Purpose: Langerhans Cell Histiocytosis (LCH) is a rare disease characterized by heterogeneous lesions containing CD207+ Langerhans cells and lymphocytes that can arise in almost any tissue and may cause significant morbidity and mortality. After decades of research, the pathogenesis of LCH remains speculative. This study was performed to test the prevailing model of LCH pathogenesis that lesions arise due to malignant transformation of epidermal Langerhans cells (LCs).

Method: LCH CD207+ cells were isolated from LCH lesions, control LCs were isolated from normal skin, and gene expression was compared. Similarly, gene expression in LCH lesion CD3+ cells was compared to gene expression in peripheral blood CD3+ cells from LCH patients with active disease.

Results: Compared to control epidermal CD207+ cells, the LCH CD207+ cells yielded 2900 differentially-expressed probes. Expression of many genes previously associated with LCH, including cell-cycle regulators, pro-inflammatory cytokines and chemokines were not significantly different from control LCs in our study. The study also identified several interesting genes not previously associated with increased expression in LCH including genes involved in regulation of cell cycle (CDC2A, AFF3, SMYD3, HOXB7), apoptosis (BAX, BCL2L1, CFLAR) signal transduction (DUSP4, JAK3, PRKCA, TLR2, TLR4, SOCS3, JAG2), tumor invasion and metastasis/tissue invasion (CEACAM6, MMP1, TGFB1), myeloid cell maturation (DUSP4, CD14, CD14, CD33, ITGA2B, ITGAX, ITGAM, CD300LF) and lymphocyte trafficking (SPP1, VNN1, NRP1, CCR1). A large number of the cells with decreased or absent expression in the LCH-CD207 cells are involved in cell-cell adhesion, including TACSTD1.

Compared to the peripheral CD3+ cells from LCH patients, the LCH lesion CD3+ cells yielded only 162 differentially-regulated probes, and the expression profile of the LCH lesion CD3+ cells was consistent with an activated regulatory T cell phenotype, including increased expression of FOXP3 and CTLA4. SPP1 had the highest relative expression in both LCH lesion CD207+ and CD3+ cells.

IL-17 is a proinflammatory cytokine recently associated with LCH pathogenesis. In this study, IL-17 expression was absent from control and LCH CD207+ cells. Very little IL-17 expression was detected in T cells from LCH lesions, but abundant message was detected from tonsil lymphocytes.

Conclusion: We propose a revised model of LCH pathogenesis in which lesions do not arise from epidermal Langerhans cells, but from accumulation of bone-marrow derived immature myeloid dendritic cells that recruit activated lymphocytes. Until the cell of origin can be identified, perhaps “LCH” should return to “Histiocytosis X”.

Purpose: To describe recent advances in the neurosurgical treatment of low-grade gliomas in children

Method: The author reviewed 5 years of experience with the use of intraoperative MRI, ultrasound, and image-guidance in the surgical treatment of low grade gliomas

Results: These technologies were deemed to be important in the total excision of these tumors in approximately 50% of surgical candidates.

Conclusion: Technological advances in the operating room appear to have led to greater operative safety and improved surgical results

Purpose: To give an update on the molecular genetics and novel targeted therapies in pediatric low grade glioma

Method: Using primary tumor material, in vitro and in vivo models, the understanding of the molecular origin of low grade gliomas in children has recently made significant progress with the identification of BRAF/MEK pathway alterations in a high percentage of pilocytic astrocytoma in children

Results: The first specific mutation identified was the KIAA1549-BRAF fusion protein leading to constitutive activation of the MAPK pathway due to loss of the BRAF auto-inhibitory domain. Subsequently, several other fusion proteins involving BRAF and CRAF as well as activating BRAF mutations were identified pointing towards loss of regulation of auto-inhibition as the common molecular theme in the molecular pathogenesis of pilocytic astrocytoma. Using lentiviral gene-transfer, we for the first time were able to generate a mouse model for pilocytic astrocytoma, that is ideally suited for preclinical testing

Conclusion: As several compounds targeting the BRAF/MEK pathway are clinically available, novel treatment options for pediatric low grade glioma are beginning to emerge

Purpose: Advances in the treatment of rare pediatric cancers are hampered by the low number of patients, which limits the design of effective clinical trials, the use of...
SIOP ABSTRACTS

different systems for staging and definition of risk factors, which restricts options for collaborative trials, and our limited knowledge on their biology, which restricts investigation of new therapies. Successful clinical research initiatives in those malignancies will have to prioritize the development of international collaborations that address those constraints.

Method: The Children’s Oncology Group Rare Tumor Committee is developing overarching initiatives in those areas, with the following objectives: 1) To develop evidence-based international consensus on disease definition and risk stratification that can be employed to identify groups of patients with a homogeneous prognosis and develop risk-adapted strategies that maximize efficacy and minimize toxicity; 2) To develop methodological innovations in clinical trial design for pediatric rare tumors; 3) To develop standard operating procedures that will facilitate the conduct of international intergroup trials and the creation of an international network for the study and research of pediatric rare cancers; 4) To enhance epidemiological and biological studies that may provide etiological and mechanistic information by characterizing the role and interaction of specific environmental, gene, and pathway aberrancies, and leveraging genome-wide approaches to define molecular mechanisms that address those constraints.

Results: Ongoing initiatives in adrenocortical carcinoma, liver tumors, retinoblastoma, and germ cell tumors are being developed exploring this model.

Conclusion: The successful development of international collaborative initiatives that address relevant clinical, epidemiological and biological questions may help advance cure for pediatric rare malignancies.

SL016 ANTIANGIOGENESIS: EMERGING PARADIGMS AND BIOMARKERS

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Purpose: The seminal hypothesis put forward by the late Dr. Judah Folkman in 1971 has resulted in antiangiogenesis as the fourth modality of cancer treatment. The approval of bevacizumab, an anti-VEGF antibody, in combination with chemotherapy, as well as the approval of oral multi-receptor tyrosine kinase inhibitors that include VEGF receptors as one of their targets have changed the practice of oncology for metastatic colorectal, lung, breast, renal cell and hepatocellular carcinomas.

Methods: The approval of this agents has also raised many questions: How do these therapies work in patients? Is their mechanism of action in patients the same as originally envisioned for antiangiogenic agents? Is it the same as demonstrated in animal models? Why is the overall survival benefit so modest? Why do some patients benefit from these therapies and others not? How do we select the former? Why do tumors stop responding? What new pathways should be targeted to prolong the duration of response and survival without increasing toxicities? How do we tailor these new therapies to individual patients? How do we schedule them with existing conventional therapies or other Food and Drug Administration (FDA) approved molecular therapeutic agents?

Results: The answers to these very basic questions are not known for most approved agents and would require sophisticated multi-disciplinary clinical trials tightly integrated with equally sophisticated preclinical studies.

Conclusion: In my presentation, I’ll attempt to answer these questions with our own preclinical and clinical data, present emerging paradigms and biomarkers for personalizing anti-angiogenic therapy for cancer and other diseases, and speculate where this nascent field is heading in the next several decades for the treatment of cancer and other diseases.

SL020 THE QLIC-ON STUDY: MONITORING HEALTH RELATED QUALITY OF LIFE IN CHILDHOOD ONCOLOGY – PROVIDING PATIENT REPORTED OUTCOMES TO PEDIATRIC ONCOLOGISTS IN CLINICAL PRACTICE

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Purpose: Children with cancer can experience health related quality of life (HRQOL) problems. These problems are not always systematically discussed by their pediatric oncologist. Aim is to develop a patient reported outcome (PRO) intervention to make pediatric oncologists aware of HRQOL problems, and to study the effectiveness of this PRO intervention in terms of patient management (advice), satisfaction, communication and feasibility.

Method: In a multicenter sequential cohort study (QLIC-ON: Quality Of Life In Childhood Oncology) children with cancer participated immediately after end of treatment (control period: March 2006–January 2008, intervention period: January 2008–November 2009). Shortly before the first three follow-up consultations with the pediatric oncologist, the child (8–18 years) or parent (about children aged 0–7 years) completed a digital HRQOL questionnaire. Results of this questionnaire were summarized per item and in graphs on the QLIC-ON PROfile. The QLIC-ON PROfile was presented to the pediatric oncologist in the intervention group during the consultation to facilitate communication about HRQOL issues. To maximize the effect pediatric oncologists received a training beforehand. The three consultations were evaluated afterwards with questionnaires for the child, parent and pediatric oncologist. One third of the consultations were audio taped. First analysis concerned t-tests.

Results: 272 children with cancer were approached, 191 participated (response 70.2%) of which 84 completed the control and 74 the intervention period. Older children refused more often to participate than younger. Participants in the control and intervention period were socio-demographically and medically equal. Advice: there were no significant differences between control and intervention group. Satisfaction: overall, pediatric oncologists in the intervention period were more satisfied with communication with parents during the third consultation (p < .05). Furthermore, parents in the intervention group were more satisfied during the first consultation with information received (p < .01). Communication: emotional (p < .05) and total psychosocial functioning (p < .05) were significantly more frequently discussed in the intervention group. In addition, significantly more time was spent on emotional and cognitive functioning (p < .05) in the intervention group. The pediatric oncologist initiated significantly more often the discussion regarding emotional functioning (p < .01) in the intervention group. Feasibility: 95.2% of the pediatric oncologists and 75.3% of the parents evaluated the QLIC-ON PROfile as an addition to current health care. Finally, the average consultation duration was significantly shorter (p < .05) in the intervention group compared to the control group (20 min vs 23 min).

Conclusion: These first results are promising. The QLIC-ON PROfile is especially effective in assisting pediatric oncologists in discussing topics within the emotional HRQOL domain. Furthermore, both pediatric oncologists and parents are positive about the use of the QLIC-ON PROfile. With adaptations using internet the QLIC-ON PROfile will be easy to implement in clinical practice in the future and helpful in monitoring and facilitating communication about HRQOL.

SL022 COMPUTERIZED COGNITIVE TRAINING FOR SURVIVORS OF PEDIATRIC CANCER

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Purpose: Neurocognitive late-effects in survivors of CNS-impacting childhood cancer are well-established in the literature. Specifically, deficits in attention and working memory are among the most common neurocognitive findings, problems which may subsequently impede survivors’ ability to acquire new information at developmentally-appropriate rates. Therefore, interventions targeting these skills may improve functioning in childhood cancer survivors with late-effects. The present study evaluated the feasibility and preliminary efficacy of a computerized, home-based working memory training program known asCogMedRM, originally developed to treat children with ADHD, with CNS-impacted childhood cancer survivors. It was hypothesized that participants who successfully completed the intervention would
show increases in attention and working memory at the end of the intervention period as compared to children who completed a “low-dose” version of the program. **Method:** 20 survivors of ALL and brain tumors aged 8–16 years with documented attention and/or working memory deficits participated in a randomized, controlled trial of a 25-session computerized, home-based working memory intervention. The program, CogMed RM, targets visual-spatial working memory skills through intensive practice of gamelike exercises. Survivors completed measures of intelligence (WAIS), memory (WRAML2), attention (CPT-II, Conners’ Rating Scales), and quality of life (PedQLTM) at baseline. Memory, attention and quality of life measures were repeated post-treatment (and 3-months later). Feasibility and acceptability data was collected after 12 and 25 sessions. **Results:** Compliance rates for the trial were high (Mean = 98.1% of sessions completed, SD = 6.0%). Feasibility and acceptability indicate high levels of participant and parental satisfaction with the intervention. Indeed, 94.4% of parents reported that they were somewhat or very satisfied with their child’s participation in the intervention, and 68.7% of children indicated that they either often or always enjoyed their training sessions. Further, data from the Cogmed Training Index, a program-specific score that is used to gauge children’s progress with WM skills targeted by the Cogmed tasks, indicated that the participants achieved a mean training index improvement of 31 (SD = 11, range = 15–54), very similar to that of a sample of 550 children with ADHD who have completed the program with a mean index improvement of 26.2. Finally, survivors completing the adaptive version evidenced increases in attention (d = 56) and WM (d = 53; as measured by the Wide Range Assessment of Memory and Learning – Second Edition) and decreases in parent-rated attention problems (d = 50; as measured by the Conners-3 Parent Rating Scale) as compared to survivors completing the non-adaptive version. **Conclusion:** This pilot study of a home-based, computerized cognitive-training intervention provides initial evidence of the feasibility, acceptability, and preliminary efficacy of a computerized intervention for pediatric cancer survivors with attention and working memory problems. Further study of this approach with a larger sample is warranted. **SI023**

**SISOM: ELECTRONIC SUPPORT TO IMPROVE COMMUNICATION AND PATIENT-CENTERED CARE FOR CHILDREN WITH CANCER**

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**Purpose:** To adequately help children with cancer, health care providers need to understand how the children experience their problems from their own perspective. This can be difficult, because less developed verbal and cognitive skills and adults’ communication styles may prevent children from communicating about distressing experiences with their care providers. Therefore, our team developed SiSom, an interactive assessment and communication tool designed to help children age 6–12 with cancer to report their symptoms/problems in a child-friendly, age-adjusted manner, and to assist clinicians in addressing and integrating children’s reported symptoms and problems into patient care. **Method:** The interactivity and graphical and auditory functionalities of the computer provide entirely different possibilities than questionnaires to capture children’s experiences of symptoms and problems from the child’s own perspective. SiSom uses spoken text, sound, animations and intuitively meaningful metaphors and pictures to express or depict symptoms and problems that even younger children who cannot read can respond to. **Results:** In this presentation we will briefly demonstrate the use of SiSom in “real-life” clinical consultations. We will illustrate how SiSom was adapted to children’s cognitive and emotional developmental stage, using participatory design techniques with children as design partners. Finally, we will present the results of a study that tested the effects of SiSom on patient-provider communication and patient-centered care. **Conclusion:** Preliminary evidence suggests that SiSom is an effective tool to help children communicate their experiences of their symptoms and problems. Integrating SiSom into routine clinical practice could significantly improve symptom management and patient-centered care; and thus may reduce unnecessary suffering for children with cancer.

**SI024**

**THE MOLECULAR BASIS OF ONCOGENESIS IN RHABDOID TUMORS AND IMPLICATIONS FOR THERAPY**

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**Purpose:** Specific biallelic inactivating mutations in SFN5/INI1/SMARCB1, a core subunit of the ATP-dependent SWI/SNF chromatin remodeling complex, are present in the large majority of Atypical Teratoid/Rhabdoid Tumors (AT(RT) and malignant rhabdoid tumors (MRT); highly lethal cancers of young children. Mutation of SNF5 is also the basis of an inherited cancer predisposition syndrome and mutation of another SWI/SNF subunit is associated with non-small cell lung cancers. My laboratory is focused upon elucidating the normal biology of the SWI/SNF complex, identifying the mechanisms by which SNF5 loss drives the formation of cancer, and utilizing this information to develop novel targeted therapies for these cancers. **Method:** Generation of genetically engineered Snf5-targeted mouse models, cell culture and analysis of primary human tumors. **Results:** Using mouse models we have shown that biallelic inactivation of Snf5 leads to the onset of cancer in 100% of mice with a median latency of only 11 weeks. Heterozygous mice develop rhabdoid tumors that are histologically indistinguishable from their human counterpart and conditional inactivation of Snf5 results in 85% of mice developing aggressive mature T cell lymphomas and 15% developing rhabdoid tumors. Intriguingly, the rapid cancer onset arises neither due to defective DNA repair nor due to genome instability, as we have found that the genomes of both the murine and human SNF5-deficient cancers are diploid and indistinguishable from normal cells via high-density SNP arrays. **Conclusion:** Collectively, our results provide novel insight into the mechanisms of oncogenesis by demonstrating that disruption of a chromatin remodeling complex can largely, if not completely, substitute for genomic instability in the genesis of aggressive cancer. Consequently, SNF5-deficient cancers constitute an ideal model with which to both investigate the mechanisms by which epigenetic changes contribute to oncogenesis and also to test therapeutic interventions aimed at erasing epigenetic changes that promote cancer. Our most up-to-date studies regarding the pathway mechanisms by which SNF5 loss drives oncogenic transformation, and the potential for therapeutic targeting, will be presented.

**SI025**

**FREQUENT HSNF5/INI1 GERMINE MUTATION IN PATIENTS WITH RHABDOID TUMOUR**

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**Purpose:** Germline hSNF5/INI1 mutations are responsible for hereditary cases of Rhabdoid tumours (RT) that constitute the rhabdoid predisposition syndrome (RPS). Our study provides the first precise overview of the prevalence of RPS within a large cohort of RT. **Method:** hSNF5/INI1 coding exons were investigated by sequencing and by multiplex ligation-dependent probe amplification. **Results:** Results: 74 constitutional DNAs from 115 apparently sporadic RT were analysed from 1999 to 2009. Germline mutations were found in 26 patients (35%). Data from 9 individuals from 5 RPS families were also studied. The median age at diagnosis was much lower (6.5 mo) in patients with, as compared to patients without (18.5 mo), germline mutation (p < 0.01). Nevertheless, 7/35 patients with germline mutation (20%) developed the disease after 2 years of age. The mutation could be detected in only one parent whereas germline blood DNA was wild type in the 20 other parent pairs therefore indicating the very high proportion of germ-cell mosaicism or de novo mutations in RPS. The former hypothesis could be clearly documented in one case where prenatal diagnosis was positive in a new pregnancy.
With increasing access to ART across the continent, and a renewed focus on children with malignancy in the developing world, we anticipate a change in the climate of care for HIV-positive African children with malignancy. This overview of the current literature on child malignancies stresses the need for guidelines for the management of KS.

**Method:** The challenges of clinical care in a low resource setting in general include lack of capacity for diagnostic confirmation of disease, poor investigation and staging tools. Children with HIV and cancer are unlikely to be optimally worked up and appropriately treated. The ACTG staging system has been used to guide management in adults, but requires validation in the paediatric age group.

**Results:** Recent results from Uganda show the unique nature of the KS disease process in children in this setting. Presentation with lymphadenopathy points to higher CD4 counts, while a mucocutaneous presentation suggests a picture akin to adult presentation. There could therefore be two subsets of patients requiring different therapeutic approaches. Outcome is influenced by treatment of both HIV and KS, and response seems to be better for those receiving both therapies. The clinical and immunologic improvement effected by HAART may therefore enhance the effects of chemotherapy. The role of Kaposi sarcoma virus (KSV) and the potential for specific treatment is an interesting ongoing research area.

**Conclusion:** In conclusion, the impact of expanding access to HAART on Kaposi sarcoma incidence and treatment in a resource-constrained setting is emerging. In order to take full advantage of this scenario there is a need to understand fully KS disease biology and clinical characteristics, in order to identify prognostic factors in children, as well as new treatment targets. There is a need to refine the regimen for children in order to determine proper sequencing of ART and chemotherapy. The answers will come from prospective studies done in low income settings where KS is emerging as the HIV epidemic’s partner in crime.

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**SL028**

**HIV-RELATED MALIGNANCIES IN CHILDREN: RARE AND EXOTIC OR AN EMERGING PROBLEM?**

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**Purpose:** Worldwide, 160,000 children are diagnosed with cancer each year; an incidence of 14.9 cases per 100,000 children less than 20 years of age. Over 80% of children with cancer live in developing countries.

**Method:** A staggering 430,000 new cases of HIV/AIDS occur in children under 15 years of age worldwide each year. The classification of pediatric AIDS lists primary brain lymphomas, small non-cleaved cell non-Hodgkin’s lymphomas (NHL), immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype, as well as Kaposi’s sarcoma (KS) as AIDS-defining events, while leiomysarcomas are included as a sign of a moderately symptomatic stage.

**Results:** According to the National Cancer Institute, people infected with HIV are about 800 times more likely than uninfected persons to be diagnosed with non-Hodgkin lymphoma, and, among women, at least 3 times more likely to be diagnosed with cervical cancer. However, there might be age-related and regional differences. A study from Malawi showed marked differences in the presentation of HIV infection associated with cancer in the pediatric population. The seroprevalence was 93% for children with Kaposi sarcoma, 4% for those with Burkitt lymphoma, but 31% for those with other non-Hodgkin lymphomas, 7% (1/15) for those with Hodgkin disease, and 5% (5/103) for those with other cancers. In sub-Saharan Africa, where Human Herpesvirus-8 is already endemic in many countries, the incidence of Kaposis sarcoma has risen dramatically in the HIV-era overtaking NHL in some HIV-positive cohorts. Unlike NHL it is almost completely preventable through the use of antiretroviral therapy. In a study from Zimbabwe, KS comprised 10.3% of all childhood tumors. While previously considered to be a symptom of end-stage HIV infection with minimal or no chance for cure (due to concurrent organ compromise), it is now clear that many of these malignancies can be approached with a curative intent, as long as HIV infection can be controlled.

**Conclusion:** Mother-to-child transmission of HIV infection continues to account for a substantial, although decreasing, portion of new HIV infections in many African countries. Inadequate knowledge about the availability of prevention services in antenatal settings often impedes their uptake. In Sub-Saharan Africa alone, an estimated 390,000 [210,000–570,000] children are infected with the AIDS virus, placing those that survive an increased risk of cancer. Many of these countries are poorly resourced to deal with the problem of childhood cancer. The unique endemic and epidemic distribution of infectious diseases makes the recognition, diagnosis and treatment of childhood cancer a challenge. In the absence of accurate population-based registries, health workers in these countries are struggling to adequately assess the impact of their growing cancer problem on their countries’ burgeoning populations.

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**SL030**

**TREATMENT OPTIONS FOR HIV-POSITIVE CHILDREN WITH B-CELL LYMPHOMAS**

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There is some controversy about the degree to which the incidence of B-cell Non-Hodgkin lymphoma (B-NHL) has increased in the context of HIV infection in children. While northern hemisphere data is quite compelling, studies from areas in sub-Saharan Africa where Burkitt lymphoma (BL) is endemic demonstrate only a marginal increase in B-NHL, compared to a massive rise in the incidence of Kaposi sarcoma (KS). What is well-recognised is that there is an increased incidence of unusual histology and the appearance of these B-NHLs in unusual sites. While KS occurs in the profoundly immunosuppressed, B-NHL frequently occurs, occurring in atypical sites such as the lungs, mediastinum, heart and bones. Burkitt lymphomas in these children tend to be more aggressive with a higher proportion spreading to the bone marrow and central nervous system, but DLBLs frequently behave in a more indolent fashion.

Primary CNS lymphomas (PCNSL) merit special attention. They are usually DLBLs and almost always EBV-driven. Extremely rare in the HIV-negative population, they constitute as many as 20% of the AIDS-related lymphomas reported in developed world series. Few have been described in sub-Saharan Africa but this may be a function of under-reporting, or misdiagnosis as toxoplasmosis, cerebral abscess or progressive multifocal leukoencephalopathy.

