1 million children (0-17 years Kyrgyz) (GB 0-14 years)

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Purpose: To determine the presence of MRD in B-cell lineage ALL by flowcytometry at end of Induction chemotherapy. Our objectives was to determine the presence of MRD in B-cell lineage ALL by flowcytometry at end of Induction chemotherapy, and to ascertain whether level of MRD can predict relapse and relapse free interval.

Method: A detailed history and clinical evaluation was done for all patients. Flowcytometry to detect minimal residual disease. Our objectives was to determine the presence of MRD in B-cell lineage ALL by flowcytometry at end of Induction chemotherapy, and to ascertain whether level of MRD can predict relapse and relapse free interval.

Results: Of 54 patients suspected to have a lymphoreticular malignancy were evaluated. Of these 32 were excluded. 25 patients, diagnosed as B-cell lineage ALL completed induction therapy were evaluated for MRD. MRD < 0.01 was seen in 17 Of these 1 child relapsed. MRD between 0.01-0.1% was seen in 1 patient who is in remission, MRD of level 0.1–1% was seen in 2 patients; of these one child is lost to follow up and other is in remission.

Conclusion: MRD estimation at end of induction therapy may predict the biological behaviors of children with ALL. Children with less MRD may be treated with less intensive protocols and step up therapy may be employed in children with high MRD including early IRT.

Pub966

CLEAR CELL MENINGIOMA -A CASE REPORT

Rania Fehri, Dalenda Hentati, Najat Mahjoub, Lotfi Kochhai, Hatem Friha, Mongi Maalej

Purpose: Clear cell meningioma (MCC) is a rare variant of meningiomas. It is characterized by its aggressiveness. The most common locations of the cancer are in the spinal cord and posterior fossa.

Method: We present the case of a long term recurrence of an MCC in the sacrum after a primitive tumor in childhood.

Results: A 26-year old man operated at the age of 9 years for a meningioma located in the spinal cord of the neck with complete remission. Sixteen years after, he presented with a sacral pain, paresthesia of the lower limbs and sphincter disturbance. A pelvic computed tomography was performed revealing an expansive process on the sacrum. A biopsy showed a clear cell meningioma. The tumor was considered unresectable and was managed by external beam radiotherapy. The tumor was stable on last follow up.

Conclusion: The MCC is a rare histological form of meningiomas. It occurs mainly in children and young adults. It is characterized by its potential of multiple recurrences in the central nervous system, especially in the spinal cord. Surgery is the reference treatment. Radiotherapy is indicated in cases of incomplete resection, tumor recurrence after first surgery or unresectable lesion.

Pub967

MEDULLOBLASTOMA IN CHILDREN: A RETROSPECTIVE TUNISIAN REVIEW

Salah Azizie, Institute, Radiation Oncology, Tunis, Tunisia

Purpose: Clear cell meningioma (MCC) is a rare variant of meningiomas. It is characterized by its aggressiveness. The most common locations of the cancer are in the spinal cord and posterior fossa.

Method: We present the case of a long term recurrence of an MCC in the sacrum after a primitive tumor in childhood.

Results: A 26-year old man operated at the age of 9 years for a meningioma located in the spinal cord of the neck with complete remission. Sixteen years after, he presented with a sacral pain, paresthesia of the lower limbs and sphincter disturbance. A pelvic computed tomography was performed revealing an expansive process on the sacrum. A biopsy showed a clear cell meningioma. The tumor was considered unresectable and was managed by external beam radiotherapy. The tumor was stable on last follow up.

Conclusion: The MCC is a rare histological form of meningiomas. It occurs mainly in children and young adults. It is characterized by its potential of multiple recurrences in the central nervous system, especially in the spinal cord. Surgery is the reference treatment. Radiotherapy is indicated in cases of incomplete resection, tumor recurrence after first surgery or unresectable lesion.
Institute, Tunis, Tunisia. included all the children diagnosed of medulloblastoma from 2000 to 2006 in Salah Azaiz Institute, Tunis, Tunisia.