With treatment for B-NHL varying from cyclophosphamide monotherapy in some low income countries to dose intense multi-agent strategies in the developed world, it has been difficult to establish consensus on whether HIV-positive children should be treated with the same regimens as their HIV-negative counterparts. Several factors such as the presence of HIV-related co-morbidity (e.g. chronic lung disease) and co-infection (e.g. Tuberculosis) as well as the potential for drug interactions with antiretroviral therapy (ART) have added to the confusion. Despite these issues evidence is emerging that HIV-positive children without severe co-morbidity can tolerate regimens as intense as the supportive care environment allows. Treatment with ART is mandatory, provided that myelosuppressive agents such as zidovudine are avoided. In patients with significant co-morbidity localised B-NHL can be successfully treated with regimens such as COMP or adult NHL approaches such as modified CHOP with or without Rituximab. Primary CNS lymphomas have been associated with a very poor prognosis but treatment with dexamethasone and high-dose methotrexate-containing regimes with or without...
radiotherapy can be curative. Ancillary reports of PCNSLs responsive to ART alone may represent polyclonal EBV-related lymphoproliferation.

**SL031**

**PEDIATRIC HIV-RELATED MALIGNANCIES IN SUB-SAHARAN AFRICA: THE HAART ERA**

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**Purpose:** To review pediatric HRM in the HAART era in sub-Saharan Africa.

**Method:** Comprehensive literature review

**Results:** The incidence of HIV-related malignancies (HRM) has been a focus of interest in HIV medicine & oncology. The incidence of pediatric HRM has varied from 66 per 100,000 in the US to 418 per 100,000 reported in Italy. CDC reported an HRM incidence of 2% in children (1996). The estimated pediatric HIV+ population is 3.5 million hence this translates to 70,000 cases of HRM in sub-Saharan Africa (SSA). At the Botswana-Baylor COE, where 2000 children are treated, this equates to 40 cases. The BIPAI Network provides care & treatment for > 30,000 HIV+ children in SSA. The expected caseload of pediatric HRM is 600. The total number of new cases of pediatric HIV infection is estimated at 400,000 in SSA. Expected HRM-cases in this cohort is 8,000.

The Italian Registry estimated incidence is 0.76 cases of HRM per 1000 HIV+ children/year in the HAART era. This translates to 2660 cases of pediatric HRM in SSA. Most countries in the region don’t have adequate & consistent access to HAART for their populations. Botswana has been an example of a successful HAART program with 70% of adults on HAART. Applying Italian Registry data, the Botswana COE would be expected to have 15 cases/yr, with the expected rate declining in South Africa from 1350 to 230 in the HAART era.

Most countries of SSA differ from expected cases of pediatric HRM. Most centers see less than predicted by the CDC or Italian Registry data. Given increased prevalence of factors including EBV & HHV-8 in SSA, one expects a higher caseload of pediatric HRM. Important differences between the US & Italy and SSA may account for the differences observed. Resources available are significantly different in the West. Patients initiate on HAART earlier than those in SSA & not based on a specific CD4%. Children in SSA are initiated on HAART when the CD4% drops to WHO Cat 3 or a child has a WHO Clinical Stage 3 condition. These children are more likely to experience morbidity & mortality from infection. Infants who are not identified and initiated early have a 50% mortality rate by age 2 years, most commonly from infections. The lower incidence of pediatric HRM may reflect a higher incidence of other diseases coupled with decreased access to care. It may also be a function of underascertainment, either because of misdiagnosis or underreporting both of which are liable to occur in resource-limited settings.

**Conclusion:** Notwithstanding this lower incidence one might pause to speculate whether a large cohort of survivors established on HAART won’t translate into a major rise in cancer incidence in the medium and long term.

**SL032**

**MULTISITE STUDY OF ADHERENCE TO 6MP TREATMENT IN PEDIATRIC LEUKEMIA**

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**Purpose:** An emerging body of scientific evidence suggests that children and adolescents with cancer, including acute lymphoblastic leukemia (ALL), do not take their maintenance phase medication in accord with their prescribed treatment regimens. Treatment non-adherence could have significant negative effects on the clinical course of ALL, but is not assessed routinely using objective methods in clinical care nor has it been evaluated extensively in research. Our preliminary studies demonstrated a relatively high prevalence (30%) of treatment non-adherence in a sample of adolescents with ALL receiving maintenance treatment based on a serum assay of metabolites of 6-mercaptopurine (6MP). Based on this identified need, we are now conducting an adherence promotion intervention in a randomized controlled trial (RCT).

**Method:** This study describes treatment adherence at baseline in a multisite study that is designed to test the efficacy of family centered problem-solving training to enhance adherence to 6MP treatment among children and adolescents with ALL. Thus far, 77 participants have been recruited, completed baseline, and randomized to the study. One potentially important feature of the study sample is that 43% (N = 34) of the sample are minority participants, the majority (N = 26) being Hispanic. This report describes preliminary analyses for the entire sample of adherence to treatment based on a comprehensive, objective assessment of electronic monitoring and serum assay of metabolites of 6MP, which is the primary outcome of the study.

**Results:** We replicated the original cluster analyses of metabolites of 6MP at baseline using the current sample. Three clusters were generated at baseline and showed that 43.5% of participants (n = 30) in this sample had thiguanine nucleotides (TGN) and methylated Mercaptopurine (MMP) metabolites at baseline, whereas another group showed low TGN and high MMP metabolite levels (43.5%, n = 30), and a third group showed high TGN and low MMP (13%, n = 9) metabolite levels at baseline. Absolute neutrophil count (ANC) was higher in the cluster with low TGN and MMP compared with the other groups derived by cluster analysis. Results of preliminary analyses of electronic monitoring data indicated less than optimal treatment adherence for the sample as a whole: 78.88% of the sample were taking their medication as prescribed.

**Conclusion:** Taken together, these findings underscore the need for this RCT to test a promising model of attention promotion intervention. Our preliminary data highlight the importance of using multiple methods of adherence measurement and developing novel statistical methods for integrating and analyzing data from adherence to treatment for pediatric cancer.

**SIOP ABSTRACTS**

**SIOP DIET CANCER OVERVIEW**

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United States

**Diet and Cancer: Overview**

The concept that diet is an important determinant of cancer captured the attention of biomedical community early in the 1980’s. Since then, the focus of thinking has evolved through what might be considered four paradigms. First was the possibility that carcinogens in food, such as those in cooked meat, increased risk by direct damage to DNA; support for this has been weak but neither has it been entirely refuted. The second paradigm hypothesized that dietary fat was the primary cause of the major cancers of western societies; this has not been supported by prospective studies or the recent WHI trial. A third paradigm has been that increasing consumption of fruits and vegetables would greatly reduce the risks of most major cancers; this has not been supported by prospective studies although a small benefit cannot be excluded. The most recent paradigm is that excess energy balance, manifested as overweight, increases the risks of many cancers. This paradigm is robustly supported by all forms of epidemiologic evidence, animal experiments and mechanistic studies. Many other promising areas of research on diet and cancer are still being pursued, but at this point in time overweight is second only to smoking as a clear and avoidable cause of cancer.

**SL040**

**ONCOLOGIC MANAGEMENT OF PULMONARY METASTASES**

N. Marina

United States

**Purpose:** The lung represents the most common metastatic site for patients with pediatric solid tumors. The management of these patients remains challenging. The therapeutic approach depends on the tumor type, timing of metastases (recurrence or at diagnosis) and the biological behavior of the tumor. Generally the management of these patients requires a multi-disciplinary approach. For most pediatric patients, the administration of systemic chemotherapy following a histologic diagnosis represents...
Patients with germ cell tumors and Wilm's tumor have a good prognosis, but the long-term outcome also depends on tumor type and biological behavior.

**Method:** Summary of the relevant research data to date.

**Results:** Patients with germ cell tumors and Wilms' tumor have chemosensitive tumors and their prognosis is good even in the setting of metastatic or recurrent disease. Second line systemic chemotherapy is effective and there is not always a need for the use of surgical resection and/or radiotherapy after chemotherapy. Patients with hepatoblastoma, rhabdomyosarcoma and Ewing sarcoma who present or develop recurrent metastatic disease are more difficult to manage. Though the use of chemotherapy allows the possibility of achieving disease control, long-term disease free survival in these patients is rare. Although chemotherapy appears to improve the outcome for newly diagnosed patients with osteosarcoma, the presence or development of metastases suggests the presence of a biologically more aggressive tumor and only a small proportion of patients are cured in spite of the use of aggressive management. The clinical course for patients with osteosarcoma is similar to that of patients with newly diagnosed metastatic or recurrent soft tissue sarcoma. These patients tend to have chemoresistant tumors and surgical management is critical. However, even though surgical resection provides disease control, it tends to be short-lived.

**Conclusion:** It is clear that other than for patients with germ cell tumors and Wilms' tumor, new therapeutic approaches are needed to improve the prognosis of patients with metastatic or recurrent lung disease. Administration of biological agents in the setting of minimal residual disease would appear to have the best chance of improving outcome. GM-CSF, cisplatin and gemcitabine have been tried in this setting, but so far none of these appear to effectively prolong disease control. The search continues for the identification of agents that might prevent or eradicate lung disease.

**SURGICAL TREATMENT OF LUNG METASTASES**

**L. Fuchs**

**Germany**

**Purpose:** Lung metastases regularly occur in different entities of pediatric solid tumors. Despite aggressive approaches with chemotherapy, the local treatment plays a key role for the outcome of children with primary or secondary lung metastases.

**Method:** The guidelines for treatment of lung metastases are included in the treatment protocols of different multicenter trials. Nevertheless the effectiveness of surgery on lung metastases has not been completely clarified. On one hand exists the influence of chemotherapy and radiotherapy, on the other hand modalities of data registration are rarely sufficient for a prospective evaluation of lung surgery for solid tumor metastases. It is well known that an aggressive surgical approach can be justified depending on the tumor entity. Examples are hepatoblastoma or osteosarcoma.

**Results:** The presentation focuses on the correlation between preoperative detection of lung metastases and intraoperative findings, indications for surgery in different tumor entities, the surgical approach, surgical difficulties, innovations, and complications. Data will be presented on overall and event free survival rates of children after surgery for lung metastases of different tumor entities.

**Conclusion:** Surgery of lung metastases can be performed with a good surgical outcome regardless of the patient's age. It is a safe method containing the perspective of preventing late effects through chemotherapy and radiotherapy. An interdisciplinary approach is mandatory in any case, which includes pediatric oncologists and radiologists and which is based on the recommendations of the different study protocols in pediatric oncology.

**VACCINE THERAPY FOR NEUROBLASTOMA**

**C. U. Louis, M. K. Brenner**

**Baylor College of Medicine, Center for Cell and Gene Therapy, Houston, United States**

**Purpose:** Immunotherapy is an attractive option for patients with high-risk neuroblastoma since these individuals continue to have poor long-term survival after conventional therapy. Development of an effective vaccine for neuroblastoma has been a considerable challenge due to the tumor's heterogeneity and down-regulation of major histocompatibility complex and co-stimulatory molecules, both of which may limit the efficacy of tumor-directed T cells. To date, most neuroblastoma tumor vaccines have been composed of cellular extracts or whole cell products that allow multiple tumor antigens to be presented. Our own group has focused on whole cell vaccines that are amenable to genetic modification as a way to enhance anti-tumor immune responses.

**Method:** We modified neuroblastoma cell lines to secrete IL-2 and lymphactin. Local IL-2 secretion recruits T cells and natural killer cells, and induces interferon gamma release, while lymphactin, a T-lymphocyte recruiting chemokine, substantially increases the immunogenecity of IL-2 gene modified cells. Additionally, we have added a second, unmodified, cell line expressing a distinct set of tumor associated antigens to this vaccine construct. This combination of lines should increase the breadth of the resulting immune response, and thereby increase the probability of an anti-tumor response to neuroblastoma.

**Results:** Subcutaneous administration of the IL-2/lymphactin vaccine to patients with neuroblastoma led to increased local infiltration of CD4+ and CD8+ T cells, eosinophils, and Langerhan's cells. Systemically, increased NK cells and IgG antibodies to the vaccine cell line were detected in peripheral blood. Clinically, of the 28 patients treated on this study, there were 4 complete responses (2 sustained > 4 years after vaccination), 1 very good partial response, 1 partial response, and 5 patients with stable disease. Studies using the second construct are currently on going.

**Conclusion:** Cell-based vaccine therapy can be given safely and induce both immune and clinical responses in patients with a history of high-risk neuroblastoma. During this session, we will discuss the advantages and disadvantages associated with each type of vaccine construct, and the history, current clinical studies, and future directions of neuroblastoma vaccine therapy.
SIOP ABSTRACTS

after allogeneic HCT: secondary leukemia, lymphomas and post-transplant lymphoproliferative disorders and secondary solid tumors. Method: Review of the literature of solid tumors occurring after allogeneic SCT. Results: Several studies have reported that survivors of HSCT have an increased risk of developing new solid cancers with the risk rising among long-term survivors from 2% to 6% at 10 years after transplantation. Several factors contributed to this increase, including total body irradiation TBI, which has been a mainstay of the preparative regimens for allogeneic HCT until recently, primary disease, male sex, and pre-transplantation therapy. Chronic GVHD and immunosuppressive therapy have also been shown to contribute to excess risk, particularly for squamous cell carcinomas of the buccal cavity and the skin. Young age at transplantation has been reported to be a strong risk factor in some, but not all studies. Conclusion: Although these data indicate that allogeneic transplant survivors face increased risks of solid cancers, supporting strategies to promote lifelong surveillance among these patients.

SL050

THE MOLECULAR PATHOLOGY OF ACUTE LEUKEMIA

J. Downing

United States

Purpose: To identify the lesions underlying acute lymphoblastic leukemia (ALL). Method: We analyzed 800 leukemia samples using single nucleotide polymorphism arrays and genomic DNA sequencing. Results: Our analyses revealed deletion, amplification, point mutation and structural rearrangement in genes encoding key regulators of B lymphocyte development and differentiation in 60% of B-progenitor ALL. PAX5 was the most frequent target of somatic mutations, being altered in 38% of cases. The frequency of alterations varied markedly across the different genetic subtypes, with a near obligate deletion of IZKF1 in BCR-ABL1 ALL. Moreover, in an analysis of differences in copy number alterations (CNAs) between diagnostic and relapse samples, we found that 90% of relapse ALLs have acquired new CNAs, with most relapse clones arising not from the diagnostic clone but from an ancestral clone that was present as a minor population at the time of diagnosis. To explore the clinical significance of the identified CNAs, we extended these studies to a cohort of 221 high-risk pediatric ALL patients treated on a Children’s Oncology Group study. This analysis identified mutations of IZKF1 as an independent poor prognostic indicator. The occurrence of IZKF1 mutations in both high-risk BCR-ABL1 negative ALL and BCR-ABL1 positive ALL raised the possibility of kinase activating mutations in the BCR-ABL1 negative high-risk leukemias. Consistent with this prediction, we identified in a subset of the cases activating mutations in JAK1 or JAK2, and chromosomal deletion that juxtaposed the first noncoding exon of F2R378 to the coding region of the cytokine receptor like factor 2 (CRLF2), resulting in the over-expression of CRLF2.

Conclusion: Our data demonstrate that mutations in genes regulating the differentiation and development of normal B cells are a frequent event in leukemogenesis. Moreover, we demonstrated that the combination of JAK activating mutation and CRLF2 over-expression directly contribute to leukemogenesis in a subset of high-risk B-progenitor ALL.

SL053

BEST PRACTICES IN INFORMED CONSENT

L. Fallowfield

United Kingdom

It is an ethical imperative that patient/parental consent to medical procedures or treatment is given freely and that it is both informed and educated. This requires, as far as is reasonable, that all the necessary facts, implications and consequences are given in an appropriate manner that is non-coercive and comprehensible enough to enable understanding. The information needed is usually conveyed verbally by healthcare professionals (HCPs) with complementary and supplementary written or other audio-visual material. Unfortunately, as far as consent to clinical research is concerned, and despite the many institutional and government guidelines developed in different countries, there are several studies showing that patients are often:-- unclear that they are participating in research, have a dubious appreciation about their rights to decline, are unclear about other treatment options that might have been available and maybe unaware about the primary aims of the studies in which they are involved. Some recent educational initiatives have been shown to improve the communication skills of HCPs when eliciting informed consent to clinical trials (Jenkins et al, BMI, 2005, but appraisal of some of patient information sheets written supposedly after comprehensive review by institutional review boards, patient groups and others, often obfuscate rather than illuminate. Information sheets are still being written at a level requiring far too high a literacy level for many patients, making their usefulness in assisting informed consent debatable. There is also increasing concern that much of the information given to cancer patients and their relatives has more to do with preventing litigation rather than genuinely helping patients arrive at an informed decision about treatment options and/or clinical trial entry. Trust in the doctor is often cited as the primary reason for consent to clinical trials suggesting that verbal communication may be the most salient factor guiding decision-making. We need continued communication skills training for HCPs at all levels and considerable improvements in the written materials provided to anxious parents agonising about the best treatment choices for their sick child.

SL054

ETHICAL ISSUES IN CLINICAL TRIALS IN THE DEVELOPING WORLD

M. Kruger

South Africa

Purpose: Developing countries bear close to 90% of the burden of disease, having access to 10% of available health care. This highlights the need to conduct clinical trials in developing countries where communities have multiple belief systems and cultures, and often a non-Western interpretation of disease. Method: Against this backdrop there are a number of ethical issues to address, which is the focus of this paper. Results: These issues include the vulnerability of the research participants, the informed consent process, the acceptable standard of care, the need for ancillary care, the lack of ethics review capacity and need for post trial benefits. The vulnerability of the research participants is illustrated by their lack of knowledge regarding the research process or alternative treatments, as well as their expectation that researchers will provide the essential medical care during research. Informed consent is problematic, since not all societies focus on first person consent and the consent process should take into consideration the local culture and traditions. genuine understanding and voluntary participation is a prerequisite, which may be difficult to establish in a context where there are huge disparities between the researchers and the participants’ knowledge and belief systems. The statement “I do understand” during the informed consent process of a potential research participant does not always indicate true understanding of the content of the informed consent document, but reflect a way of expressing respect towards the researcher, who is deemed more knowledgeable. Trial participants may also be intimidated to ask questions since they are in awe of the researcher/physician’s knowledge and status in society. Trial counsellors, who translate the information into the local language, may interpret the information in such a manner that reflects their belief system rather than the true content of the information. Other issues include the scientific design and standard of care, which will be discussed using the example of the perinatal HIV preventative clinical trials, which sparked tremendous controversy in the 1990’s, with the current consensus agreement that the best available treatment constitute standard of care. The lack of ethics review expertise to review clinical trials are currently addressed by numerous Fogarty International sponsored capacity-building training programs. Post trial benefits is another issue and to achieve this it is advisable that the researchers reach an agreement with the local health authorities prior to the initiation of the clinical trial to ensure access to these novel therapies by clinical trials.

Conclusion: In conclusion it is essential that we take the best interest of poor populations to heart since the neglect of their health may threaten the health of all. In paediatric oncology we should improve the access to cancer therapy through well-designed clinical trials adjusted to the local context of developing countries.

SL055

ASSENT IN PEDIATRIC RESEARCH

M. Broome

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Purpose: The solicitation of assent for children for research trials has been discussed in the literature for 2 decades. Assent is broadly defined as a child’s affirmative agreement to participate in research (NIH, 2009). However, a lack of clear guidance in the federal regulations that guide the ethical practice of research and informed consent from children who are potential participants has resulted in assent practices that vary widely. These practices often depend on the individual investigator or team to operationalize their procedure based on the anecdotal approaches to soliciting and
documenting assent from children most often found in the literature. In spite of the Institute of Medicine Report (2004) and recommendations of others (Broome et al., 2005; Ungar, 2006) devoted to the ethical conduct of clinical research involving children, practices remain varied. Theoretical arguments remain related to age of assent and the appropriateness of healthy children being allowed to make their own decisions about assent for research. The issue of ‘honoring’ dissent by a child is also debated in the literature.

Method: Comparisons of actual practices across multiple centers have clearly demonstrated continued variations (Kimberly, et al., 2006) related to both research compensation and child assent. In one study of consistency across 3 different research protocols under the jurisdiction of 69 Institutional Review Boards, both practices related to compensation and assent were evaluated. This study reported substantial variation. Compensation was determined using 3 different factors (e.g. time, expenses, and inconvenience) and the amount of monetary compensation varied as well. Only 50% of the forms employed to document assent used a separate form from the official consent document.

Results: This presentation will review the guidelines, recommendations, empirical studies related to child assent for research.

Conclusion: Recommendations for improving consistency and adherence by investigators will be discussed.

IPSOSL002 DIFFERENT TECHNIQUES FOR TISSUE DISSECTION IN PEDIATRIC SURGICAL ONCOLOGY- AN OVERVIEW

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Purpose: Conventional electrosurgery has been used for many years in pediatric surgical oncology. In recent years, novel techniques and devices have been introduced. The aim of this paper is to review these devices and to assess their applicability in pediatric surgical oncology.

Method: Besides conventional electro surgery including HF-surgery, other techniques (Argon-Plasma-Coagulation, radiofrequency surgery, hydro surgery, ultrasound dissection, and vessel sealing techniques) are compared.

Results: Different devices are useful for different tasks in pediatric surgical oncology. Conventional electro surgery is preferable for dissection of smaller vessels and tissue. Argon-Plasma-Coagulation might be used for tumor debulking. Radiofrequency surgery is a “cold-cut-technology”, which is helpful for tissue dissection with little damage to the surrounding tissue. Hydro surgery seems to be preferable for dissection of parenchymal organs. Ultrasound dissection can be used for tissue dissection and vessel sealing.

Conclusion: This paper gives an overview over different dissection techniques and might help to estimate the usefulness according devices in pediatric surgical oncology.

IPSOSL003 COOLING, CLAMPING AND BENCH RESECTION IN NEPHRON-SPARING SURGERY

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Purpose: Nephron-sparing surgery (NSS) continues to develop as a standard of care for select renal masses in both the adult and pediatric urology practice. Advanced ablative and complex reconstructive procedures in a hemostatically controlled field have evolved to make this surgery safer. This review will address the current techniques and technologies being used for hemostatic control during NSS.

Method: Relevant treatment strategies with respect to the surgical approach, methods of hemostatic control, acceptable time of warm ischemia, and cooling techniques will be reviewed and collated from the most recent peer-reviewed literature related to NSS.

Results: Methods of hemostatic control favor soft vascular clamping for larger tumors that are more endophytic and central. Smaller exophytic lesions may be managed without renal vascular control using a variety of coagulative and hemostatic tools. Data related to warm renal ischemia suggest that the time used for tumor excision and renal reconstruction should be 30 minutes or less.

Conclusion: Many promising techniques for NSS are being developed currently, most geared toward improved hemostasis and collecting system repair. These techniques and products have made, and will continue to make, this surgery less demanding and more universally accepted.

GUEST LECTURES (GL)

GL001 WORLD CHILD CANCER

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2St Jude Research Hospital, Oncology, Memphis, United States
3International Society of Paediatric Oncology, Paed Onc, Amsterdam, Netherlands

Purpose: Aims: To attempt to reduce the global inequality in treatment of children with cancer worldwide.

Method: Method: To create twinning partnerships between hospitals in resource limited and resource rich countries using “seed funding” from philanthropic donors.

Results: Background: World Child Cancer was created as a charity in 2007 by the International Confederation of Childhood Cancer Parents’ Organisations in collaboration with SIOP and with the support of St Jude Research Hospital. In each project it aims to: raise awareness of the early signs of cancer; promote timely diagnosis; improve protocol treatment rates; increase survival and decrease abandonment; provide practical and emotional support for children/families, and improve supportive/palliative care.

Progress: Using a project template developed by St Jude and twinning methodology pioneered by them and many SIOP members, we are providing $40,000 per year for initially 5 years, alongside mentoring to centres who have requested help. We have opened four projects in Malawi, Mexico, the Philippines and Colombia. Volunteer mentors/ambassadors have been recruited worldwide. Four more projects are planned for 2010 (Nepal, Namibia, Ghana and Mozambique) and four more each year up to 2012 (new requests already received from China, India, Bangladesh). The recipient country determines the needs/required support (eg drugs and equipment, staff training and retention, refurbishment of facilities, public awareness campaigns). World Child Cancer provides long-standing mentorship and technology transfer wherever possible. Recipients provide progress reports and are assisted in developing parent support groups and to seek longer term sustainability funding beyond the 5 year initial funding from World Child Cancer.

Conclusion: Carefully planned twinning would appear the optimal way to deliver support in this field.

More information is available at www.worldchildcancer.org or by emailing info@worldchildcancer.org. Offers of help in mentoring/ambassadorial roles and of course bids from needy countries/centres are welcomed.

GL002 BLOCKING THE HEDGEHOG PATHWAY AS A THERAPEUTIC OPTION IN PEDIATRIC LIVER TUMORS

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Accumulated data suggest that activated Hedgehog (Hh) signaling significantly contributes to development of cancer in a variety of organs. The purpose of the current study was to determine the role of Hh signaling in pediatric liver tumors. Expression level of different Hh target genes was measured by real-time PCR, activity of Hh signaling by reporter assays, influence of cyclopamine and recombinant hedgehog interacting protein (HhIP) by cell viability and apoptosis assays, and epigenetics by bisulfite sequencing and methylation-specific PCR.

Here, we demonstrate that Hh signaling is activated in hepatoblastoma (HB), the most common liver tumor in childhood. Downstream Hh target genes such as GLI1, GLI2, BCL2 and PITCH1 showed a strong transcriptional upregulation in HB compared with normal liver tissue. In line with an autocrine stimulation of the Hh pathway, overexpression of the ligand encoding HhIP gene was found in the majority of HB cases. Consequently, blocking Hh signaling with the antagonist cyclopamine had a strong inhibitory effect on proliferation of HB cells with an activated Hh pathway. We further demonstrate that decreased cell viability is caused by a massive induction of apoptosis, as evidenced by morphological changes, phosphatidylserine membrane asymmetry, and proteolytic cleavage of caspase 3 and poly(adenosine diphosphate-ribose) polymerase. Most interestingly, the HhIP gene is transcriptionally silenced by CpG island promoter methylation in HB. Consistent with this, treatment with a DNA-
demethylating agent restored HHIP expression. Strikingly, restoration of HHIP function by adding the recombinant protein to HB cell cultures impaired HB survival. The cranial radiation group had lower mean FA and higher mean ADC than the chemotherapy group. Strikingly, restoration of HHIP expression by adding the recombinant protein to HB cell cultures impaired HB survival.

GL003

CEREBRO-CEREBELLAR CONNECTIONS IN PEDIATRIC BRAIN TUMOR PATIENTS: IMPACT ON WORKING MEMORY

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Purpose: Pediatric posterior fossa (PF) tumors are treated surgically, with radiation and chemotherapy being reserved for residual or malignant cases. Cranial radiation has been associated with delayed cognitive dysfunction. Working memory has yet to be fully examined in this population. JMRI, MEG, and lesion studies have implicated both the cerebellum and dorsolateral prefrontal cortex (DLPFC) in working memory. After radiation, working memory functions were impaired in patients with localized tumors and those with control groups. Method: Forty-one patients treated for PF tumors (29 of which were treated with surgery and radiation, 12 of which were treated with surgery only) and 26 controls were examined. We used diffusion tensor imaging (DTI) to delineate cerebellar-DLPFC tracts and perform probabilistic tractography to delineate and investigate the structural integrity of cerebellar-DLPFC tracts. Results: Bilateral tracts connecting the cerebellum with the DLPFC were delineated in all participants. The cranial radiation group had lower mean FA and higher mean radial diffusivity within the cerebellar regions of the cerebellar-DLPFC tract compared to the control group. Poorer working memory scores were observed for the cranial radiation group (WMI = 88) compared to the control group (WMI = 102), p < 0.05, and these lower working memory measures were correlated with reduced FA and higher radial diffusivity (r = -0.334, p < 0.01 and r = -0.312, p = 0.05, respectively) within the entire cerebellar-DLPFC pathway. Conclusion: Identifying differences in the integrity of white matter for specific pathways is an essential step in attempting to localize the regional effects of PF tumors and their treatment methods. Integral to this study is the finding that working memory function may be dependent on the integrity of cerebellar-DLPFC connections.

GL004

A MEDICATION DIARY-BOOK FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS IN INDONESIA: TREATMENT OUTCOME FROM A RANDOMIZED TRIAL

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Purpose: Event-free survival of childhood acute lymphoblastic leukemia (ALL) in Yogyakarta, Indonesia was low (20%). The aim of the study was to evaluate the effectiveness of using a diary-book in the outcome of childhood ALL. Method: A randomized study was conducted with 109 childhood ALL patients in a pediatric oncology centre in Yogyakarta, Indonesia. Both the intervention and the control groups received a structured parental education program and donated chemotherapy. The intervention group received a medication-diary book to assist reminding parents and families to take oral chemotherapy and present for scheduled appointments or admissions. Event-free survival estimate (EFS) at 3 years was assessed. Results: Among childhood ALL patients whose mothers had a high educational level (senior high school or higher), the EFS estimate at 3 years in the intervention group was significantly higher that the EFS estimate in the control group (62% vs. 29%, p = 0.04). No significant difference was found in EFS estimate at 3 years between the intervention and the control groups in childhood ALL whose mothers had low educational level (26% vs. 18%, p = 0.86). Conclusion: In a resource-limited setting, a medication-diary book is useful to improve the EFS estimate in childhood ALL patients especially in those whose mothers had a high education level. For parents with a lower educational level the diaries should be made simpler, and more support and education is necessary to help them to use it. Keywords: Medication-diary book, childhood acute lymphoblastic leukemia, treatment outcome

ORALS (O)

O001

SURGICAL TREATMENT OF PULMONARY METASTASES IN CHILDREN: EXPERIENCE FROM A SINGLE INSTITUTION

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Purpose: To evaluate the efficacy of lung metastases surgical treatment in children with different kinds of extrapulmonary malignancies. Method: We studied the outcomes of 28 pts, 3–17 y.o. (Me = 7 ys) with different kinds of malignancies after lung lesion’s removal. Most of them were with osteosarcoma (N = 15) and Ewing’s sarcoma (N = 6). Other pts had soft tissues sarcomas (N = 2), germ cell tumors (N = 2), chondrosarcoma (N = 1). Wilms tumor (N = 1) and hepatocarcinoma (N = 1). All lesions were diagnosed by CT and resected by thoracotomy or sternotomy. All the patients underwent protocol therapy. Results: CT has underestimated the number of lung lesions; we detected more lesions during surgery in 16 (59.3%) pts and bilateral affection in 2 (7.2%) pts while CT showed less number of metastases and only unilateral affection instead of bilateral. 331 lung lesions were removed. 237 (71.6%) lesions were morphologically confirmed as malignant, in 4 (14.3%) pts - as benign. 58 (24.5%) metastases were located deeply in the parenchyma. They could not have been detected visually during surgery procedure and were found only by manual palpation. The most (78.7%) of 94 benign lesions were focused on hyperpigmentation (31 lesions) and intrapulmonary lymph nodes (43 lesions); all of them were subpleural. The observation time for all patients was 4–71 mths (Me = 25 mths). 16 (66.7%) patients with morphologically confirmed metastases are alive. The observation time for 15 pts with osteosarcoma was 10–70 mths (Me = 23 mths), OS was 50%, PFS was 47%. Conclusion: Lung metastasectomy can improve the outcome in stage IV pediatric cancer. Manual exploration by thoracotomy remains the procedure of choice.

O002

VATS (VIDEO ASSISTED THORACIC SURGERY)- THE OPTION IN ONCOLOGICAL SURGERY OF THORAX IN CHILDREN

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IS THORACOSCOPY VALUABLE FOR RESECTION OF NEUROGENIC TUMORS IN CHILDREN?

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Purpose: To evaluate the value of thoracotomy for resection of neurogenic tumors in children through a review of the literature.

Method: From January 2006 to December 2009, 10 patients aged 3 months to 4.5 years (mean: 2.3 years) underwent thoracotomy for tumor resection in a single institution. They were 8 localized and 2 stage IV neuroblastomas. Tumor was associated to an opsoclonus-myoclonus syndrome in one case and was diagnosed later in the course of the disease.

Results: All procedures were completed successfully except in one patient where the procedure had to be interrupted due to too close adhesions of the tumor with the aorta. A chest tube was left in all cases for a mean of 2.5 days. Operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Preoperative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology in about half of the patients to have a pre-operative histopathological diagnosis.

Conclusion: As previously reported in few reports of literature, our series confirm that thoracotomy is a safe and efficient procedure for resection of neurogenic tumors in children.

TIME OF PRESENTATION OF PULMONARY METASTASES IN THE PROGNOSIS OF PEDIATRIC PATIENTS WITH OSTEOSARCOMA. A SINGLE INSTITUTION EXPERIENCE

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Purpose: The lung is the most common site for metastatic spread in osteosarcoma. Twenty percent of cases are detected at diagnosis, while almost 80% of patients develop lung metastases during treatment or follow-up. Metastatic disease in osteosarcoma has prognostic significance.

The study is designed to evaluate the prognostic impact of the time of presentation for lung metastases in pediatric patients with osteosarcoma.

Method: Medical records for patients between 7 and 15 years of age, with diagnosis of osteosarcoma and lung metastases, treated at the National Institute of Pediatrics in Mexico City, between 2000 and 2008 where retrospectively reviewed.

Results: We found 250 patients with diagnosis of osteosarcoma. Ninety two patients were eligible for the study. 47 females and 45 males. The most common site of primary tumor was the distal femur (51%), followed by humerus (21%), and tibia (14%). Most were osteoblastic osteosarcomas (42%), Chondroblastic (25%), and fibroblastic (10%) tumors were also seen.

Survival was evaluated in four different groups, according to the time of presentation of pulmonary metastases:

- Patients with lung metastases at initial diagnosis (20%) had a 2yr and 5yr DFS of 34% and 12% respectively.
- Metastases diagnosed during neoadjuvant chemotherapy (12%) had 27% and 9% DFS. Patients developing metastases during their treatment (7%) had 24% and 8% DFS. Patients who developed lung metastases during follow up (41%) had 48% and 29% DFS, respectively.
- Patients in group 4 showed the highest survival rates, whereas patients who developed metastases due to chemotherapy had the poorest survival.

Conclusion: The time of presentation of pulmonary metastases has an impact on disease free survival in pediatric patients with osteosarcoma. Metastases developed later in the course of the disease have a more favorable prognosis, probably because they are produced in slow growing cellular nests, while metastases developed during treatment represent chemo-resistant cells.

MALIGNANT GERM CELL TUMORS - OUTCOME ANALYSIS

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Purpose: To audit the outcome of patients with Malignant Germ Cell Tumors (GCT) treated in a public hospital in New Delhi, India.

Method: A retrospective study was performed in the Department of Pediatric Surgery at MAMC, Delhi by retrieving data from the records of operated children with Malignant GCTs from 1998 to 2009. The patients with immature or mature teratomas and CNS Malignant GCTs were excluded.

Results: 23 children, (M:11, F:12), mean age of 3.6 years were studied. Primary sites of origin were gonad in 11 (47%) and extragonadal in 12 (53%). Considerable delay in presentation ranging from 1 month to 5 years was noted in 13(56.52%). Misdiagnosis contributed to delay in 6 (26%). Tumor markers such as Alpha-feto-protein, and radiological imaging such as ultrasonography, CT-scan were performed in all the patients. Fine needle aspiration cytology (FNAC) or trucut biopsy was obtained in about half of the patients to have a pre-operative histopathological diagnosis. Pre-operative chemotherapy was given in 8 (34%), which altered the histology from malignant to benign in 48/50%. All patients underwent surgical resection. Histopathological examination of excised specimens revealed yolk sac tumors in 7, dysgerminomas in 2, mixed (yolk sac and embryonal carcinoma) in 2 and in embryonal germ cell tumor in 2. Histopathology was unspecified in 8 other malignant GCTs. Adjunct chemotherapy was administered to 18 patients, mainly BEP, none received radiotherapy. 33% in the study completed treatment. Overall mortality was 34.8%. Recurrence rate was 21%. The disease free survival (DFS) for 2 years was 42.8% and for 5 years 14.2%.

Conclusion: Poor results are multi-factorial due to delayed presentation, non-compliance, and misdiagnosis. Whether down-staging the tumor by pre-operative chemotherapy and inadequate therapy thereof as a cause for poor outcome needs to be evaluated further. The need to upgrade the surgical oncology facilities and training in our country is evident.

NEUROENDOCRINE TUMOURS (NET) OF THE APPENDIX IN CHILDREN AND ADOLESCENTS – RESULTS AND RECOMMENDATION OF THE GPOH-MET 97 TRIAL

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**Purpose:** Evaluation of current German guidelines for treatment of NET of the appendix.

**Method:** Examination of clinical presentation, histopathological parameters (tumour size, tumour localisation, infiltration of the mesenterium, presence of lymphovascular space invasion (CD31), Ki-67 proliferation index), occurrence of micro metastases in regional lymph nodes and outcome of 180 children aged 4.5 to 18.3 years (mean 13.1 years) which were admitted to a national prospective interdisciplinary multicenter trial (GPOH-MET 97) from 1996 to 2009.

**Results:** Clinical presentations were in 80% symptoms of acute appendicitis and in 20% chronic abdominal pain. All tumours were found incidentally after appendectomy. In 60% an inflammation of the appendix, in 34% an visible tumor and in 6% a normal appendix were found. Paraffin embedded tumour specimens from 85% of the patients were re-evaluated by a reference pathologist. A second operative intervention was performed in 44 of all re-evaluated cases. Micro metastases in regional lymph nodes were detected in 16% (N = 7) of re-operated patients. The tumour size of 15 mm was the optimal cut-off in predicting lymph node metastases (sensitivity 86%, specificity 67%). Patients with tumours > 15 mm showed metastases in 35.5% (6 of 17) and patients with tumours U 15 mm in 3.7% (1 of 27). Since none of the patients showed a relapse or distinct metastases, the presence of micro metastasis in the removed lymph nodes are the only events in the follow up (up to 11.5 years, mean 3 years). The data suggest, that almost 85% of the re-operations were "unnecessary" because in only 16% micro metastases were found.

**Conclusion:** Right hemicolectomy as the standard therapy should be therefore only recommended in patients with tumours > 15 mm. A long term follow up is necessary to evaluate the clinical significance of the micro metastases.

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**O007**

**EXPERIENCE WITH THE MANAGEMENT OF INCIDENTALLY DIAGNOSED APPENDICEAL CARCINOIDs**

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**Purpose:** Incidentally diagnosed appendiceal carcinoids in children are rare, and controversy exists as to appropriate management, in particular the role of right colectomy. This study reviews our experience with the histopathology, followup, and outcome of patients with localized incidental appendiceal carcinoid.

**Method:** With IRB approval, we retrospectively reviewed medical records of 7 consecutive patients treated at our center for incidental appendiceal carcinoids between January 1992 and September 2009. Details concerning histopathology, tumor size, location in the appendix, demographics, and followup were obtained from patient charts. Patients had initial staging as well as followup octreotide scans and measurement of urinary 5-hydroxyindoleacetic acid (5-HIAA).

**Results:** All patients had an incidental finding of carcinoid after appendectomy performed for acute appendicitis. The median followup was 3 years, range (7 months to 7 years), and the median size was 7 mm (range, 6 mm to 1.7 cm). Five locations were known, four of which were found to be in the tip and one of which was at the base of the appendix. Three of 7 patients had mesoappendiceal invasion, as shown on pathology. One patient (carcinoid at the base of the appendix) with a positive appendiceal margin and partial appendectomy underwent removal of the base of the appendix. No patient underwent a right hemicolectomy. Urinary 5-HIAA levels remained within normal levels (3-15 mg/24 hr), and octreotide scans showed no residual, metastatic, or recurrent disease during the period of followup. All patients are currently alive without disease.

**Conclusion:** Patients with incidental appendiceal carcinoid with no evidence of metastases can be safely managed with observation using octreotide scans and measurement of urinary 5-HIAA. Right hemicolectomy can be avoided.

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**O008**

**RISK OF MALIGNANCY INDEX FOR PREOPERATIVE EVALUATION OF PEDIATRIC OVARIAN TUMORS**

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**Purpose:** Preoperative prediction of malignant potential in pediatric adnexal tumors can guide operative decisions regarding stage and use of laparoscopy. This study aimed to assess the use of risk-of-malignancy indices developed from complementary radiological and clinical parameters for cancer-risk prediction.

**Method:** Fifty-five girls under 19 years of age underwent surgery for suspicious or symptomatic adnexal masses between 2004–2009. Clinical and biochemical parameters, and blinded scores of ultrasound and computed-tomography features were correlated by multivariate logistic regression and by comparison of areas under receiver-operator characteristic curves (AUC). Study end-points were histological classification of tumors as benign or non-benign, and AUCs of tested algorithms.

**Results:** From 47 benign and 8 non-benign tumors studied, the best 2 predictive indices were developed. A logistic regression model developed included the following parameters: (1) hormone-related symptoms, (2) maximum diameter of the largest solid component, (3) enhancement or flow in a septum or solid papillary projection. This predictive index gave an AUC of 0.864, negative predictive value of 97.9%, specificity of 95.8%, and sensitivity of 85.7%, and could correctly classify 46 (98%) benign and 6 of the 8 non-benign tumors. A second index was developed by comparison of AUCs, and included the following imaging parameters: (1) large maximum diameter - more than 15 mm above 12 years old, or more than 7mm under 12 years old, (2) septal thickness more than 3mm, (3) ascites, (4) internal irregular cyst wall, (5) multiloculated or solid lesion, (6) radiologist’s impression. This predictive score gave an AUC of 0.916, negative predictive value of 95.7%, specificity of 97.8%, and sensitivity of 77.8%, and could correctly classify 45 (96%) benign tumors and 7 of the 8 non-benign tumors.

**Conclusion:** Risk of malignancy indices can accurately discriminate between benign and non-benign adnexal masses in children. Their application may guide operative management decisions before histological confirmation is available.

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**PHASE I DOSE ESCALATION STUDY OF INTROOPERATIVE RADIATION THERAPY IN RADIATION RECURENT POSTERIOR FOSSA TUMORS: FINAL RESULTS**


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**Purpose:** Thyroid Cancer (TC) is uncommon in children. The prognosis depends in the histology. Differentiate thyroid carcinoma (DTC) is often diagnosed in advanced stages with lymph node involvement and distant metastasis; however, with an appropriate treatment it has a good prognosis. Prognosis in medullary carcinoma (MTC) depends in surgical resection, reason why advanced disease at presentation has bad outcomes. To present demographic, histological characteristics and management of TC in our institution.

**Method:** Retrospective review of 27 cases diagnosed with TC over a 10 years period.

**Results:** Twenty-two second DTC and 5 MTC. Median age was 10 year-old (4–16 years), 9 male and 18 female. 14/27 had thyroid enlargement at presentation; 6 had familiar history of TC (2 DTC and 3 MEN II syndrome), 1 was diagnosed in screening post cervical radiation, 17/27 presented lymph node invasion, and 10/27 distant metastases at diagnosis. All patients underwent total thyroidectomy and central neck dissection, associated with adjuvant radiosioine treatment in DTC patients. Surgical complications were 6 transitory hypoparathyroidism, 1 phrenic paralysis, and 1 insufficient lymph node dissection. Local recurrence was 7.4% (4 patients), they underwent a second surgery. All patients received thyroid hormone replacement with levothyroxine. Follow up was done in all patients with clinical evaluation, thyroid function tests including thyroglobulin levels, cervical and chest images. One patient with MC presented disease progression despite several respective surgeries; all other patients are currently disease free (median follow up 41 months (3-115)).

**Conclusion:** TC is uncommon; there is a predominance of females. DTC frequently presents lymph node involvement at diagnosis, has a high recurrence rate, but mortality is low. Neither local disease at diagnosis or recurrences affect survival in children. MC is a different disease, requires early surgical management which improves prognosis, we recommend early thyroidectomy in patients with familiar MEN II syndrome.
Purpose: To report the final results of a phase-I intraoperative RT (IORT) dose-escalation protocol using the Photon Radiosurgery System (PRS) in children with radiation-recurrent posterior fossa (Pf/Pt) tumors. Method: Eleven children mean age 9 yrs (4-14 yrs) with Pf/Pt ependymomas were accrued on this protocol. PRS has a 50 kV x-ray source that delivers high RBE (1.4-1.5) RT to the surgical cavity. All patients were pretreated with multiple surgeries. RT (59.4 Gy) and chemotherapy. All had gross total tumor resection prior to IORT. The 3 dose levels were 10 Gy, 12 Gy and 14 Gy prescribed to a depth of 2 mm from applicator surface. IORT applicator size ranged from 1.5–3 cm, dose rate ranged from 77–170 Gy/min and treatment times ranged from 5.8–16.4 minutes. The primary end point was the development of irreversible RTOG grade 3 or higher toxicity within 3 months of IORT.

Results: Mean follow was 33 months (8–96 months). Follow up after 10 Gy, 12 Gy and 14 Gy was 208 months, 101 months and 61 months respectively. No patient developed any irreversible grade 3 or higher toxicity. All six children after 12 Gy and 14 Gy developed RT-induced MRI changes (diffuse enhancement and T2 signal hyperintensity) in the tumor bed 2–4 months post RT. These changes resolved spontaneously 6–8 months later. One patient who had multiple surgeries, chemotherapy, 59.4 Gy RT and gamma knife radiosurgery (12 Gy) prior to 10 Gy IORT, developed sub-acute infarct in the brain stem with normal MRA 4 years and 7 days after IORT. She has residual facial numbness and mild arm weakness with stable MRI findings. 7/11 had local control, 4/11 had neuraxis relapse and 5/11 are alive. The 3yr local control, disease-free and overall survival rates were 60%, 28% and 48% respectively.

Conclusion: IORT doses of 10–14 Gy to 2 mm depth using the PRS can be safely delivered after tumor resection in children with radiation-recurrent Pf/Pt ependymomas. The MTD was not reached. Survivors should be monitored for late RT-induced vasculopathy.