**Results:** There were included 23 patients, 17 boys and 6 girls, with ages between 2 and 13 years (average age 7.52 years). Main complaints were headaches and vomiting (91.3%) secondary to increased intracranial pressure. Time to diagnosis varied between 2 and 90 days (median 15 days). Cerebellar syndrome was the most common clinical findings (65.2%) with ataxia involving the lower extremities. 60.9% were high risk patients. 47.8% of patients had a complete resection. 47.8% an incomplete resection and one patient biopsy only. Therapy consisted of chemotherapy (65.2%) and radiation therapy (60.9%) for children older than three years of age. Fourteen patients achieved a complete remission. A relapse was diagnosed in the follow-up of 26.1% of the children with a median time to relapse of 12 months (range, 5–33). Sequelae were noted in 27.3% of the survivors, mainly with cerebellar and ocular alterations. Overall 5-year survival rate was 42%, with a median survival time of 32 months. Only risk category was found to significantly influence survival.

**Conclusion:** The survival rate of children with medulloblastoma was poor, and the rate of sequelae was high. Much remains to be achieved in understanding the pathogenesis, critical pathways responsible for medulloblastoma, and molecular risk stratification, and in devising treatment strategies with even better survival and less long-term sequelae.

**Pub070**

**KIMURA DISEASE AS A CAUSE OF PERSISTENT LYMPHADENOPATHY**

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**Purpose:** Kimura disease is a chronic inflammatory disorder of unknown etiology that most commonly develops as painless, unilateral cervical Lymphadenopathy or subcutaneous masses in head and neck region. It is reported to be associated with nephritic disease in 15-19% of cases. There are not many case reports of Kimura disease in children from India. The basis of association is not well understood probably an underlying T cell and related cytokine defect.

**Method:** A 13-year-old child presented to pediatric nephrologist with complaints of swelling in left sub mandibular and post auricular region for 2 months. Patient had been a known case of nephritic syndrome for past 2 ½ years. Prednisolone was stopped 1 month back before the appearance of this swelling. Patient was given antibiotics but no response was observed.

**Results:** Child was referred to us from nephrology clinic. Lymph node biopsy was done which showed marked widening of Para cortical region with follicles in between. The paracortical region showed numerous eosinophils with occasional eosinophilic micro abscesses. Few germinal centres show proteinaceous material. Absolute eosinophilic count was 4400 and IgE levels were 3782. The case was diagnosed as Kimura disease. Child was put on oral dexamethasone for 4 weeks followed by tapering over 2 weeks then 5-day pulse of dexamethasone every month for 6 months was given. Child had recurrence of swelling after 4 months of stopping steroid. Was again put on 5-day pulse of dexamethasone every month and doing fine till date.

**Conclusion:** Kimura disease should be considered in differential diagnosis of cervical Lymphadenopathy.

**Pub071**

**CRITERIA NORM OF IMMUNOLOGY IN SUBPOPULATIONS LYMPHOCYTES OF THE BONE MARROW AT CHILDREN**

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**Conclusion:** To study subpopulations lymphocytes in bone marrow of children at which the diagnosis of malignant tumors has been excluded during carrying out of complex inspection. Method: The characteristic of mature lymphocytes subpopulations (D45 ++), to research among them NK-cells, and also -cytotoxic cells and their subpopulations by three-colored flow cytometric.

**Results:** Our data have confirmed presence of the expressed proportion of mature T-cells (D3 +) in a bone marrow of the child. Heterogeneity of mature T-cells of a bone brain on markers of activation, co-stimulation to molecules and CD57 is established. Feature in B-lymphocytes in bone marrow of children of younger age is presence of expressed proportion D19+CD5 + lymphocytes.

**Conclusion:** This group can serve in the further as group of comparison at carrying out of researches at children sick of malignant tumors.