0001

USE OF INTRA ABDOMINAL EXPANDERS (IAE) IN THE PREVENTION OF RADIOTHERAPY (RT) INDUCED TOXICITY TO THE PELVIS

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Method: from 1987 through 2008, 29 children and young adults – mean Y (17m-23y) – were managed with an IAE prior to RT. They were 4 pathological groups (Ewing: 18, RMS: 7, osteosarcomas: 3, carcinoma: 1). Chemotherapy (CT) was administered in 29/29 (heavy regimen: 12, including Busulfan: 11), and surgery in 15/29. BO/BL displacement required 1 or 2 IAE removed within a month post RT. RT was delivered with megaradial photons ± neutron boost in 2. Mean total dose was 51.6 Gy (41.4–60), dose per fraction (dpf) 1.8–2.5 Gy. CT-based 3D dose distribution (allowing DVH evaluation to BO+BL) was performed in 8/29. In 4/8 cases, pre + post implantation CTs were available for dosimetric intercomparisons. Clinical acute and late toxicity were recorded retrospectively according to the CTC/CTE v3 score.

Results: with a mean 80 m F-Up (3-253), 27/29 patients completed RT and were evaluable. Tolerance to IAE was excellent in all, except minor to mild discomfort in 3/27 [11%]. Acute BO/BL tolerance to RT was excellent in 22/27 [81%] and poor in 5/27 [19%] since it motivated RT interruption (diarrhea: 4, urinary obstruction: 1). Late BO/BL tolerance was excellent in 23/27 [85%], and impaired in 4/27 [15%] (1g 1 BO, 1g 3 BO, 1g 4 BO, 1g 4 BO + BL). Higher toxicity was associated with the concomitant use of a neutron boost, multiple surgical procedures, dpf > 2.0 Gy, and TD > 55 Gy, DVH intercomparison in 4, evidenced marked reduction of V50-BL, and V40-BO following IAE implantation (mean pre vs post implant: 18 to 10%, and 16 to 8% respectively)

Conclusion: IAE represent a safe, simple, and efficient BO/BL sparing, that should be promoted esp. for toxic CT regimens combined with high dose RT.

0012

REIRRADIATION FOR PROGRESSIVE DIFFUSE INTRINSIC PONTINE GLIOMA AND SUBSEQUENT RADIOGRAPHIC CHANGES

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Purpose: Progression after definitive treatment of diffuse intrinsic pontine glioma (DIPG) is accompanied by severe neurologic deficits and morbidity. We describe a series of patients treated with second course of radiation therapy (RT) for DIPG and the subsequent radiographic changes. Previously, MR imaging changes have been reported to poorly correlate with survival.

Method: Five patients completed reirradiation treatment for progressive DIPG at our institution. Each patient was presented at multidisciplinary conference prior to reirradiation. Patient’s clinical records were reviewed, including post treatment MR imaging. Progression after initial therapy was verified with both clinical course and imaging. All relevant imaging was reviewed by the treating team including a single radiologist experienced in pediatric neuro-oncologic imaging.

Results: Time from initial course of RT to reirradiation was 8 to 28 months. Initial RT was 54 to 55.8 Gy with concurrent chemotherapy. Time to initial progression was 5 to 16 months. All patients had progression on salvage chemotherapy. Reirradiation was 18 to 20 Gy in 2 Gy fractions with concurrent chemotherapy. Four patients had significant clinical improvement in symptoms with improvement in speech (n = 2), ataxia (n = 3), and ocular movements (n = 3). Two patients were not ambulating prior to radiation but did so after treatment. Acute toxicity reported was fatigue (n = 2), alopecia (n = 2), decreased appetite (n = 1). Follow up MRI for four patients demonstrated objective improvement after therapy. All patients’ MRI showed decrease in tumor size. One patient had accompanied increase in T1 post contrast enhancement and also demonstrated shortest duration of clinical response.

Conclusion: Reirradiation might be a feasible option to improve symptoms and further delay progression. This may be considered in select patients, particularly those with prolonged response to initial therapy and long interval since initial radiation. In our small series, enhancement on MRI correlated with progression of clinical symptoms and may be useful for monitoring response to treatment.

0013

PROTON THERAPY (PT) IN PEDIATRIC MALIGNANCIES: THE ORSAY EXPERIENCE

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Method: 108 children were managed between 1994 and 2007 with protons for part (64) or full treatment course (44). Selected indications mainly concerned low-grade malignancies located close to critical structures in the brain, orbit, and head and neck regions that were classified in 5 subgroups (craniopharyngiomas:33, cerebral gliomas:15, bony sarcomas:34, soft tissue sarcomas: 11, others:15). Children (med. age: 11 years, range: 2-17.5) were treated with a mid 50 to 70 Cobalt-Gray Equivalent (CGE) according to the tumour type (range: 43–72) using conventional fractionation and stereotactic alignment. General anaesthesia was required in 7 cases.

Results: With a median follow-up of 28 months (range: 3–164), 5 Y OS/DFS are 88/72, and 5-Y OS significantly superior in benign processes compared with malignant ones (p.05). By subgroups, 5 Y OS/DFS were: craniopharyngiomas: 100/
PRELIMINARY ANALYSIS OF SECONDARY LEUKEMIA IN CHILDREN TREATED WITH IMRT FOR BRAIN AND HEAD & NECK TUMORS

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Purpose: Compared to conventional radiotherapy, intensity modulated radiation therapy (IMRT) is associated with a greater volume of normal tissue exposed to low dose radiation. This is secondary to the use of more fields and increased leakage radiation from delivering more monitor units. Because of the body’s exposure to low dose radiation, many have speculated that IMRT may be associated with an increased incidence of secondary leukemias. The purpose of this study is to determine the frequency of secondary leukemias in a group of children treated with IMRT for brain and head and neck tumors at 1 institution.

Method: From 1995 to 2006, 260 patients < 19 years of age received IMRT for a brain or head and neck tumor at The Methodist Hospital. There were 152 boys and 108 girls treated at a median age of 8 years. Tumor types were as follows: medulloblastoma 61, ependymoma 42, other low grade glioma 34, sarcoma 32, craniopharyngioma 25, germ cell tumor 11, high grade glioma 9, nasopharyngeal carcinoma 6, retinoblastoma 5 and other 35. IMRT delivery was through the Peacock (MIMCd) device using 10 MV photons in 182 (70.0%); the rest of patients received plan and shoot IMRT using 6 MV photons. Median follow-up time was 63.3 months.

Results: Only 1 patient developed a secondary leukemia (AML) at 7 years after IMRT for embryonal rhabdomyosarcoma of the face. He had a p53 mutation and received 4500 cGy in 25 fractions over 5 weeks to the primary site using the Peacock system. He was also found to have an osteosarcoma in the irradiated field 4 years after IMRT.

Conclusion: At a median follow up when most secondary leukemias are expected to occur, our preliminary findings showed that only 1 of 260 patients treated with IMRT developed a secondary leukemia.

CENTRAL VENOUS CATHETER PLACEMENT IN CHILDREN WITH NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA: IS EARLY PLACEMENT ADVISABLE?

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Purpose: Central venous catheters (CVC) are essential in the management of patients with malignancies. However, in patients diagnosed with acute lymphoblastic leukemia (ALL), the optimal timing for placement is unclear. We sought to determine whether early CVC placement in children diagnosed with ALL at a higher risk, would be associated with a higher complication rate while in induction therapy. The risk factors were also investigated.

Method: We evaluated surgery-related complications and associated risk factors in children with ALL diagnosed from December 2004 to January 2009 at our institution. Complications including infection, thrombosis and CVC malfunction were evaluated in the first 30 days after CVC placement. Risk factors included demographics, CVC type, blood count and clinical condition at the time of the CVC placement.

Results: Of 172 patients, 139 received externalized tunneled catheters (50% with ANC < 500 at placement) and 33 totally implantable access ports (TIAp) (15% with ANC < 500). There were 17 episodes of bloodstream infection (ANC < 500 in 10 patients), for a 30-day incidence of 9.8% (CI 5.9%–15.1%); There were no surgical site infections. No CVC was removed due to infection. One catheter (0.5%) was removed due to malfunction. Early thrombosis occurred in only 1 patient. Surgical related complications were not influenced by catheter type, patient’s age, BMI or fever at the time of placement. The infection rate increased in the presence of ANC < 500 at the time of placement (14.2% vs. 6.8%; p = 0.12), but this was not statistically significant.

Conclusion: Early placement of CVC at the time of diagnosis of ALL, was associated with an extremely low surgical complication rate with no catheters requiring removal due to infection. Utilizing our current protocols concerning preoperative preparation, surgical management and postoperative CVC care, early placement of a long term CVC is safe in children with newly diagnosed ALL even in children with severe neutropenia.

INCIDENTS AND COMPLICATION OF TOTALLY IMPLANTED VASCULAR ACCESS DEVICES: A PROSPECTIVE STUDY

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Purpose: Totally implanted vascular access devices are frequently used for repeated blood samples or intravenous treatments. This prospective study aims at identifying risk factors associated with infections, obstructions and surgical complications of these devices in pediatric oncology patients.

Method: From January 2006 to January 2008, all children older than one year with a diagnosis of solid or blood cell malignancy were included. Insertion was performed by the surgeon according to a standardized protocol after landmark-guided puncture of the subclavian or internal jugular vein by a senior anesthesiologist. Post-operative care was standardized. Each manipulation was prospectively recorded by oncology nurses. All patients were screened for surgical complications one month post-surgery. Minimal follow-up was 6 months.
SIOP ABSTRACTS

O018

SPINAL CORD COMPRESSION IN CHILDREN WITH WILMS’ TUMOUR

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Purpose: Neoplastic infiltration of the spinal canal leading to cord dysfunction is a rare complication of Wilms tumour and may result from cord compression, displacement by tumour or vertebral body collapse, ischaemia or intra-spinal metastasis. Controversy persists concerning the primary treatment of affected children.

Method: Retrospective review of 406 children with Wilms tumour of whom 5 (1.2%) developed spinal cord compression during treatment.

Results: Neurological symptoms had been present from one week to twelve weeks prior to presentation. Three patients were already receiving treatment for Wilms tumour when neurological symptoms developed. All patients had metastases to liver and/or lung and one additionally had bilateral synchronous renal tumours. Imaging studies showed epidural masses with paraspinal disease, cord displacement and compression. Abnormal signalling from vertebral bodies was seen in three patients. Four patients have died. Of two who showed neurological recovery one relapsed in the spinal canal after 4 months. Histology showed triphasic Wilms tumour in all patients with one showing diffuse anaplasia. Epidual biopsies showed perineural, intraneural and lymphovascular spread of disease.

Conclusion: One patient was offered palliative care only. Three children received chemotherapy and regional radiotherapy. One patient received chemotherapy and surgical decompression.

O019

SUPERIOR VENA CAVA SYNDROME IN MEDIASTINAL TUMORS

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Purpose: Superior Vena Cava syndrome in a child, becomes a medical/oncologic life-threatening emergency and prompt and appropriate management is crucial for survival. This brief report highlights the importance of rapid institution of therapy which otherwise could lead to mortality as has happened in one of our cases.

Method: During 2006 to 2009 all children who presented to the Department of Pediatric Surgery with SVC syndrome were retrospectively evaluated. The demographic details, clinical details, radiographic features, associated complications, histopathological features, tumor characteristics, and form of therapy instituted, overall outcome, cause of mortality were studied in detail.

Results: 6 boys between 2-6 yrs of age with a mean age of 3.8 years, presented with features of SVC syndrome. All the children were admitted to the Intensive care unit and prompt medical management was instituted. CT-Guided biopsy was done for 3, primary surgical excision for 1 and open biopsy for 1 child. 3 children had Mediastinal T-cell Lymphomas, 1-B-Cell lymphoma, 1-Germ cell tumor and 1-Thymoma. The first child with thymic mass underwent primary surgical excision and the other with germ cell tumor received upfront chemotherapy followed by surgical excision. The second child in this short series of patients succumbed to severe respiratory compromise inspite of adequate ventilatory care while awaiting histopathology report. Following this unfortunate event, all children with mediastinal masses and SVC Syndrome were given steroid therapy immediately post-biopsy, which provided significant relief in 3 of the 4 children(75%). None of the children received emergency radiotherapy. The overall outcome showed 1 year DFS of 83%(5/6) and a 2 year DFS of 75% (3/4).

Conclusion: Superior vena cava syndrome could be fatal. The lesson learnt from this study emphasizes the need to institute treatment protocols including steroids even before a histological diagnosis is established to prevent mortality due to this condition which is completely preventable.

O020

NAT2 GENE POLYMORPHISMS AND RISK SUSCEPTIBILITY TO CHILDHOOD ACUTE LEUKAEMIA

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Purpose: Maternal exposures to a variety of carcinogens, such as those found in cigarette smoke, diet, drugs and environment during pregnancy are associated to the etiology of childhood acute leukemia (AL). These compounds are acetylated by NAT2 resulting in activation or detoxification of a variety of heterocyclic amine drugs and carcinogens. Individuals may be classified as rapid or slow acetylators according to the rates at which drugs are acetylated by NAT2. Epidemiological studies suggest that NAT2 acetylation polymorphisms may modify the risk of childhood AL. To identify the distribution of NAT2 polymorphisms in Brazilian children and the effects of the polymorphisms on the development of childhood AL, we performed a case-control study.

Method: DNA samples from 194 childhood AL cases and 285 age-matched controls were analyzed. The genotypes were assessed by PCR-RFLP and the phenotypes of subjects were defined as rapid- or slow-acetylators based on their genotypes.

Unconditional logistic regression methods were used.

Results: Point mutations at positions 191 and 341 were more frequent in children with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) than in control group (7.3% and 9.7% vs. 3.7%, respectively of 191 position; and 46.5% and 48.6%, respectively of 341 position). NAT2 slow-acetylation alleles were associated to an increased risk of ALL and AML (odds ratio [OR] = 2.29; 95% confidence interval [CI], 1.69–3.11; and OR = 2.80; 95% CI, 1.55–5.07; respectively), due to a high frequency of NAT2*5A allele within the leukemia group. On the other hand, because of the underrepresentation of NAT2*4 and *12A alleles in leukemia group, NAT2 rapid-acetylation alleles were associated with a protection role of ALL and AML (OR = 0.44; 95% CI, 0.32–0.59; and OR = 0.36; 95% CI, 0.20–0.65; respectively).

Conclusion: Our findings suggest that NAT2 slow-acetylation phenotype increases the risk of ALL and AML development in Brazilian children.

O021

CANCER IN INFANTS IN MOSCOW REGION: EPIDEMIOLOGIC CHARACTERISTICS

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Purpose: The aim of the study was to assess the main epidemiologic characteristics of cancer in infants in Moscow Region (MR), Russian Federation. Method: The data on patients were retrieved from the database of Childhood Population-based Cancer Registry of MR, which was established in 2000. Only infants with the established diagnosis of cancer during 1990-2008 living on the territory of MR were included in this study. The study period was divided into two
parts: retrospective (1990–2000) and prospective (2001–2008). Morphological diagnoses were stratified according to ICD-O-3, subsequently tumors were grouped according to ICCC-3. Age-specific incidence rate (IR) was calculated per 100,000 infants. Overall survival (OS) was calculated by the Kaplan-Meier method.

Results: 113 cancer cases were registered during 1990–2008 years that comprised 6% of all cancer cases in children 0–14 years old. The male-to-female ratio was 1:2.1: The incidence rate (IR) of cancer in infants was 9.0 per 100,000 in 1990–2000 and 15.4 per 100,000 in 2001–2008. The main diagnostic groups of cancer in infants were leukemia – 20 (17.7%), renal tumors – 19 (16.8%), neuroblastoma – 17 (15.0%). Only 4 (5.7%) cases were diagnosed during the first month of life. The cancer IR during 2001–2008 years was 2.7 for leukemia, 2.4 for neuroblastoma, 2.1 for renal tumors. The OS of patients with all types of tumors diagnosed during 2001–2008 was 65% with a median follow-up of 29.5 months. The OS of patients with neuroblastoma was 91%, renal tumors – 67%, CNS tumors – 57%, leukemia – 33%.

Conclusion: The results of our study showed the distinct epidemiologic features of cancer in infants. The analysis revealed variations in incidence in Russia as compared to the data from international cancer registries. Establishment of childhood population-based cancer registry as a key element of cancer control enables us to improve the registration of childhood cancer.

0022
QUALITY OF MANAGEMENT OF ADOLESCENTS WITH CANCER IN FRANCE

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Purpose: For adolescents, the main explanations of not achieving an outcome as good as in children are the relatively poor registration in clinical trials, biological differences of several sub-types of cancer, in some of them the choice of treatment regime, and perhaps the risk of poor treatment observance. The aim is to evaluate pathway of care and quality of management for adolescents with cancer.

Method: The methodology is based on Childhood Cancer Registries, including all cases of cancer among 15–19 years, diagnosed from 2006 to 2007, living in 6 French Regions (covering rate: 40%). Data (diagnosis and treatment delays, management with multidisciplinary decisional approach, care pathway) were collected retrospectively in medical records.

Results: For all cancers, the median times for diagnosis and treatment delays were respectively 8 weeks and 2 days. About 55% of adolescents with cancer were managed with multidisciplinary decisional approach, depending on diagnosis (36% for epithelial tumours and 78% for bone or soft-tissue sarcomas). Before diagnosis, in 60% of cases a general practitioner referred the adolescent for investigation of symptoms suggestive of cancer to specialists (versus 6% for paediatricians). After diagnosis, for haematological malignancies, referent physicians were mainly adult haematologists (51%), paediatric haemat-oncologists (40%); for solid tumours: paediatric haemat-oncologists (24%), adult oncologists (14%), surgeons (39%), other medical specialists (26%). About 37% of the 15–19 years old patients were entered into clinical trials (respectively 23%, 8% and 6% into paediatric, adult and common trials).

Conclusion: Compared with children, pathway of care for adolescent with cancer is heterogeneous because collaboration between paediatrics and adult medicine is not well established. But it is necessary to elaborate National recommendations for the treatment of adolescents with cancer. The evaluation of their quality of care and their treatment modalities at the population level, providing a non-biased view, could be brought by the extension of Childhood Cancer Registries.

0023
DESCRIPTIVE EPIDEMIOLOGY OF CANCER IN AYA IN THE STATE OF SÃO PAULO, BRAZIL

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Purpose: Cancer in AYA is almost 3 times more frequent than in childhood and it has a unique pattern regarding tumor type distribution. This study aimed to describe the epidemiology profile of cancer in AYA in the state of São Paulo, Brazil, applying a special scheme to classify cases in this age group.

Method: A descriptive epidemiological study was conducted, using data from the network of hospital-based cancer registries (RHC-SP) in the period of 2000–2005, for AYA (15–24 years). Cases were classified according to the scheme proposed by Birch et al, which has 10 groups. Cases were analyzed according to sociodemographic and clinical variables.

Results: 3731 cases were registered in the period. Most cases were diagnosed in males (52.6%), in the age group 20-24 years (52.5%), with education level equivalent to high-school (41.3%). Overall, there was a predominance of Hodgkin’s disease, specified subtype (9.2%), gonadal germ-cell tumors (7.3%), osteosarcoma (6.4%), thyroid carcinoma (6.0%), and NHL; specified type (6.0%). Among males, gonadal germ-cell tumors were the most frequent tumor type (11.3%), followed by osteosarcomas (8.4%), while for females thyroid carcinomas and Hodgkin disease, specified type were the most common (9.8% each). An analysis of those tumors with valid information on staging revealed a predominance of stages I and II (56.5%). Chemotherapy alone (55.2%) was the therapeutic choice most commonly employed. For those cases without a previous diagnosis, median interval between first consultation and diagnosis (ICD) was 3 days and between diagnosis and treatment (IDT) was 2 days. Significant differences between mean ICD and IDT across the 10 diagnostic groups were observed (p<0.001).

Conclusion: Tumor type distribution is similar to that observed in other geographic regions, although it is noteworthy a higher frequency of osteosarcomas. Short intervals for diagnosis and treatment suggest that access to proper oncology assistance has been guaranteed.

0024
ACCUMULATION OF SEGMENTAL ALTERATIONS DETERMINES PROGRESSION IN NEUROBLASTOMA

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Purpose: Neuroblastoma is characterized by two distinct types of genetic profiles, consisting of either numerical or segmental chromosome alterations. The latter are associated with a higher risk of relapse, even when occurring together with numerical alterations. We explored the role of segmental alterations in tumor progression and the possibility of evolution from indolent to aggressive genomic types.

Method: Array-based comparative genomic hybridization data of 394 neuroblastoma samples was analyzed and linked to clinical data. Results: Integration of ploidy and genomic data indicated that pseudo-triploid tumors with mixed numerical and segmental profiles may derive from pseudo-triploid tumors with numerical alterations only. This was confirmed by the analysis of paired samples, at diagnosis and at relapse, as tumors with a purely numerical profile at diagnosis frequently acquired segmental alterations at relapse. New segmental alterations were also usually observed at relapse in cases with segmental alterations at diagnosis. Such an evolution was not linked to secondary effects of cytotoxic treatments since it was observed even in cases treated with surgery alone. A higher number of chromosome breakpoints was correlated with higher age at diagnosis, higher stage of disease, and a higher risk of relapse and a poorer outcome.

Conclusion: These data provide further evidence of the role of segmental alterations, suggesting that tumor progression is directly linked to the accumulation of segmental
alterations in neuroblastoma. This possibility of genomic evolution should be taken into account in treatment strategies of low- and intermediate risk neuroblastoma and should warrant biological reinvestigation at the time of relapse.

**O025**

**TUMOR CELL DETECTION IN AUTOLOGOUS STEM CELL HARVESTS IN PATIENTS WITH HIGH RISK NEUROBLASTOMA**

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**Purpose:** The presence of minimal residual disease (MRD) detected by real-time PCR in autologous stem cell harvests in children with high-risk neuroblastoma seems to be associated with an unfavourable outcome, however to date the prognostic impact of MRD in autologous harvests and the reinfusion of autologous harvests, 12% (9/75) PBSC harvests and 14% (8/55) CD34⁺ harvests. This was as a result of expansion of the PCR target due to amplification of the PCR target in normal bone marrow (BM) and peripheral blood stem cells (PBSC). In this retrospective multicenter study, harvests of a large patient cohort were studied using a recently described optimal panel of PCR targets (Stutterheim et al. Clin Chem 2009).

**Method:** In total, 37 BM harvests, 75 PBSC harvests and 55 CD34⁺ selected harvests from 167 high-risk patients were retrospectively collected at 2 Dutch and 12 German centers between 1986 and 2009. In 137 patients the harvest was reinused. Of those, 25 PBSC before CD34⁺ selection, 44 CD34⁺ selected harvests and 68 unselected harvests (28 BM and 40 PBSC) were tested. RQ-PCR was performed with six neuroblastoma specific markers: PHOX2B, TH, DDC, GAP43, CHRNA3, and DBH. The prognostic impact of MRD in autologous harvests and the identification of contaminated harvests were assessed using Kaplan-Meier plots and log-rank tests.

**Results:** Presence of neuroblastoma mRNA was detected in 46% (17/37) BM harvests, 12% (9/75) PBSC harvests and 14% (8/55) CD34⁺ harvests. This was associated with poor survival (5 years overall survival (5-OS), 23.4 ± 8.2% versus 45.6 ± 4.5% p = 0.008). In 2% (24/112) of the patients an MRD positive harvest was reinused, which was associated with poor outcome (5-OS 30.5 ± 10.5% versus 55.4 ± 5.7% p = 0.03).

**Conclusion:** Our series of autologous stem cell harvests is the largest series described up till now. In this series, BM harvests were more often contaminated than PBSC or CD34⁺ selected harvests. Both the presence of MRD in the harvests and reinfection of a contaminated harvest were associated with worse outcome.

**O027**

**IDENTIFICATION OF NEW CANDIDATE GENES IN PROGRESSION OF NEUROBLASTOMA USING OMICS ANALYSIS**

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**Purpose:** Neuroblastoma (NBL) is biologically heterogeneous and demonstrates both favorable and unfavorable outcomes. Genome-wide genetic aberrations and expression using microarray was already reported (PSI 25:031:2009, 20:33:2004, JP41:2032:2006). In this study, proteome and microRNA (miRNA) data were combined to evaluate the mechanism of neuroblastoma progression.

**Method:** From 200 NBL tumor samples analyzed by Affymetrix SNP and expression arrays, 40 tumor samples were selected, including 42 favorable cases which regressed or matured spontaneously and 20 unfavorable cases who died of tumor progression. 10 NBL cell lines were also examined. The miRNA expression levels and cellular contents were examined by Agilent microarray and LC-MS analysis using mass spectrometers with ESI module.

**Results:** About 2,000 peaks were extracted from the LC-MS data and 450 genes were listed by expression array. The comparison between these two data sets showed that MYC-induced and cholinergic pathways are activated in unfavorable tumors and apoptosis pathways including neuron-differentiation and sphingomyelin metabolites were upregulated in the favorable ones. The data of SNP array showed that the genes including DDX1, NAG, NME1, MAC30 located in the amplified and genetic gained loci activated this pathway in unfavorable tumors. The data of miRNA array showed that the activated pathways in unfavorable tumors were regulated by miRNA located in the genetic aberrated loci (miR-30c, 34a, 137and 186 in 1p, etc.). Gene dosage is correlated with the expression levels of located gene and miRNA, consequently regulating the pathways including networks of sphingolipid, apoptosis, IL6, and MMP1.

**Conclusion:** Omics analysis from gene to protein revealed the main activated pathway in unfavorable and favorable NBLs. The aberrations of gene dosage might regulate the expression of genes and miRNA and consequently regulate the malignant grade of NBLs. Further pathway analysis provided important candidates of indicators for risk assessment and of therapeutic targets for unfavorable NBLs.
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O028

NEUROSURGICAL HYPOthalamic Lesions and Postoperative Outcome in Childhood Craniopharyngioma - Results of the Multinational Prospective Trial

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Purpose: Despite high overall survival rates (92%) in patients with childhood craniopharyngioma, quality of survival is frequently impaired due to sequelae resulting from hypothalamic involvement of CP such as severe obesity. Method: Multivariable analyses of risk factors and descriptive analyses of overall (OS) and event-free survival (EFS) rates were performed in 117 patients from Germany, Austria and Switzerland, recruited prospectively (2001-2006) and evaluated after 3 yrs of follow-up (KRANIOPHARYNGEOM 2000). Body-mass-index (BMI) and QoL (PEDQOL) at diagnosis and 12 and 36 mo after diagnosis were analyzed in relation to neuroradiological reference assessment of tumor localization and a score of post-surgical hypothalamic damage (anterior, posterior or no hypothalamic lesions). Results: We observed a 3-yr-OS of 0.97 ± 0.06 and a 3-yr-EFS of 0.50 ± 0.05, indicating high recurrence rates after complete resection (CR) [n = 47; 3-yr-EFS 0.63 ± 0.09] and high progression rates after incomplete resection (IR) [n = 66; 3-yr-EFS 0.31 ± 0.07]. The risk of an event decreased by 80% after CR compared to IR (HR = 0.20 [p < 0.001]). Irradiation (XRT) had protective effects on EFS. XRT-patients had an 88% lower risk of progression compared to patients without XRT (HR = 0.12 [p < 0.001]). Growth hormone therapy had no impact on 3-yr-EFS. BMI-SDS at diagnosis was similar in patients without and with hypothalamic involvement of anterior/posterior hypothalamic areas. Surgical lesions of posterior hypothalamic areas were associated with increases in BMI-SDS during the first 12 mo (+2.2BMI-SDS; p < 0.01) and 36 mo (+3.2BMI-SDS; p < 0.01). Post-surgical QoS deteriorated in patients with posterior hypothalamic lesions. Postoperative increases of BMI (>2 SD) were associated with lowest QoS. Conclusion: We conclude that tumor recurrences/progressions are occur early after initial treatment of craniopharyngioma. Growth hormone therapy had no impact on high recurrence/progression rates observed during short-term follow-up. A radical surgical strategy leading to damage of posterior hypothalamic areas is not recommended. XRT was efficient in preventing recurrences/progressions.

O029

Changes of Peripheral Alpha-Melanocyte-Stimulating Hormone in Childhood Craniopharyngioma

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Purpose: Craniopharyngioma is associated to severe morbidity including hypothalamic dysfunction related to tumour growth and/or post-operative damage. After incomplete resection, radiotherapy reduces recurrence rate although its place is debated especially in younger children. Improving dose-gradient to critical structures and reducing brain exposure, protontherapy (PT) offers reconsidering post-operative RT according to clinical presentation.

Method: From 1994–2007, 33 craniopharyngioma, median age 9[4–16], were irradiated, at relapse in 16 cases; and as part of a combined prospective approach following conservative subtotal resection in 17 patients with hypothalamic...
Involvement (starting 2004). One patient required general anaesthesia. Multidisciplinary follow-up includes serial imaging and neurocognitive evaluation in all recent cases. Total dose 54–55 GyE, conventionally-fractionated, was delivered using mixed photon-proton approach (until 2004), or protontherapy only. Results: Comparative dosimetry (3DCRT/IMRT/protons) in 2 cases, showed benefit of proton-beams for: critical organs (non-abutting chiasma, brain-stem, cochlea); temporal lobes; whole brain exposure. At median FU 38 mths [3–163], 2 in-field relapses were observed at 49 and 40 mths and were operated showing necrosis. 1 relapse occurred along surgical access-route after 56 mths. In three cases, cystic component increased during or after protontherapy completion. Monitoring of the cysts showed subsequent shrinkage. All children had hypopituitarism with diabetes insipidus prior PT. No PT-related optic-neuropathy was observed. In children irradiated after several surgeries, neuro-psychological evaluation emphasised altered short-term memory, social and emotional functioning, and significant school difficulties. In children treated prospectively with conservaive approach, results show reduced morbidity with lower rate of obesity and behavioural disorders when preserving hypothalamus.

Conclusion: Preliminary results of combined approach with conservaive surgery for cranio/opharyngioma with hypothalamic involvement suggests reduced morbidity without jeopardizing tumour control. Long term follow up is required including longitudinal analysis of neurocognition and quality of life. With the potential to decrease risk of late-sequelae and second malignancies, protontherapy is a promising tool, especially for younger children.

O031
DISEASE CONTROL AFTER REDUCED VOLUME CONFORMAL AND INTENSITY-MODULATED RADIATION THERAPY FOR CHILDHOOD CRANIO/OPHARYNGIOMA
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Purpose: To estimate the rate of disease control after conformal radiation therapy using reduced clinical target volume (CTV) margins and determine factors that predict for tumor progression. Method: Eight-eight children (median age 8.5 yrs, range 3.2–17.6 yrs) received conformal or intensity-modulated radiation therapy at St. Jude Childrens’s Research Hospital between 1998 and 2009. This included those prospectively treated from 1998–2003 using a 10mm CTV, defined as the margin surrounding the solid and cystic tumor targeted to receive the prescription dose of 54Gy. The CTV margin was subsequently reduced after 2003 yielding two groups of patients: those treated with a CTV margin greater than 5 mm (n = 26) and those treated with a CTV margin less than or equal to 5 mm (n = 62). Disease progression was estimated on the basis of additional variables including sex, race, extent of resection, tumor interventions, target volume margins and the frequency of weekly surveillance MR imaging during radiation therapy. The median follow-up was 5 years.

Results: There was no difference comparing progression-free survival based on CTV margin (> 5 mm vs. ≤ 5 mm) at 5 years, 88.1 ± 6.3% vs. 96.2 ± 4.4% (P = 0.6386). There was no difference based the planning target volume (PTV) margin (or combined CTV+PTV). The PTV was systematically reduced from 5 to 3mm during the time period of the study. Factors predictive of superior progression-free survival included Caucasian race (P = 0.00175), absent CSF shunting requirement (P = 0.0066) and treatment protocol (P = 0.0032). Patients whose treatment protocol included a higher number of weekly surveillance MRI imaging evaluations had a lower rate of tumor progression.

Conclusion: These results suggest that targetted volume reductions for radiation therapy using smaller margins are feasible and safe but require careful monitoring. We are currently investigating the differences in outcome based on host factors, tumor volume and target volume coverage to explain the results.

O032
EFFECT OF FACTORS RELATED TO SURGERY ON LOCAL RECURRENCE IN WILMS’ TUMOUR
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Purpose: To assess the influence of surgery related factors on local recurrence rate in children with Wilms tumor treated with NWTS-5 and the impact of postoperative complications on delayed or reduced intensity of treatment.

Method: Children evaluated in this study were retrieved from the records of NCI, Cairo University. We identified all randomized and followed patients (eligible patients treated according to the NWTS-5, on whom operative and pathology narratives had been submitted to the statistical center. A total of 62 patients who met these criteria were identified. Local recurrence was defined as recurrence in the original tumor bed, in the retroperitoneum, or within the abdominal cavity or pelvis, but did not include children with hematogenous hepatic metastases only. Special attention was given to surgical complications and its impact on local recurrence rate and the intensity of the post-surgical treatment and on possible late effects, which may affect both morbidity and mortality.

Results: Data sets from 62 of registered patients with Wilms tumor who were treated on the NWTS-5 were evaluated. Median follow-up was 3.2 years. Bilateral Wilms tumor was observed in 6.4% of the cases. Intraoperative tumor rupture rates were 19% in primarily operated patients versus 25% in patients with bilateral tumor after preoperative chemotherapy. The absence of lymph node biopsy (in 12/62 of cases) was associated with an increased relative risk of recurrence, which was largest in children with stage II disease. Delayed or reduced intensity of treatment in children with postoperative complication correlated with lower EFS (p-value = 0.002).

Conclusion: Surgical rupture of the tumor must be avoided as tumor spill proved to be a major factor increasing the risk of local recurrence. Lack of definite data on lymph node status in our patients was positively correlated with increased local recurrence rate though not statistically significant.

Keywords: Wilms tumor, surgery, childhood
RENAZENAL FUNCTION IN THE TREATMENT OF BILATERAL WILMS-TUMORS.

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Purpose: Therapy of bilateral renal tumors is different from unilateral tumors. Nephron sparing surgery is required in all cases at least at one side without disregarding radicalness. In the follow-up both cure of tumor disease and development of renal function have to be regarded. We present our results from 15 consecutive cases placing emphasis on renal function.

Method: From 2004 to 2007 we treated 15 patients with bilateral renal masses. After chemotherapy (14 pat.) we performed a partial nephrectomy (PN) in 23 renal units (11 bilateral PN/PN) and a total nephrectomy (N) in 7 RU. All N were classified as stage I or II. 6 of PN showed a stage III postoperatively. Histology revealed a WILMS-tumor in 27 RU. Renal function was monitored by calculation of creatinine-clearance (CC), microalbuminuria, electrolytes, BUN and creatinine in serum, DMSA-scan, and blood pressure respectively. Follow up is 3 years (mean).

Results: Two patients died. Regarding kidney function patients with N/PN revealed lower CC than patients with a PN/PN (median 94 (range 28,5–102) vs median 128 (range 43–148) ml/min/1,73 m2). No patient showed microalbuminuria nor had serum electrolyte imbalances. Of the 2 patients with the lowest CC the first underwent N/PN with less preservation of healthy kidney parenchyma, whilst in the 2nd patient additional irradiation after PN/PN possibly accounts for the renal failure. In 6 of 10 patients with increased preoperative blood pressure the values returned back to normal postoperatively. 3 of the remaining 4 patients receive antihypertensive therapy. All had a N/PN operative procedure.

Conclusion: In our series, we see a relapse free survival of 87% in the treatment of bilateral WILMS tumors in this follow-up. PN/PN whenever possible results in better renal function and reduced need for antihypertensive treatment compared to N/PN with an adequate outcome from the oncological point of view.

O037

CLINICO-PATHOLOGIC FINDINGS PREDICTIVE OF RELAPSE IN CHILDREN WITH STAGE III FAVORABLE HISTOLOGY WILMS TUMOR: THE IMPORTANCE OF LYMPH NODES
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Purpose: Stage III designation in National Wilms Tumor Study-5 (NWTS-5) was determined by four pathologic criteria: positive lymph nodes (LN), peritoneal implants, residual disease and tumor rupture. Recent studies revealed that 17% of patients did not have lymph nodes sampled at surgery. The purpose of this study is to determine the prognostic significance of each of the stage III criteria.

Results: At a mean cross-sectional follow-up of 12 years, all measurements of serum creatinine were within normal limits. However, nephrectomized patients in comparison with those treated with NSS still presented higher mean serum creatinine SDS (0.68 ± 0.5 SD vs 0.14 ± 1.1 SD; p = 0.009). Stratification of serum creatinine SDS for postoperative interval showed a significant decrease of values in nephrectomized patients (r2 = 0.48; p = 0.017) and stable values within the lower range in patients treated with NSS (r2 = 0.004; p = 0.84). Notably, two nephrectomized patients returned to a serum creatinine SDS below 1 only 16 years after surgery.

Conclusion: In comparison with NSS, NP is followed by a longer period of adaptive renal hyperfunction, that in some patients may continue nearly for two decades. Long-term follow-up is needed to detect if sustained hyperfunction causes renal damage in predisposed children.
RNA INTERFERENCE MEDIATED SILENCING REVEALS TEL/AML1 IS DISPENSABLE FOR LEUKEMIC CLONE SURVIVAL

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Purpose: Translocation (12;21), the most frequent chromosomal aberration in childhood acute lymphoblastic leukemia (ALL), results in TEL/AML1 fusion gene. Hybrid TEL/AML1 protein was shown to play a role in preleukemia establishment, but its relevance for leukemia persistence is not yet clear.

Method: To address this question and to explore the possibilities of a potential TEL/AML1-targeted therapy we applied RNA interference to silence TEL/AML1 fusion gene in leukemia cells.

Results: To identify efficient siRNA system we designed and tested eleven different oligonucleotides targeting the TEL/AML1 fusion gene. The mix of two of most efficient siRNAs silenced the TEL/AML1 mRNA by 61%. After two rounds of siRNA transfection we achieved an average of 74% and 86% TEL/AML1 protein knock-down in U937 and U937-6 leukemic cell lines, respectively. Despite the intuitive expectation derived from studies on other fusion oncornogenes, TEL/AML1 silencing neither decreased cell viability, nor induced apoptosis. On the contrary, TEL/AML1 depletion was accompanied by the modest but significant increase in the fraction of S-phase cells and corresponding rise in the proliferation rate. Opposite effects on cell cycle distribution and proliferation were induced by AML1 silencing, supporting our hypothesis that TEL/AML1 blocks previously documented AML1 protein role in G1/S progression through the cell cycle.

Conclusion: LN involvement is highly predictive of relapse and mortality in stage III FHWT, strongly supporting the need for LN biopsy in all children with WT.

OLIGOCLONAL ORIGIN OF FUNCTIONALLY DISTINCT LEUKEMIC STEM CELLS IN INFANT ACUTE LYMPHOBlastic LEUKEMIA

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Purpose: Recent findings have challenged the cancer stem cell (CSC) hypothesis, and whether a stochastic or hierarchical model best reflects the biology of human tumors is still an open debate. With regard to ALL, the existence and the identity of a candidate leukemia-initiating cell (L-IC) is even more controversial.

Method: Through combined immunophenotype-FISH analysis, in vivo xenotransplantation assays and PCR clonal analysis, we assessed the leukemia-initiating potential of phenotypically different BM subsets, purified from t(4;11)/ MLL-AF4 positive infant ALL patients at diagnosis.

Results: Although multiple BM subsets within the B-committed CD19+/CD34- compartment can serve as L-IC in NOD/SCID mice, we observed functional differences in terms of kinetics, penetrance and immunophenotypes of engraftment, between NG2+ and NG2−, as well as CD34+ and CD34− L-ICs. Furthermore, our data suggest that each purified L-IC subset is further clonally heterogeneous, as multiple independent subclones co-exist and compete between each others to generate leukemia.

Conclusion: This is the first study reporting that in MLL-AF4 positive infant ALL, phenotypically and functionally distinct L-ICs exist, which self-renew and regenerate predominantly themselves, rather than giving rise to a more differentiated progeny of non-tumorigenic cells. We proposed an alternative model, which might possibly reconcile conflicting results with regard to previously proposed stochastic versus hierarchical models. Our findings provided new insights into the dynamic behavior of co-existing and competing leukemic clones and their contribution to the diversity of L-ICs, which might help to unravel the dismal prognosis and the frequent occurrence of relapse in this high risk leukemia.
**O042**

**INCREASED INTERFERON-ALPHA SIGNALING DURING MEGAKARYOCYTE ONTOGENY: IMPLICATIONS FOR THE SPONTANEOUS RESOLUTION OF DOWN SYNDROME TRANSIENT MYELOPROLIFERATIVE DISORDER**

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**Purpose:** About ten percent of infants with Down syndrome (DS) are born with a transient myeloproliferative disorder (DS-TMD) that spontaneously resolves within the first few months of life. However, the basis for this resolution remains unknown. Acquired mutations leading to exclusive production of a short isoform of the transcription factor GATA-1 (GATA-1s) occur in all cases of DS-TMD, and knock-in mice that exclusively produce GATA-1s have hyperproliferative megakaryocytes during early fetal liver hematopoiesis, but not during post-natal bone marrow hematopoiesis. The purpose of this study was to further understand the basis for the developmental stage-specific effects of GATA-1s on megakaryocyte proliferation in order to gain insights into DS-TMD pathogenesis.

**Methods:** Highly purified populations of megakaryocyte progenitor cells (MkPs) were immunophenotypically isolated from embryonic day 13.5 (e13.5) fetal liver or adult bone marrow of wild type mice, and their gene expression patterns were directly analyzed by cDNA microarray analysis.

**Results:** We found striking upregulation of the interferon-alpha (IFN-alpha) receptor and multiple IFN-alpha responsive genes including Il20r3, Il20s, Ifi1-1, Ifi8, and Ifi6m in the bone marrow versus fetal liver derived MkPs. The expression differences in IFN-alpha responsive genes were confirmed at the protein level by in situ immunohistochemistry. Addition of IFN-alpha to e13.5 fetal liver MkPs from GATA-1s knock-in mice reduced their hyperproliferation in a dose-dependent manner in vitro. Conversely, injection of neutralizing IFN-alpha/beta antibodies, but not control IgG, into adult GATA-1s mice increased megakaryocyte numbers 3 to 4-fold compared to wild type mice.

**Conclusion:** Increased IFN-alpha signaling during megakaryocyte ontogeny contributes to the developmental stage-specific effects of GATA-1s on megakaryocyte hyperproliferation, and possibly the spontaneous resolution of DS-TMD.

Interestingly, the gene encoding the IFN-alpha/beta receptor is located on human chromosome 21. We speculate that this may contribute to the selective pressure for GATA-1s producing mutations in trisomy 21 fetuses.

**O043**

**SIMILAR RESULTS ARE CURRENTLY OBSERVED IN THE LMB AND BFM STUDIES FOR B-CELL NON HODGKIN’S LYMPHOMA AND B-AL ALLOWING FUTURE COMMON STUDIES**

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**Purpose:** In order to study the possibility of doing a common study on rituximab for B-cell lymphoma with the different groups using BFM or LMB schemes, data of the 2 more recent French LMB and German-Austrian-Switzerland NHL-BFM studies were pooled to analyse and compare their results. In LMB, patients were stratified in 3 risk groups (A,B,C) depending on resection, stage and CNS involvement, and received 2, 4/5 or 8 courses of chemotherapy. In BFM, patients were stratified in 4 groups (R1,R2,R3,R4) adding LDH level in the stratification and received 2,4,5 or 6 courses. Although courses were differently designed and drug dosages were different in the 2 regimens, drugs were the same: HDMTX, corticosteroid, vincristine, cyclophosphamide (+/−ifosfamide), ara-C (HD in advanced stages), doxorubicin, and +/−VP16.

**Method:** Data of the BFM 95 (Blood 2005), the ongoing 04 studies, the SFCE part of the FAB/LMB 96 (Blood 2007, BJH 2008) and the ongoing LMB 2001/03 studies were merged.

**Results:** There were 691 patients in the LMB (07/96-12/05) and 935 patients in the BFM (04/96-12/05) studies. For the following analysis, 42 PMLBL were excluded, and results given for LMB and BFM in this order. 4y EFS was 90% and 89% respectively (NS). By stage (st), 4y EFS was: 98% and 97% for st1, 96% and 98% for st2, 92% and 88% (NS) for st3, 85% and 76% (NS) for st4, 81% and 81% (NS) for B-AL, 79% and 72% for the CNS+ (NS). If considering the higher risk patients: st3 with high LDH (> twice the upper normal value, or >500), st4 and B-AL, 4y EFS was 85% (n=566) and 84% (n=393).

**Conclusion:** These 2 regimens developed in parallel since 1981 using same drugs obtain similar results. This encourages an international collaboration based on a common regimen, especially addressing the question of rituximab in higher risk patients.

**O044**

**CYTOKINE INDUCED KILLER (CIK) CELLS FOR CELL THERAPY OF ACUTE MYELOID LEUKEMIA (AML): IMPROVEMENT OF THEIR IMMUNE ACTIVITY BY EXPRESSION OF CD33-SPECIFIC CHIMERIC RECEPTORS (CARS)**

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**Purpose:** CIK cells are ex-vivo expanded cells with potent antitumoral activity. CIK cells infusion in acute myeloid leukemia patients relapsing after allogeneic hematopoietic stem cell transplant is well tolerated, but limited clinical responses were observed. To improve their effector functions against acute myeloid leukemia, we genetically modified CIK cells with CARs specific for the CD33 myeloid antigen. **Method:** SFG retroviral vectors coding for anti-CD33-zeta and anti-CD33-CD28-OX40-zeta CARs were used to transduce CIK cells. Transduced cells were in vitro
characterized for their ability to lyse leukemic targets (4- hours-51Chromium-release and 6-days co-cultures assays on stromal mesenchymal cells), to proliferate (3H-thymidine-incorporation assay) and secrete cytokines (Flow cytometry assay) after contact with acute myeloid leukemia cells. Their activity against normal CD34+ hematopoietic progenitors was evaluated by analysing the colony-forming unit capacity after co-incubation.

**Results:** CIK cells were efficiently transduced with the anti-CD33.CARs, maintaining their native phenotype and functions and acquiring potent cytotoxicity (up to 80% lysis after 4-hours) against different acute myeloid leukemia targets, as also confirmed in long-term killing experiments. Moreover, introduction of the anti-CD33.CARs was accompanied by a prominent CD33-specific proliferative activity, with a release of high levels of immunosupstimulatory cytokines. The presence of CD28-OK493 CAR endodomain was associated with a significant amelioration of CIK cells anti-leukemic activity. Importantly, anti-CD33.CARs-transduced CIK cells showed a transient toxicity against normal hematopoetic CD34+ progenitors.

**Conclusion:** Our results indicate that anti-CD33.CARs strongly enhance anti-leukemic CIK functions, suggesting that CIK cells transduced with these molecules might represent a promising optimized tool for acute myeloid leukemia immunotherapy.

O045

**PHASE II STUDY OF LOW DOSE METRONOMIC (LDM) CYCLOPHOSPHAMIDE (CTX) AND VINORELBINE (VN) FOR RECURRENT OR RESISTANT PEDIATRIC TUMORS**

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**Purpose:** Low-dose chemotherapy (CT) without scheduled breaks (LDM) has been shown to inhibit angiogenesis in preclinical models.

**Method:** A two-staged Simon accrual design was adopted for this phase II study aimed at evaluating the activity and toxicity profile of the combination of vinorelbine and CTX in Rhabdomyosarcomas, non RMS soft tissue sarcomas (NRSTS), Ewing’s sarcomas, Osteosarcomas, Neuroblastomas and Medulloblastomas.

Vinorelbine 25 mg/m² i.v. was administered on days 1, 8 and 15 with CTX 25 mg po qd. Twenty patients less than 15 years had pharmacokinetic evaluation of vinorelbine. Results: Between December 2003 and December 2008, 117 patients (52% males) aged 1–24 years (median 12) were enrolled, of whom 114 were evaluable. There was a median of 3 prior chemotherapy regimens (range 1–12 and 35% had received high dose CT with PBSC rescue; 35% had received radiation therapy. Median number of courses was 2 (range 1–36) and 15 patients received more than 6 courses. Response after 2 cycles: 3 CR (3%) 17 PR (15%), 21 SD (18%) and 71 PD (65%). Median PFS was 2.1 months, PFS at 6 months was 28% [21%–37%]. Complete and partial best responses were observed in 22/114 patients: 18/50 RMS (36%), 1/7 undifferentiated sarcoma, 2/15 Ewing, 1/15 neuroectoderm, 0/11 other NRSTS, 0/10 osteosarcoma, 0/7 medulloblastoma. Neutropenia occurred in 28% of the courses, but with fever in only 7% of them. Only 5 patients presented 1 episode of minor reversible hematuria.

**Conclusion:** Metronomic chemotherapy combining vinorelbine with cyclophosphamide has clinical activity and low toxicity in recurrent or resistant RMS.

These results form part of the basis of the ongoing EpSSG trials. Data on pharmacokinetics will be available.

O046

**TRANSITION OF ADV-TK GENE TRANSFER APPROACH FROM ADULT TO PEDIATRIC ONCOLOGY**

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**Purpose:** Novel therapies are greatly needed to improve the outcome of current cancer therapies in pediatric oncology without added morbidity. Adv-tk, an adenoviral vector containing the HSV thymidine-kinase gene, plus prodrug is cytotoxic to tumor cells and stimulates anti-tumor immunity. Adv-tk has shown synergism with surgery, radiation and chemotherapy. Multiple adult and one pediatric study in retinoblastoma have demonstrated a safe dose range with some objective responses. Significant adult data in multiple tumor types support launching similar studies to evaluate Adv-tk in pediatric oncology.

**Method:** A Phase Ib/2a trial was conducted in newly diagnosed adults with malignant glioma. Adv-tk was delivered via tumor bed injection at surgery followed by valacyclovir for 14 days. Synergy with radiation was maximized by overlapping it with HSV-tk expression and prodrug activation. The phase Ib study evaluated 3 dose levels, 3x10e10, 1x10e11 and 3x10e11 vector particles. The phase 2a is an expansion of dose level 3.

**Results:** Median survival is 15.8 months and progression free survival is 10.2 months with 33 evaluable subjects to date: 12 from the phase Ib (3 each in 1st two dose levels, 6 in dose level 3), and 21 from the phase 2a. There has been no dose limiting toxicity. Radiation was started on average by day 7 (range 4–12) and temozolomide was administered after valacyclovir without decreased toxicity. T cell infiltrate was found in 4/6 resection pathologies. Similar studies in pancreatic, prostate and ovarian cancers have also demonstrated safety and potential efficacy of combinations with radiation, surgery and chemotherapy.

**Conclusion:** Adv-tk and prodrug can be safely delivered concurrently with surgery and chemoradiation in adult patients. A Phase I study recently opened for pediatric malignant glioma and a study is planned for pediatric extra-cranial solid tumors, particularly neuroblastoma.

O047

**CANCER PATIENTS’ AND PARENTS’ ATTITUDES TOWARDS BANKING OF TISSUES FOR RESEARCH**

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**Purpose:** Ethics and regulations increasingly mandate patient consent for banking of tissues for research. Little is known about what factors influence willingness to donate tissue.

**Method:** We surveyed adult patients and parents of pediatric patients within 90 days of their first visit to the Dana-Farber Cancer Institute (DFCI) to assess their willingness to donate excess tissues for research. Using a factorial survey design, we presented respondents with 4 vignettes that systematically varied along 3 dimensions: cation of samples (anonymized vs. coded); site of research (DFCI, other academic centers, commercial companies); and nature of research (genetic versus non-genetic). Logistic regression analyses accounting for clustering within respondents were used to estimate the independent effects of these 3 factors, as well as sociodemographic characteristics and trust in scientists (scale range 1–4), on willingness to donate. Due to multiple testing, associations were considered significant if 2-sided p < 0.01.

**Results:** 505 patients (372 adults, 133 parents, response rate 50%) completed surveys. Depending on the combination of factors, willingness to donate tissue for cancer research ranged from 72–98%. In regression analyses, 3 factors were associated with willingness to donate tissue: linkage of samples to respondents’ identities (odds ratio [OR] 0.5, 99% confidence interval [CI] 0.2–0.9), research at commercial companies (versus at DFCI OR 0.2, CI 0.1–0.5), and trust in scientists (OR 2.7 per 1-point increase in trust, CI 1.4–5.2). Performance of genetic analyses, sharing of tissues with
other academic institutions, age, sex, race and education were unassociated with willingness to donate tissue. Willingness did not differ between parents and adult patients.

Conclusion: Most adult cancer patients and parents of pediatric patients are willing to donate tissue for future research. Linkage of samples to patients’ identities, sharing of tissue with commercial companies, and lower trust in scientists are associated with decreased willingness to donate tissue for research.

0048

CURRENT BARRIERS FOR SUCCESSFUL TREATMENT OF CHILDREN WITH SARCOMA IN LOW INCOME COUNTRIES: A CLOSER LOOK

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Purpose: Despite the advances made in the treatment of pediatric acute leukemia, a significant survival gap between pediatric bone and soft tissue sarcomas between high and low income countries (LIC) persists. Lack of sophisticated multidisciplinary care, high risk of acute and long-term morbidities, and socioeconomic factors represent major limitations to care for these patients. We aimed to better understand barriers to treatment of pediatric sarcomas in Central America.

Method: A 110 item questionnaire was developed and distributed among pediatric oncologists in the six largest Central American countries. We analyzed descriptive information on cancer incidence and infrastructure, and subjective questions on perceived barriers to care (scaled 1–5 with rising level of contribution).

Results: The assessment showed that access to reference protocols, imaging studies, first-line chemotherapy agents, pediatric subspecialty providers, urgent laboratory data, and hospital beds was satisfactory. However, the following situations arose as potential barriers: significant patient load per oncologist, disproportionate burden of metastatic disease, inconsistent formal multidisciplinary review of staging and treatment plan, inconsistent adherence to oncologic surgical techniques and reporting of microscopic margins in pathology reports, and predominance of bi-dimensional cobalt-based radiation therapy. Cronbachs alpha reliability score on scaled questionnaire was 0.93 (goal ≥ 0.7). Major barriers (scaled > 2 in > 80% responders) included familial socioeconomic constraints, parental fear of surgery (particularly disabling surgery), difficulties achieving clear surgical margins, and lack of appropriate surgical materials such as bone allografts and endoprostheses. Other items perceived as important barriers (scaled > 2 in > 60% responders) included uncertainty in pathologic interpretation, high abandonment rates, and difficulty with communication and coordination of multidisciplinary case review.

Conclusion: Initiatives to improve treatment of children with sarcoma in LIC are warranted. Early diagnosis strategies, capacity building in cancer pathology, improved radiation therapy infrastructure and a focus on multidisciplinary case review are identified as keystones in this endeavor.

0049

KAPOSI SARCOMA IN SOUTH AFRICAN CHILDREN

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Purpose: Despite the advances made in the treatment of pediatric acute leukemia, a significant survival gap between pediatric bone and soft tissue sarcomas between high and low income countries (LIC) persists. Lack of sophisticated multidisciplinary care, high risk of acute and long-term morbidities, and socioeconomic factors represent major limitations to care for these patients. We aimed to better understand barriers to treatment of pediatric sarcomas in Central America.

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Conclusion: Initiatives to improve treatment of children with sarcoma in LIC are warranted. Early diagnosis strategies, capacity building in cancer pathology, improved radiation therapy infrastructure and a focus on multidisciplinary case review are identified as keystones in this endeavor.

0050

NOVEL RISK STRATIFICATION MODEL FOR INTRACRANIAL PEDIATRIC EPEMDYOMA BASED ON DNA COPY-NUMBER ALTERATIONS

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Purpose: Ependymoma compromises the second most common malignant brain tumor in childhood. The clinical course of intracranial ependymoma is unpredictable based on clinical variables. So far, no molecular markers have been successfully translated into clinics to stratify patients according to disease risk.

Method: In total, we studied 292 primary tumor samples from patients with intracranial ependymoma for DNA-copy-number aberrations, either by array-CGH (10K-BAC-arrays, n=170) and its clinical signi

Results: Based on our array-CGH results, we were able to define a novel molecular staging system consisting of three genetically distinct subgroups: i) low-risk group (34%: n=41) including tumors with gain of chromosomes 9,15q,18,6 and loss 1p,q; ii) intermediate-risk group (41%: n=51) characterized by balanced cytogenetic profiles especially for chromosomes 1q,9q,15q,18,6 and the CDKN2A-locus (5-year-OS=77%); iii) high-risk group (25%: n=30) comprised by tumors harboring gain of 1q and/or homoygous deletion of CDKN2A (5-year-OS=33%). Interestingly, these cytogenetic risk-groups showed a significant overlap with transcriptome-based
subgroups identified by unsupervised hierarchical-clustering. By integrating cytogenetic subgroups with mRNA-based subgroups specific for infratentorial and supratentorial localization, we could define high- and low-risk groups, respectively. High-risk infratentorial ependymomas are characterized by the overexpression of immune-response genes CXCL1 and II-8, which have been shown to define tumor self-seeding cells.

**Conclusion:** A novel staging model for intracranial ependymoma consisting of three subgroups based on cytogenetic aberrations could be deciphered. Integrating gene expression and genomic data, we were able to identify subgroup-specific genes, which may be used as surrogate markers for certain biological subgroups to stratify patients in future clinical trials.

**O051**

**THE PROTO-ONCOGENE LIM AND SH3 PROTEIN 1 ON 17Q CONTRIBUTES TO METASTATIC DISSEMINATION OF MEDULLOBLASTOMA**

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**Purpose:** Medulloblastoma is the most common malignant brain tumor and one of the leading causes of cancer-related mortality in children. Treatment failure is mainly observed in children harboring tumors with metastatic dissemination at the time of diagnosis, which typically carry an isochromosome 17 or gain of 17q, a common cytogenetic hallmark of intermediate and high-risk medulloblastoma. The aim of this study was to evaluate the association of LASP1 mRNA abundance with 17q gain and metastatic disease. To identify the oncogene(s) targeted by 17q gain, mRNA expression analysis was performed in an independent cohort of 101 primary medulloblastoma samples. Protein expression was analyzed by immunohistochemistry in a large cohort of uniformly treated patients (n = 798). To verify the predictive power of LASP1 protein expression, we analyzed overall survival and tumor progression in medulloblastoma cell lines demonstrated a strong reduction of cell migration and decreased proliferation upon LASP1 knockdown, further indicating an important role for LASP1 in the progression and metastatic dissemination of medulloblastoma.

**Conclusion:** In conclusion, we have identified LASP1 as an important player in the metastatic medulloblastoma which additionally has a high potential to serve as a molecular biomarker for outcome prediction in future prospective studies. Furthermore, LASP1 comprises an excellent novel candidate proto-oncogene for future targeted therapy approaches in high-risk medulloblastoma.

**Objective:** To identify the oncogene(s) targeted by 17q gain, mRNA expression and genomic data, we were able to identify subgroup-specific genes, which may be used as surrogate markers for certain biological subgroups to stratify patients in future clinical trials.

**Result:** Genes constituting an independent novel prognostic marker for overall survival and tumor progression in medulloblastoma. Three established medulloblastoma cell lines demonstrated a strong reduction of cell migration and decreased proliferation upon LASP1 knockdown, further indicating an important role for LASP1 in the progression and metastatic dissemination of medulloblastoma.

**Conclusion:** In conclusion, we have identified LASP1 as an important player in the metastatic medulloblastoma which additionally has a high potential to serve as a molecular biomarker for outcome prediction in future prospective studies. Furthermore, LASP1 comprises an excellent novel candidate proto-oncogene for future targeted therapy approaches in high-risk medulloblastoma.

**O053**

**DNA COPY NUMBER CHANGES AND KIAA1549-BRAF FUSION GENE DETECTION IN 125 PEDIATRIC LOW-GRADE GLIOMAS**

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**Purpose:** Embryonal tumors with abundant neuropil and true rosettes (ETANTR) and Ependymoblastoma (EBL) are highly malignant embryonal neoplasms characterized by the presence of ependymoblastic multilayered rosettes typically occurring in children below six years of age. It remains uncertain whether these two tumors really comprise distinct entities. To elucidate molecular characteristics of these embryonal tumors we analyzed the presence of 19q13.42 amplification which we previously identified in a single ETANTR by array-CGH.

**Method:** In the present study, we investigated this locus by FISH in 41 tumors which had morphologically been diagnosed as EBL or ETANTR. In addition four tumors (2 EBL and 2 ETANTR) were studied by array-CGH.

**Result:** Notably, FISH analysis revealed 19q13.42 amplifications in 37/40 samples with appropriate hybridization signals (93%). Among tumors harboring the amplification, 18 samples were identified as EBL and 19 as ETANTR. The remaining tumors (2 EBL and 1 ETANTR) only showed a polysomy of chromosome 19. Analysis of 7 recurrent/metastatic tumors revealed that the proportion of nuclei carrying the amplification was further increased (up to 80–100% of nuclei) in comparison to their primaries. These findings might be explained by a selective growth advantage for tumor cells harboring the 19q13.42 amplification. Array-CGH analysis disclosed 19q13.42 amplification in all 4 tumors studied. In addition, we found a few small regions of DNA copy-number aberrations harboring potent oncogenes and tumor suppressor genes, although their biologic relevance for the pathogenesis of these tumors requires further investigation.

**Conclusion:** In conclusion, 19q13.42 amplification constitutes a characteristic cytogenetic aberration occurring in virtually all embryonal brain tumors with ependymoblastic rosettes. This finding suggests that ETANTR and EBL may comprise a single biological entity. Thus, FISH analysis of the 19q13.42 locus helps to identify a subset of primitive neuroectodermal tumors with distinct morphology, biology, and clinical behavior.
Purpose: Low-grade gliomas (LGG, WHO grades I and II), particularly pilocytic astrocytoma, are the most common primary brain tumors seen in children, however their underlying biology is poorly understood. Fusions between the genes KIAA1549 and BRAF were recently identified in LGGs. Here, we present the results of a study evaluating the frequency of KIAA1549-BRAF fusions in LGGs and the possible association with TP53 mutation status.

Method: A total of 125 LGGs were included in the study. Tumor samples were collected from patients treated at the German Cancer Research Center, Clinical Cooperation Unit Pediatric Oncology, Heidelberg, Germany. KIAA1549-BRAF fusions were identified by direct sequencing of all coding exons (2 to 11). Immunostaining, array-based genomic hybridization analysis, and clinical data were correlated with TP53 mutation status.

Results: SNP array data were analyzed using the bioconductor and dCHIP software packages. 7q34 gain was identified in 51/67 PAs. Of these, 50 were confirmed to contain KIAA1549-BRAF fusions by PCR and sequencing, the remaining sample had insufficient cDNA for testing. Sixteen PAs showed no apparent 7q34 gain by SNP array analysis; of these 6 were subsequently found to contain KIAA1549-BRAF fusions. Gain of 7q34 was also identified in 2/2 PMAs, both contained KIAA1549-BRAF fusions. The NF1 case did not show 7q34 gain, and did not contain a fusion gene. KIAA1549-BRAF fusions were also identified in 9/12 PAs and 1/3 PMGs tested using PCR and sequencing alone.

Conclusion: KIAA1549-BRAF fusions were found only in PAs or myxoid tumors related to PA, confirming the high prevalence of fusions within PAs and indicating the importance of identifying additional biological markers within the wider classification of LGGs.

O054

TP53 MUTATION STATUS IS A POTENTIAL PREDICTIVE MARKER IN MEDULLOBLASTOMA

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Purpose: Medulloblastoma (MB) is the most common malignant pediatric brain tumor and frequently harbors 17p allelic loss (chromosome locus of TP53). In rare cases, an association between this embryonal tumor and Li-Fraumeni Syndrome (TP53 germline mutation) is observed. Previous studies describe sporadic TP53 mutations as rare events in MB with a recent report depicting TP53 mutations as unfavorable prognostic factor.

Method: Mutation analysis of TP53 was performed in a total of 321 primary MB by direct sequencing of all coding exons (2 to 11). Immunostaining, array-based genomic hybridization analysis, and clinical data were correlated with TP53 mutation status.

Results: 5.9% (19/321) of tumor samples harbored TP53 mutation with a strong positive correlation between TP53 mutation and p53-immunopositivity rendering immunostaining an excellent surrogate marker for TP53 mutation. Interestingly, no association of TP53 mutation with 17p allelic loss was observed and TP53 mutations were significantly overrepresented in the prognostically favorable WNT-subgroup characterized by CTNNB1 mutations (8/19 = 42.1% of tumors with TP53 mutations showed concomitant CTNNB1 mutations). Survival analysis revealed no correlation between TP53 mutation status and patient outcome in our large cohort mostly treated according to a protocol including postoperative radiotherapy followed by maintenance chemotherapy consisting of 8 cycles of vincristin, cisplatin and lomustine.

Conclusion: Biologically, TP53 mutation may constitute a late event in MB tumorigenesis since it occurs in all molecular subgroups. Possible explanations for the contradictory results concerning the prognostic value of TP53 mutation status in MB include the application of different cumulative doses of alkylating agents depending on the respective treatment protocols, the largely different frequency of tumors of the WNT-subgroup in the two study cohorts, and the possible inclusion of previously unidentified patients with Li-Fraumeni Syndrome.

O055

STRATIFICATION OF CHILDREN AND ADOLESCENTS WITH MEDULLOBLASTOMA BY HISTOLOGICAL AND BIOLOGICAL PARAMETERS IN SIOP-EUROPE PNET CLINICAL TRIALS

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Purpose: Treatment selection for medulloblastoma, the most common malignant brain tumor of childhood, has historically been based on clinical risk factors including age at diagnosis, M-stage, and extent of tumor resection.

Method: The recent prospective randomised PNET4 clinical trial, conducted by the SIOP-Europe PNET group, aimed to identify and validate histological and biological parameters of prognostic importance. Forthcoming trials are planned to investigate the utility of validated markers for improved treatment stratification.

Results: In PNET4, medulloblastoma patients between 3 and 21 years without metastases were treated by radiotherapy (conventional or hyperfractionated) and chemotherapy between 2001–2006. Complete analysis of a full set of biological parameters was achieved in 179/139 cases. In preliminary analyses, three risk groups were identified: 1) Favourable-risk: Patients with beta-catenin nuclear accumulation, absence of significant postoperative residual tumor, and without large-cell/anaplastic histology, MYC or MYCN gene amplification, 2) Intermediate-risk: Patients without beta-catenin accumulation but fitting all other criteria described in (1), and 3) High-risk: Patients with large post-operative residual, large-cell/ anaplastic histology or MYC or MYCN amplification. The next SIOP-Europe medulloblastoma trials (PNET5, PNET6), will use combined biological, pathological and clinical factors for treatment stratification. Feasibility studies are currently underway across SIOP-E partner countries, to establish systems for rapid, quality controlled, centralised pathology review and molecular diagnostics, to support these trials.

Conclusion: Histological and biological risk factors of prognostic value have been identified and will be applied prospectively in forthcoming SIOP-E PNET trials, aiming to improve risk-adapted treatment stratification, survival rates and quality of survival.
0058  
DOES SURGERY HAVE A ROLE IN THE TREATMENT OF LOCAL-RELATED RHABDOMYOSARCOMA? EXPERIENCE OF THE ITALIAN STS COMMITTEE

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Purpose: Patients with non metastatic Rhabdomyosarcoma (RMS) have a cure rate of 50% to 90%, but up to one-third of them experience a recurrence, mostly local. Second-line treatment is not standardized as for new-diagnosed tumors. Aim of this analysis has been to evaluate the role of surgery in the multimodal therapy of RMS local relapses (LR).

Method: We analysed the patients enrolled in two consecutive Italian Studies (RMS88 and 96): among 509 evaluable patients, 89 experienced LR, in 789 cases associated to a regional nodes involvement. Considering first-line local treatment, 10 were IRS I, 12 IRS II (5 of them were irradiated), 67 were IRS III and the delayed local treatment had been surgery in 13 cases, surgery + radiotherapy in 11, radiotherapy in 27 and none in 16.

Considering the treatment after the LR, data were insufficient for 20 cases. 39/69 underwent a surgical excision (Surgery Group, SG), mutulating in 10, with (22) or without/not known (17) radiotherapy respectively; 30/69 did not receive any surgical treatment (No-Surgery Group, NS), however 20/30 received radiotherapy.

Results: Overall Survival (OS) after LR was 39% (27/69) (mean follow-up of 59 months: range 1–226). OS of SG patients was 54% (21/39): 64% (14/22) with and 41% (7/17) without radiotherapy. 2 patients developed a second RL, cured with further treatment. Mutulating surgery did not improve survival compared to conservative surgery (40% vs 59%).

OS of NS patients was 20% (6/30): 30% (6/20) with and 0% (0/10) without radiotherapy. 1 patient developed a second RL, cured with further treatment.

Conclusion: The treatment of recurred RMS represents a challenge: in our experience patients with LR had a severe prognosis (OS ~40%). SG patients had a better outcome than NS patients (p = 0.0096) and those treated with resection plus radiotherapy had the best outcome; patients who did not receive any local treatment had an unfavourable outcome.

0059  
FIRST LINE LIVER TRANSPLANTATION FOR HEPATOBLASTOMA AFTER CHEMOTHERAPY

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Purpose: Unresectable hepatoblastoma (HBL) should be considered for liver transplantation(LT) as first line surgery in absence of visible extrahepatic disease according to SIOPEL protocol. We report the experience of our institution.

Method: We reviewed charts of patients treated with a first line LT for HBL after pre-operative chemotherapy according to SIOPEL. 3 or 4 protocols, from 2001 to 2009, focusing on waiting time, type of donor and outcome.

Results: Twelve SIOPEL PRETEXT IV, and 1 PRETEXT III P- patients, including 2 children with pulmonary metastasis at diagnosis were included. All patients but one have been referred to our centre soon after diagnosis of HBL. The schedule of current SIOPEL protocol could be respected in all patients, because of priority access to cadaveric donation obtained from experts of the Agence de la Biomédecine, the French national authority of organ procurement. The 12 patients referred initially received a cadaveric graft and the patient referred after pre-operative chemotherapy received a graft from living related donor.Eight of the 13 patients could receive post operative chemotherapy. With a mean follow-up of 3 years (range 1.4–5.1), 10 patients are alive and 3 are dead (2 teenagers from metastatic relapse, and the last one, tumor-free during 2 years, from heart failure). Among the 10 survivors, 8 (including 3 without post-op chemo) are in first CR, one (initially with intracardiac extension) is in second CR after removal of 2 successive lung mets, and one after excision of remaining tumor in origin of portal vein, and second LT for removal of secondary HBL in graft.
A PHENOMENOLOGICAL STUDY TO EXPLORE THE EXPERIENCES OF NEW NURSES ON A CHILDREN’S CANCER WARD

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Purpose: The focus of this study was to explore the experiences of nurses new to a children’s cancer ward and to understand how these experiences affected their role, care delivery and ability to make clinical decisions.

Results: The rich narratives from this study illustrated the experience and meaning of being a children’s nurse new to children’s cancer nursing. Furthermore, it raised critical questions regarding the educational and psychological support required for children’s cancer nurses, in particular new nurses. This presentation will present all aspects of the study that has implications for the ongoing mentoring and support of new nurses.

JOB SATISFACTION SURVEY AMONG PEDIATRIC ONCOLOGY NURSES

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Purpose: A descriptive cross sectional design was carried out by using quantitative data obtained through self-administered questionnaires. Our tool was the ‘job satisfaction survey’ to examine job satisfaction among 25 pediatric oncology nurses from SHIRAZ University of Medical Science (IRAN).

Results: The satisfaction for pediatric oncology staff nurses had been calculated using mean and standard deviation and results revealed that (N:25, Mean:2.3) and this is an indication of dissatisfaction.

Conclusion: This research study reports on Child Health Nurses (CHN’s) perceptions of the impact of paediatric oncology education on their practice. Using a phenomenological approach, this study explores this phenomenon in depth, constructing meaning through the individual participants’ ‘lived experiences’ (Van Manen 1990). A purposive sample of CHN’s participated in semi-structured interviews within their clinical environment. The interviews were digitally recorded and transcribed verbatim. Transcribed data were analysed with assistance from the software package QSR NVivo (Bryman 2008).

Results: Findings suggest that formal paediatric oncology nurse education is perceived to positively impact on the practitioners practice. The practitioners felt empowered through the newly found knowledge, confidence and attitude gained from the education received.

Conclusion: This study explored the knowledge, attitudes and beliefs of nurses who administer chemotherapy to children and young people.

EXPLORING THE WORK OF NURSES WHO ADMINISTER CHEMOTHERAPY TO CHILDREN AND YOUNG PEOPLE

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Purpose: This study explored the knowledge, attitudes and beliefs of nurses who administer chemotherapy to children and young people.

Method: The study involved a national postal survey of nurses working within the 21 cancer centres in the UK and Ireland. The questionnaire included 25-items addressing the attitudes, beliefs and concerns regarding nurses’ roles, support mechanisms and educational preparation related to administration of chemotherapy. Mann Whitney U-tests was used to identify differences between variables and relationships between variables using Spearman’s ‘d’ test.

Results: 286/307 (56%) questionnaires were returned. The majority of nurses worked in in-patient +/-outpatient (78%) settings and most gave chemotherapy on a daily basis (61%). The median time working in oncology was 10 [range 0.5–32] years and time administering chemotherapy was 8 [0.1–32] years. Most had completed a chemotherapy workbook (n = 245; 86%) but only 66 (26%) had competed an update. Aspects of administration that caused the most worry included treatment side-effects, extravasation, dealing with allergic/anaphylactic reactions and knowledge deficits in colleagues. 9/17 aspects this was more so in lower banded nurses (p < 0.05). The
questions related to worry were subdivided into three domains: Education, Safety and Support. There was no significant difference in worry according to level of nurse education but those with an oncology qualification had less Knowledge-related worry (p=0.05). The attitude questions were subdivided into three domains: Education, Emotions and Communication. There was no difference in attitude according to level of education or having an oncology qualification. There were significant correlations between time qualified, time working in oncology and the number of years administering chemotherapy and the three worry domains (ranging from r=-0.14 to r=-0.24, all p<0.05); and attitude to chemotherapy (ranging from r=0.12 to r=0.26, all p<0.001).

Conclusion: This presentation will present the method and focus on the findings that have implications for education and training.

0064

A NOVEL NURSE RESEARCH MENTORSHIP PROGRAM TO PROMOTE EVIDENCE BASED PRACTICE

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Purpose: The first Nurse Researcher Workshop funded by the Alex’s Lemonade Stand Foundation (ALSF) will take place in the spring of 2010. ALSF evolved from a child’s lemonade stand into a national fundraising program for childhood cancer care. This nonprofit organization has established a program for novice nurse researchers that includes both educational and mentorship components. The goals of the twoday workshop are to train pediatric oncology nurse researchers in the mechanics of designing research questions, securing funds, implementing research, and disseminating research findings. A critical piece of this program is the ongoing support following the workshop through a one on one mentorship at the applicant’s institution to facilitate the implementation phase.

Method: Applicants were required to submit essays describing how the workshop would impact the novice nurse researcher, a description of research interests and their impact on children with cancer, letters of recommendation, and a curriculum vitae.

Results: Nineteen nurses were accepted into the program following a vigorous review process. A broad spectrum of pediatric oncology nurses’ research ideas throughout the United States will be presented at the workshop. An example of the development of a research concept and nurse researcher/mentor relationship will be explored in detail using this applicant’s research pursuits - caregiver stress and development of a telephone based support group for parents of children who have been recently been

Conclusion: This presentation will present the method and focus on the findings that have implications for education and training.

0065

THERAPEUTIC RELATIONSHIPS: HONORING THE SPACE BETWEEN US

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Purpose: From diagnosis of cancer to off treatment or palliation, children and families are vulnerable and look to nurses for support and advocacy. Without meaningful relationships with children and families, nurses cannot fulfill their professional and ethical obligations. The difference between a caring therapeutic relationship and an over-involved relationship is narrow. Recognizing this and taking a proactive stance to ensure that we give our patients and their families our best, without harming ourselves, is an important skill to develop, with implications for ourselves, colleagues, and the children and families for whom we care.

Method: Using the best evidence as a basic foundation, we will use a case study approach to explore the nature of nurse/health care professional (HCP)/patient/family relationships. We will offer an opportunity for participants to develop a personal self-care plan that will (1) help them identify stressors that may impact their ability to maintain professional therapeutic relationships, (2) offer strategies to help them individualize their care plan as they turn complex emotional situations into therapeutic ones, and (3) demonstrate a feedback loop so they can keep their personal care plan active and relevant.

Results: Participants will have an opportunity to learn more about the ways that HCPs may protect the space between their own power and the patient/family’s vulnerability by using tools that will help them develop a personal/professional care plan. They will take into consideration the internal and external stressors that may affect one’s performance, and the emotional toll of poor therapeutic relationships and boundaries.

Conclusion: Our work should not cause us harm. This session will help participants ensure that it does not. At the same time, it will help illuminate ways we can enhance the care we give to patients and families.

0066

BTG1, A GENE FREQUENTLY DELETED IN PRE-B ALL, REGULATES GLUCOCORTICOID RECEPTOR-MEDIATED GENE EXPRESSION

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Purpose: By genome-wide SNP-based array CGH we have found that about 10% of pediatric pre-B ALL cases contain a (single copy) deletion of the B cell translocation gene 1 (BTG1) gene. BTG1 belongs to a family of potential tumor suppressor genes implicated in the induction of growth arrest and apoptosis. BTG1 associates with and regulates the activity of the arginine methyl transferase PRMT1, a coactivator of nuclear receptor-mediated transcription. As BTG1 was found to be upregulated in ALL in response to synthetic glucocorticoids (GCs), we examined a role for BTG1 in GC induced therapy responses.

Method: Here we use shRNA mediated knockdown to examine the role of BTG1 in GC therapy resistance.

Results: Loss of BTG1 decreases sensitivity of pre B ALL cells to the apoptosis-inducing effects of synthetic GCs about 10,000 fold. This acquired GC therapy resistance is accompanied by a 10 fold reduction in GR protein expression as well as a loss of GC-induced gene expression. Conversely, increased expression of BTG1 restores GC sensitivity by potentiating GC-induced GR expression, a phenomenon known as GR autoinduction. In addition, we show that BTG1 potentiates GR-dependent transcription activation in a luciferase reporter assay. Moreover, PRMT1 is recruited to the endogenous GR/NR3C1 gene promoter in a BTG1-dependent manner, consistent with a role for this arginine methyl transferase in the regulation of GR-mediated gene expression.

Conclusion: Our results implicate the BTG1/PRMT1 complex in GR target gene regulation and reveal how deregulation of a nuclear receptor coactivator complex can give rise to GC resistance. Identification of these coactivators as part of the GR regulatory circuitry could offer novel opportunities for improving the efficacy of GC based therapies in ALL as well as other hematological malignancies. To what extent single copy losses of BTG1 affect GC-induced therapy responses in the patient is currently under investigation.

0067

GERMLINE GENOMIC VARIATION IN THE MTHFR AND MTRR GENES DETERMINES IMPAIRMENT OF BONE MINERAL DENSITY IN PEDIATRIC ACUTE LYMPHOBlastic LEUKEMIA

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Purpose: We have previously shown that single nucleotide polymorphisms (SNPs) occurring in the genes encoding MTHFR and MTRR are associated with decreased bone mineral density (BMD) in children with acute lymphoblastic leukemia (ALL). To determine whether these associations were due to germline genomic variation we investigated whether these SNPs were associated with differences in BMD in normal pediatric controls.

Method: We examined the association between MTHFR and MTRR genotypes and BMD in 71 healthy children and adolescents aged 10-17 years.

Results: We found that the C677T MTHFR SNP was associated with decreased BMD at the lumbar spine (p=0.03) and the C677T MTHFR SNP was associated with decreased BMD at the lumbar spine (p=0.03)

Conclusion: Our results support the hypothesis that germline variation in the MTHFR and MTRR genes is associated with decreased BMD in healthy children and adolescents.
Conclusion: the BTG1 knockdown cells is accompanied by increased expression of ASNS.

Results: The MTHFR 677C > T SNP and the MTRR 66A > G SNPs were identified as determinants of impaired BMD-TB in children treated for ALL.

Purpose: To determine whether the infusion duration of high-dose methotrexate (1 g/m²) affects the in vivo accumulation of active methotrexate polyglutamates (MTXPG) in leukemia cells, and whether the accumulation differs among major subtypes in acute lymphoblastic leukemia (ALL).

Method: As pre-induction therapy on the St Jude Total XV protocol, 356 children diagnosed with acute lymphoblastic leukemia (ALL) were randomized to receive high-dose methotrexate (1 g/m²) as a 24-hour IV infusion or a 4-hour infusion. Accumulation of MTXPG was measured in leukemia cells obtained from bone marrow 42 hours after start of the methotrexate infusion. Antileukemic effects were measured as inhibition of de novo purine synthesis and decrease in circulating leukemia cells.

Results: The 24-hour infusion produced significantly higher concentrations of MTXPG (median: 1695 pmol/10⁹ cells) than the 4-hour infusion (median: 1150 pmol/10⁹ cells; P = 0.006), and greater antileukemic effects (i.e. decrease in circulating leukemia cells; P = 0.04), and inhibition of de novo purine synthesis (P = 0.02). Among ALL subtypes, the 24-hour infusion had the greatest effect on MTXPG accumulation in hyperdiploid > 50 ALL (24-hour infusion median: 3919 pmol/10⁹ cells vs. 4-hour infusion median: 2417 pmol/10⁹ cells; P = 0.004). T-cell ALL exhibited smaller differences in MTXPG but greater antileukemic effects with the longer infusion (decrease in leukemia cells: 24-hour infusion median: 88.4% vs 4-hour infusion median: 51.8%; P = 0.008). In ALL with the t(12;21)(ETV6-RUNX1) subtype (~23% of all patients), infusion duration had no significant impact on MTXPG accumulation or antileukemic effects.

Conclusion: Infusion duration of high-dose methotrexate is an important determinant of intracellular accumulation of active methotrexate in ALL cells. However, the impact differs among ALL subtypes, with longer infusion particularly beneficial in hyperdiploid and T-cell ALL. Our data suggest that 4-hour infusion could potentially be used to reduce hospitalization time and healthcare costs for patients with t(12;21)(ETV6-RUNX1) ALL.

O070

ASPARAGINASE THERAPY IN THE ALL-BFM 2000 TRIAL - A FOLLOW-UP OF 127 PATIENTS

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Purpose: Therapeutic drug monitoring (TDM) of asparaginase (ASNase) activities and follow up of all patients treated according to the ALL-BFM 2000 protocol between 08/1999 and 10/2005 at the university hospital of Muenster.

Method: 127 patients (median age 5 years, [range: 14 yrs – 18 yrs]) diagnosed with ALL were evaluated. ASNase activities were monitored throughout all ASNase containing elements (induction, reindensification). Treatment started with 5,000 U/m² E.Coli ASNase during induction followed by 10,000U/m² E.coli during reinensification. In case of allergic reactions patients received second line
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treatment with 1,000U/m² PEG-ASNase and third line ASNase treatment 25,000U/m²
Erwinia-ASNase.

Results: 9/124 patients (7%) had insufficient ASNase activities and/or allergic
reactions after E.coli-ASNase during induction. 10 patients dropped out after
induction, 2 patients were added for reinduction monitoring.

107 patients were monitored throughout reintensification. 76 (out of 86) pat continued
reintensification with first line E.coli (71%), 10 patients started reintensification with
PEG-ASNase for clinical reasons during induction. 18 pat were consecutively
switched to PEG-ASNase. 3 patients (17%) were not to re-establish sufficient
activities afterwards. 21 patients were switched to PEG-ASNase (1,000U/m²) for
reintensification without allergic reactions to E.coli ASNase and 15 out of 21 patients
(71%) passed reintroduction treatment on the basis of “front-line” PEG-ASNase for
reintensification with sufficient activities. Thus, at least 71% finished reintensification
after up front PEG-ASNase with sufficient ASNase activities. 80% of all patients
reached end of reintroduction protocol without need of Erwinase.

Conclusion: This clinical-pharmacological monitoring of ASNase therapy
demonstrates that treatment with E.coli-ASNase front- and PEG-ASNase second-line
is as effective as E.coli follow-ASNase followed by Erwinase, as published recently
(Vroooman L et al, 2010). Compared to data using front-line treatment with PEG-
ASNase for reintensification, this monocentric dataset reveals no major differences of
the current concept with regard to patients with insufficient activities after induction
and reintensification.

0071

TOXICITY AND EFFICACY OF DEXAMETHASONE AND METHYLPRERNSISOLONE USED IN INDUCTION TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS OF MULTICENTER CONTROLLED ALL MB 2002 STUDY

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Purpose: To compare toxicity and efficacy of dexamethasone 6 mg/m² and
methyprednisolone 60 mg/m² used during induction treatment of childhood acute
lymphoblastic leukemia (ALL).

Method: A randomized multicenter study ALL-MB 2002 was performed in 37
pediatric oncology/hematology centres in Russia and Belarus. The induction
treatment accordingly ALL-MB 2002 employed a 6 week phase with dexamethasone
or methylprednisolone, vincristin, daunorubicin (once for standard risk (SRG) [day 8]
and twice for intermediate risk (IMRG) [day 8 and 22] patients) and triple intrathecal
therapy. Between 01.05.2002 and 10.12.2006, 1072 newly diagnosed ALL patients
aged 1–18 years were randomly allocated to dexamethasme 6 mg/m² (n = 546) or
methylprednisolone 60 mg/m² (n = 526) during induction.

Results: Almost identical number of patients achieved remission on day 36: 522/546
in dexamethasone group (95.6%) and 502/526 in methylprednisolone group (95.4%).
Induction death rate was 3.3% (18/546) in dexamethasone group and 3.8% (20/526) in
methylprednisolone group (p = 0.74), and remission death rate (RD) was 4.2% (23/546) and 7.4% (39/526) respectively (p = 0.026). There was an identical relapse rate
(15.8%) in both groups. The 8-year event-free survival (ePFS) was 74% ± 2% and
71% ± 2%, correspondingly (p = 0.23).

There were no differences in respect of PFS, ID and RD between dexamethasone
and methylprednisolone depending on risk groups, but cumulative risk of isolated CNS
relapse for both SRG and IMRG was significantly lower in dexamethasone group
compared with methylprednisolone group (1.64% ± 0.01% vs 3.67 ± 0.01%,
p = 0.04). The detailed retrospective toxicity analysis of 271 randomised non-selected
patients has shown that severe and non-severe non-lethal infectious complications
during induction as well as during first 100 days after diagnosis were identical in both
groups.

Conclusion: The use of dexamethasone 6 mg/m² during induction compared with
methylprednisolone 60 mg/m² was not associated with higher ID, RD and non-lethal
acute toxicity, but led to better CNS disease control in a setting of Moscow-Berlin
protocol.
expression. Treatment with 5-Aza-2'-deoxycytidine resolves gene expression of SFRP2 offering a possible future treatment approach, especially for refractory YST and CC.

Supported by a grant from the Medical Faculty’s Research Commission of the Heinrich-Heine-University Düsseldorf

O073

STAGE I GERM CELL TUMORS: OUTCOME OF A WATCH AND WAIT STRATEGY

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Purpose: Clinical trials in both men and boys have demonstrated that for patients with stage I testicular germ cell tumors (GCT) close observation after surgery reserving chemotherapy only for those with residual or recurrent disease results in excellent event free and overall survival. A similar strategy for girls with stage I ovarian GCT was assessed as part of the current COG protocol AGCT0132.

Method: Girls with ovarian germ cell tumors were included on the observation trial only if patient had evidence of a malignant germ cell tumor histology (yolk sac, choriocarcinoma or embryonal carcinoma) and had undergone full radiologic and operative staging, including cytologic examination of either ascitic fluid or peritoneal washings. Tumor markers (AFP and B-HCG) were followed every 3 weeks and imaging of chest/abdomen and pelvis were obtained every 3 months.

Results: 25 girls with stage I ovarian tumors were enrolled; 11 girls had evidence of residual or recurrent disease as evidenced by rising tumor markers (5), new radiologic evidence of disease (1), or both (5). The Kaplan-Meier estimate of the 2 year EFS is 50.2% (95% confidence interval 28.2-68.7%). Median time to event was 1.7 months (range 1-7.8). Median follow up on those without events is 26 months (range 0.6-60). Association with surgical approach, histology, and other predictors of relapse will be described. Overall survival however is >95% (not lower than expected).

Conclusion: Girls with stage I ovarian germ cell tumors appear to have a higher rate of protocol-defined disease progression (p = 0.08). However, at least at this point in follow-up, salvage with three cycles of “compressed” bleomycin, etoposide and cisplatin appears to be excellent with no diminution in overall survival.

O074

TREATMENT WITH PE FOR INTERMEDIATE-RISK GERM CELL PEDIATRIC PATIENTS FROM THE BRAZILIAN GCT-99 PROTOCOL.

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Purpose: Assessment of two drugs with standard doses in three days/cycle for intermediate-risk (IR) germ cell patients.

Method: The Brazilian GCT-99 protocol was the second cooperative study where children were registered from May-99 to October-2008, with a total of 533 patients. We have followed 156 patients admitted in this IR group. We have used the Children’s Oncology Group (COG) staging system. Were included testicular tumors EI/II (no teratoma), ovarian EI (no dysgerminoma/teratoma) and EI/III (no teratoma) and extragonadal EI (no teratoma). These patients have received 4 cycles of PE (cisplatin = 35 mg/m²/daily x 3 and Etoposide-170 mg/m²/daily x 3). If partial remission or in progression after the 3rd cycle, second arm was added with 3 cycles of IVB (Hosamamide, Vinblastine and Etoposide).

We show here 3 years-EFS (by Kaplan-Meyer methods). Differences between groups were assessed by long-rank test.

Results: A total of 123 patients have been analyzed. The primary site was 23 testicular, 84 ovarian and 6 extragonadal. Treatment was PE for 113 patients (91.8%) and 5 drugs (PE+IVB) for 10 patients (7 testicular and 3 ovarian). The 3y-EFS was 86.5% for the PE group and 88.8% PE+IVB group (p = ns). In a univariate analysis no results statistically significant have been found for primary site, presentation at diagnosis (R0 x R1/R2), histology, but for testicular EI vs EIII the curves were statistically significant (94.4% x 63.6%, p = 0.003).

Conclusion: Preliminary results suggests that two drugs in a standard dosage used for 3 days/cycle is enough for gonadal IR group. However, testicular group probably needs a better ganglionar imaging evaluation and a better control from the board of our group to help the doctors before and during the reevaluations.

O075

PAEDIATRIC MEDIASTINAL GERM CELL TUMOURS: ARE ALL PATIENTS HIGH RISK?

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Purpose: Although most paediatric patients with extracranial malignant germ cell tumours (MGCTs) have an excellent prognosis, patients with mediastinal primaries seem to have a higher risk of treatment failure. For MGCTs at most sites prognosis is influenced by additional factors of age and histology. Analysis of a large, combined dataset of US and UK MGCTs was undertaken to refine understanding of prognostic factors for mediastinal primaries.

Method: A combined US/UK dataset of 1027 paediatric MGCTs was created during 2009. Patients were treated between 1983 and 2005 on platinum based protocols (GC1, GC2, P9047, P9048, P9747, AGCT01P1, AGCT0132). UK treatment was predominantly carboplatin based in contrast to cisplatin based in the US. Prior published data indicate outcomes to be comparable.

Results: There were 65 patients with mediastinal MGCT (48 M,17 F) aged 0–10 yrs, 32 < 10yrs, 32 >10yrs. Histology was germinoma 4, embryonal carcinoma 1, choriocarcinoma 2, yolk sac tumour 21, mixed 28, missing 9.

For mediastinal primaries a distinct pattern emerges with 2 peaks, < 5 and >10yrs. A significantly greater percentage of patients are male, >10yrs and have Stage 3/4 tumours than MGCTs overall. Male predominance is particularly marked >10yrs (90%, M, 10% F).

Overall mediastinal MGCTs had 72% EFS at 4yrs, 95% CI [59.0, 81.3] and all MGCTs 85% [82.7, 87.7]. p = 0.004. For patients < = 10 EFS was 82%[63.9, 91.4] compared to 61%[41.2, 75.7] for patients over 10. When compared to other MGCTs in < = 10 yrs EFS was 82% and 86%[82.9, 88.7] respectively. In contrast in patients over 10 yrs EFS was 61% compared to 84%[78.3, 87.8] for other MGCTs, p = 0.003.

Conclusion: Creation of a large dataset has clarified the difference between the good prognosis of patients < = 10 and the distinctly worse outcome in patients > 10 with mediastinal MGCTs. This may define a group where future therapeutic intensification is justified.

O076

PROGNOSIS AND OUTCOME OF OVARIAN GERM CELL TUMORS – FINAL RESULTS OF THE GEMMA MAKE 96-TRIAL

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Purpose: Most germ cell tumors (GCTs) in the pediatric population are localised in the ovary. Teratoma account for about 50% of this group. Ovarian tumors if localised have an excellent prognosis with event-free survival rates of nearly 100%, whereas only little is known about risk factors for prognosis in this disease group.

Method: We analyzed 470 children and adolescents with ovarian GCTs registered between 01.01.1996 and 31.12.2005 in the MAEKi (96) trial. 37 patients were identified as tumors in both ovaries, 13 developed a metachronous disease. 4 patients suffered from a 2nd malignancy (ALL, PNET, Glioma, Medulloblastoma). Children with malignant GCTs have been treated with a risk-stratified therapy considering histology and stage. Patients with ovarian disease only are treated with surgery and a watch and wait-strategy. Patients with dissemination either into surrounding tissue (FIGO II) or metastases (FIGO III-IV) received a platinum-based chemotherapy.

Results: 396 protocol patients were reported, median age was 11 years. Mature and immature teratoma were diagnosed in 196 patients, dysgerminoma in 50 and secreting GCTs in 150 patients. The event-free survival in patients with malignant GCTs, FIGO stage I to III is 0.78 ± 0.08 (CR = 167/192, median survival: 48 months). The event-free survival in patients with FIGO stage IV is 0.50 ± 0.20 (CR = 3/6, median survival: 9 months). In 5/6 patients with FIGO IV a YST was diagnosed: 4/5 patients had metastases in lung and liver, 1/5 patient showed only regional metastases. 1/6 patient had a mixed malignant GCT (CHC, YST, dysgerminoma) with metastases in the spleen and died of diffuse bleeding. 

Conclusion: Although the prognosis is excellent for stage I to III patients under protocol treatment, patients with FIGO stage IV are not sufficiently treated with conventional chemotherapy. Therefore up front intensification seems necessary to improve outcome.

Supported by a grant of the Barbara und Hubertus Trettiner foundation

O077 PROGNOSIS AND OUTCOME OF TESTICULAR GERM CELL TUMORS (GCTs) – FINAL ANALYSIS OF THE GERMAN MAHO 94/98 AND THE MAKEI 98/96 TRIALS.

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Purpose: In the German MAHO/MAKEI trial patients (pts) were treated with a risk-stratified therapy considering the parameters localisation, stage and histology. Testicular pts with mature and immature teratoma or pure Yolk Sac (YST) Lugano stage Ia received a watch-and-wait strategy after tumororchidectomy. All other pts were treated with a cisplatin based chemotherapy.

Method: We analyzed 165 children and adolescents with testicular GCTs registered between 01.01.1996 and 31.12.2005. 120 protocol pts with a median age of 2 years and an overall survival (OS) of 0.97 ± 0.02 (alive / dead = 116/119; median survival: 29 months) are discussed.

Results: 60/120 pts without chemotherapy were reported, 59/60 of those pts had teratoma or pure YST Ia (age < 10 years). 60 pts received chemotherapy: leading diagnosis was YST in 7 pts, Embryonal Carcinoma in 34 and Choriocarcinoma in 19, Seminoma were not found. 11 patients were < 10 years, 3 had an extended disease (Lugano IIc-IIIc). 49 pts were > 10 years, 11 pts had Lugano Ia-Ib, 7 pts showed Lugano Ia-IIb, none relapsed. 31 patients were diagnosed with Lugano Ic-IIc. 9/31 pts relapsed, the event-free survival (EFS) is 0.68 ± 0.09, median survival: 25 months). 5/9 relapsed pts showed at diagnosis haematogenous metastases outside the lung. (EFS: 0.44 ± 0.17, median survival: 11 months).

Conclusion: Prognosis in testicular GCT is excellent but depends on stage, histology and age. Lugano IICc and mixed histology were reported in patients > 10 years only. 

Patients with haematogenous metastases outside the lung have the most unfavourable prognosis and need upfront treatment intensification.

Supported by a grant of the Barbara und Hubertus Trettiner foundation

O078 HIT-SIOP PNET4 – A RANDOMISED MULTICENTRE STUDY OF HYPERFRACTIONATED (HFRT) VERSUS STANDARD RADIOTHERAPY (STRT) IN CHILDREN WITH STANDARD RISK MEDULLOBLASTOMA (MB)

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Purpose: The first aim of this study was to compare whether HFRT is superior to STRT for survival and late effects. A second aim was to collect tumor material from a large uniformly treated group of patients in order to study biological markers for future risk grouping.

Method: Patients over 4 years with standard risk Medulloblastoma (MB) where randomised to craniospinal HFRT 1.0 Gy twice daily (36 Gy craniospinal, 60 Gy posterior fossa, 68 Gy residual tumor) or STRT 1.8 Gy daily (23.4 craniospinal, 54 posterior fossa). Thereafter chemotherapy with Cisplatin, CCNU and Vincristine was given in 8 courses.

Results: Between 2001 and 2006 339 patients were included (211 M, 128 F) from ten countries. Randomisation assigned 170 patients to HFRT and 169 STRT. Central review of pathology was performed in 97%. Sixtythree pts (19%) have relapsed. One child died in remission. Mean/Md follow up for children in remission is 52/48 months. EFS at 3 and 5 y FU is 0.82 ± 0.02 and 0.79 ± 0.03 with no significant difference between the two arms. Patients with residual tumor > 1.5 cm³ had a significantly increased risk for relapse. The pattern of relapse will be discussed. Survival 3y after relapse was 0.08 ± 0.05. Complete analysis of the whole set of biological markers planned was achieved in 50% of the patients.

Conclusion: There was no significant difference in EFS between the two radiotherapy arms. Longer follow up may reveal a benefit of either RT arm for late effects. The patients can be stratified according to clinical and biological data into three risk groups for future studies.

O079 CHILDHOOD AND ADOLESCENT CNS TUMOUR SURVIVORS’ EVALUATION OF PROVIDED INFORMATION DURING AND FOLLOWING TREATMENT

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Purpose: To study CNS tumour survivors’ informational needs, and satisfaction with extent and quality of information provided during and after treatment.

Method: In a population-based cohort of 697 > 18 years old childhood and adolescent CNS tumour survivors, 531 survivors provided data (78% response rate). Information was studied using a questionnaire including areas similar to those of the EORTC QOL-INFO26 inventory. It covered issues about medical tests, disease and treatment, monitoring of late effects, and psychological- and rehabilitation services. We also asked respondents to evaluate the quality of information.
Results: On the whole, 53% of survivors reported no, or only minor, satisfaction with the extent of information. 263 survivors (52%) expressed need for more information than provided, and 4 survivors (1%) wanted less. Greatest amount of information was received about medical tests, followed by information about disease and treatment. Least information was received for “other services”, including psychological support and rehabilitation services, for which half of survivors (54% and 49%, respectively) reported that they had received no information whatsoever. The information provided was found useful (to some extent/very much) by 53%, while 33% found it useful to only a minor degree, and 14% not at all useful. Survivors listed that they had additional information needs, beyond what was provided, in the domains of late effects, illness education, rehabilitation, and possibilities for getting psychological support. Only 26% told that they had received written information.

Conclusion: A considerable proportion of survivors indicate dissatisfaction with provided information. Although the wish for written information was evident, only one fourth of survivors told that they had received such. Unmet information needs regarding late effects, services beyond primary cancer treatment, and psychological support should be acknowledged. High quality comprehensive care and follow-up should more effectively address issues where information to childhood CNS tumour survivors is evidently unsatisfactory.

O080

OUTCOME FOR CHILDREN’S CANCER AND LEUKAEMIA GROUP (CCLG) PATIENTS TREATED WITH RADIOTHERAPY (RT) IN THE FIRST INTERNATIONAL CONSORTIUM LOW-GRADE GLIOMA STUDY (LGGI)

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Purpose: To report EFS and OS for children with LGG treated with RT in the LGGI study and to report impact of RT dose on outcome.

Method: Between March 1995 and November 2007 154 eligible children aged 1.2–20.3 years (median 9.2) were treated with RT at diagnosis (55), after observation (51), after chemotherapy (33) or after observation then chemotherapy (15). Predominant primary site was midline supratentorial in 79(51.3%) and histology pilocytic astrocytoma in 86(55.8%).

Results: Median follow-up from start of RT was 5.0 years (range: 3 months – 11 years). Forty-four (28.6%) relapsed after RT and 21 (13.6%) died following relapse. Five-year EFS and OS from commencement of RT were 70.7% and 87.2% (95% CI 61.4%, 78.1% and 80.4% 92.5%) respectively.

Conclusion: The outcomes in this group of children with low-grade glioma, treated with RT, are comparable with other international series. Relapse rate post-RT is lower than that reported for the whole series. The prognostic value of the extent of resection remains to be defined. The group of patients with post-RT chemotherapy had more than twice the risk of further progression compared to those treated with RT alone.

O081

NEUROBEHAVIORAL FUNCTIONING IN PEDIATRIC BRAIN TUMOR PATIENTS AFTER PROTON BEAM RADIATION TREATMENT

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Purpose: Radiation therapy is integral in treating pediatric brain tumors. However, photon radiation (XRT) is associated with neurobehavioral sequelae, including decrements in IQ and difficulties with attention/executive skills. Proton beam radiation (PBT) provides better targeting of tumors than XRT, sparing surrounding healthy tissue. Therefore, radiation-related neurobehavioral deficits should be reduced relative to reports of XRT effects. This study examines changes in neurobehavioral functioning in pediatric brain tumor patients treated with PBT at MGH.

Method: Since 2004, baseline (BL) neurobehavioral testing has been routinely conducted with brain tumor patients receiving PBT. To date, 56 have received follow-up testing (M = 2.1 years, SD = 1.3). Neurobehavioral functioning was assessed in: 1) IQ; 2)emotional/behavioral functioning; 3)adaptive abilities, and 4) executive functioning.

Results: Three standardized parent rating scales were administered: Behavior Assessment System for Children. 2 Scales of Independent Behavior- Revised, and Behavior Rating Inventory of Executive Functioning.

Conclusion: At two-year follow-up, IQ and neurobehavioral functioning remained intact and stable in this proton treated cohort. While findings are preliminary, they compare favorably to reports from photon radiation treatment. Data collection is ongoing and will refine these preliminary findings.

O082

CEREBROCEREBELLAR CONNECTIONS IN PEDIATRIC BRAIN TUMOR PATIENTS: IMPACT ON WORKING MEMORY

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Purpose: Pediatric posterior fossa (PF) tumors are treated surgically, with radiation and chemotherapy being reserved for residual or malignant cases. Cranial radiation has been associated with delayed cognitive dysfunction. Working memory has yet to be fully examined in this population. fMRI, MEG, and lesion studies have implicated both the cerebellum and dorsolateral prefrontal cortex (DLPFC) in working memory function. We strived to delineate cerebellar-DLPFC white matter tracts in patients and healthy control children, examine the structural integrity of these tracts, investigate working memory differences in patients versus controls and relate working memory function to structural integrity of cerebellar-DLPFC tracts.

Method: Forty-one patients treated for PF tumors (29 of which were treated with surgery and radiation, 12 of which were treated with surgery only) and 26 controls were seen for evaluation working memory function assessment using the Wechsler Intelligence Scale for Children. We used diffusion tensor imaging (DTI) and probabilistic tractography to delineate and investigate the structural integrity of cerebellar-DLPFC tracts.

Results: Bilateral tracts connecting the cerebellum with the DLPFC were delineated in all participants. The cranial radiation group had lower mean FA and higher mean radial diffusivity within the cerebellar regions of the cerebellar-DLPFC tract (FA = .43) compared to the surgery only (FA = .41) and control groups (FA = .41), p < 0.01. Poorer working memory scores were observed for the cranial radiation (WMI = .88) and surgery only (WMI = .98) groups relative to controls (WMI = 1.02). p < 0.05, and these lower working memory measures were correlated with reduced FA
and higher radial diffusivity ($r = 0.334$, $p < 0.01$ and $r = 0.312$, $p < 0.05$, respectively) within the entire cerebellar-DLPFC pathway.

**Conclusion:** Identifying differences in the integrity of white matter for specific pathways is an essential step in attempting to localize the regional effects of PF tumors and their treatment methods. Integral to this study is the finding that working memory function may be dependent on the integrity of cerebellar-DLPFC connections.

**O083**

SELF-EVALUATION IN MULTIPLE DOMAINS IN ADULT SURVIVORS OF CHILDHOOD CNS TUMORS

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**Purpose:** To determine the impact of childhood CNS tumour (CCNST) and treatment on domains of identity and self-esteem in adult survivors. The study also aimed at identifying risk factors that modify self-evaluation.

**Method:** The target population was a population-based nation-wide cohort of 697 adult CCNST survivors diagnosed before their 18th birthday, who were $> 5$ years beyond diagnosis date, and $> 18$ years old at follow-up. Comparison data collection addressed 2500 randomly selected general community individuals, stratified on the basis of birth year, sex, and geographical area of residence. A 6-dimensional inventory (Self-Esteem Questionnaire, SEQ-42) was used for addressing domains of identity and self-esteem. Survivors’ outcomes were contrasted with those of the non-tumour comparison group. The predictive significance of potential risk factors was evaluated in adjusted linear regression models.

**Results:** Although not apparent in all outcome dimensions, results systematically revealed a pattern of an adverse effect of illness/treatment history on identity in terms of generally affected self-evaluation. Among outcome domains where survivors reported significantly lower self-evaluation than controls were those related to: peers, school/work, body image, and self-esteem. Female survivors expressed significantly lower self-evaluation than males in several of studied domains. Oligodendrogioma, CNS germ cell tumor, medulloblastoma/PNET, and craniopharyngioma survivors expressed lower self-evaluation in certain identity-related domains, compared to patients in other diagnostic groups. In addition, visible physical sequelae adversely influenced self-evaluation in some domains.

**Conclusion:** Group level comparisons with a non-clinical sample show that adult survivors with a childhood CNS tumor history demonstrate lower self-evaluation in domains of identity and self-esteem. Depending on domain, female sex, certain types of cancer, and lower age at diagnosis increase the risk for adverse influence on self-evaluation. Compensatory measures integrated in psychological follow-up should address self-evaluation disturbance due to the cancer history, in order to enhance long-term mental health and well-being of the vulnerable population of CNS tumor survivors.

**O084**

LIPOBLASTOMA IN CHILDHOOD: A CASE SERIES

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**Purpose:** Lipoblastoma is a rare, benign tumor mainly seen in infancy and early childhood. Nearly 90% of the cases occur before three years of age. On histology lobules of mature and immature adipose tissue are separated by fibrous septa with numerous vessels. Within lobules, capillaries make a plexiform pattern and a myxoid stroma is present. We report a case series of 7 children followed in our center.

**Method:** Cases diagnosed as lipoblastoma by biopsy and followed in our hospital for a duration of 10 year were retrospectively reviewed. Clinical presentations, radiological features, treatment and follow-up of cases were evaluated.

**Results:** Seven children with lipoblastoma were reviewed. There were 4 girls and 3 boys. Median age was 17 months (range 7 months–3 years). The most common presentation was with a painless, slow growing mass. Tumors were superficial (n = 1) and deep (n = 6), location was at extremity (n = 2), pelvis (n = 2), neck (n = 1), abdomen (n = 1) and trunk (n = 1). Tumor size ranged between 2 cm to13 cm. Preoperative imaging was helpful for most of the cases. On MRI a heterogeneous, solid mass including septations and lipid features was the most common finding. All patients but one underwent total excision. Patient follow-up period ranged between 3 months to 9 years. No recurrences or metastasis were seen.

**Conclusion:** Lipoblastoma is a benign tumor which can be located superficially or deeply and sometimes can reach large size with local extension. Complete resection is the way of treatment. Although no recurrence was seen in our cases, follow-up is required as recurrences were reported, especially in incomplete resections.

**O085**

SURGICAL SPECIFICITY OF SOFT TISSUE SARCOMAS LOCATED IN THE THORAX WALL: EXPERIENCE OF THE POLISH PEDIATRIC SOLID TUMOUR STUDY GROUP

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**Purpose:** Characteristics of soft tissue sarcomas (STS) of the thorax wall remains unclear. Aim of the report is to evaluate characteristics and surgical treatment of STS located in the thorax wall.

**Method:** Polish Paediatric Solid Tumour Study Group registered 381 STS patients staged I-IV (CWS 1996 and 2002). In 29 of them (7,61%) the primary tumours were located in the thorax wall. Twenty-three cases had chemosensitive sarcomas (RME, RMA, SS, PNET), 6 had tumours of not proven chemosensitivity (LPS, mesenchymoma malignum, MPNST, HP, epithelioid sarcoma). Clinical stages of disease were I-1, II-3, III-17, IV-8 and the risk groups (CWS) were standard/1, high/22 and very high/6 pts. Seventeen pts underwent initial surgery (3-R0, 9-R1, 5-R2), 12 had biopsy only. Secondary surgery followed neoadjuvant chemotherapy in 4/5 initially R2 pts (sec.R0/R0/4) and 7/12 biopsied only (sec.R0/R0, R1/1). Eight pts underwent RTX. Systemic treatment was conducted according to CWS 96 and CWS 2002 protocols. Follow-up 24–144 months, M = 84 months.

**Results:** Sixteen of 29 pts (58.6%) are alive; 14 in 1st CR and 2 in 2nd CR after relapse. Remaining died (41,4%). Eight of 13 pts after primary (3) or secondary R0 (10) are in 1st CR. Another one is in 2nd CR, 3 relapsed and died of disease (DOD).
and 1 died of secondary AML (in 2nd CR from STS). Regarding primary (9) or secondary R1 (1), 6/10 pts are in 1st CR, 1 in 2nd CR and 3 DOD. Only 3/12 pts who had initial biopsy alone are in 1st CR (25%) and 1 (8.3%) in 2nd CR; 8 (66.7%) DOD. Surprisingly, primary biopsied nonendocrine tumors had worse outcome (3/12 CR) than those after R2 (4/5 CR) and week chance for long term CR.

0086

TREATMENT AND OUTCOME OF PEDIATRIC PATIENTS SUFFERING FROM PERINEAL/PERIANAL RHABDOMYOSARCOMA: RESULTS FROM THE COOPERATIVE SOFT TISSUE SARCOMA STUDIES

CWS-86, 91, 96 AND -2002P

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Purpose: Perineal/perianal rhabdomyosarcoma (PRMS) is uncommon. The aim of this study was to analyze the clinical course, treatment and outcome in patients suffering from PRMS treated within the Cooperative Soft Tissue Sarcoma Studies CWS-86, 91, 96 and 2002P.

Method: Patients with RMS were enrolled in the CWS-86, 91, 96, and 2002P trials, of which 36 had PRMS. All patients received three cycles of neoadjuvant chemotherapy. At week 9, patients were reassessed using CT- or MRI-scan. Depending on the tumor size, age, and response to chemotherapy, local therapy, consisting of radiotherapy and/or surgery, was initiated. After local therapy, adjuvant systemic therapy was continued.

Results: Patient’s age ranged from 0 - 17 years (mean 10 ± 7yrs); 8 patients had embryonal RMS (RME), 25 had alveolar RMS (RMA). 3 patients were excluded due to insufficient data or age above 21 years. Median follow up was 67.6 months ± 49.6.

55% of patients presented with advanced stage neoplasm (IRS-stage III). 7 patients (all RMA) had initially metastatic disease. 17 patients had locoregional lymph node involvement (ERMS: 2, RMA: 15). 5/8 patients with ERMS and 19/25 with RMA received radiotherapy (32–64 Gy). Primary tumor resection was performed in 8 patients (R0: 2, R1: 5, R2: 1). Secondary tumor resection was carried out in 11 patients (R0: 2, R1: 3, R2: 4; no data: 2). Local relapse occurred in 2 patients with ERMS and 8 patients with ARMS. 7/8 patients with ERMS and 7/25 patients with ARMS are in first complete remission.

Conclusion: Similar to RMS in other sites, histological subtype seems to be the most important predictor of outcome in PRMS as well. Patients with ERMS seem to have a better outcome due to the higher failure rate in patients with ARMS.

0087

PERIANAL/PERIANAL RHABDOMYOSARCOMA, A VERY RARE MALIGNANT DISEASE IN CHILDHOOD: RESULTS OF THE SIOP MMT STUDIES (MST 84-89-95)

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Purpose: Childhood Rhabdomyosarcoma (RMS) of the perianal/perineal region is rare with limited survival. The MMT studies (MST84-89-95) was interrogated for cases of this condition, identifying outcomes, local disease characteristics and treatment factors that may have an impact on survival.

Method: From 1983 until 2003, 2022 patients were enrolled. Only 21 (1%) had perianal/perineal RMS. One patient had incomplete surgical data, leaving 20 for analysis. The database and surgical reports were analyzed for local therapy administered, local and overall outcome data.

Results: Median age was 12 years (range 1–17 years). There were 14 male and 6 female patients. The primary tumor size was > 5cm in 16 patients. Histological subtype was alveolar (11), embryonal (7) and not otherwise specified (2). Lymph nodes were involved in 9 patients. Node negative patients (11) were designated based on clinical/radiological criteria. Primary resection was performed in 3 patients, 17 having only a biopsy. Four patients did never achieve complete remission (CR): 3 died, 1 is alive after chemotherapy (CT) conservative surgery (CS) and radiotherapy (RT). Sixteen patients achieved CR with CT alone (4), conservative surgery (10 + RT in 4) or CT (2), but 10 relapsed. Only 1 patient survived after relapse. At a mean follow-up of 7.2yrs (3.5–10.7yrs), 7 pts are alive. All received a local treatment (1 RT, 5 CS + RT in 2). Characteristics found to have an impact on survival and local relapse were initial tumor size > 5cm, regional lymph node involvement, and local therapy delivered. Histopathological subtype did not influence outcome in this patient sub-group.

Conclusion: Most patients present > 10 years of age with large tumors. Local therapy is required even when there is apparent complete response to systemic therapy. There is a trend towards improved survival with combined local modality therapy. Brachytherapy needs further evaluation in this anatomical region.
ADOLESCENT-PARENT-CLINICIAN COMMUNICATION REGARDING CANCER-RELATED SYMPTOMS

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Purpose: Pediatric oncology patients experience a myriad of disease and treatment-related sequelae. However, reports that describe the process by which adolescent cancer patients and their family members share information about these distressing events with clinicians are lacking in the literature. The specific aims of this study, in a sample of oncology patients, ages 14 to 21 years, were to elicit adolescent cancer patients’ perceptions of their patterns of communication with clinicians about their symptom experiences.

Method: After the consent/assent process, individual semi-structured interviews were conducted with 15 adolescent cancer patients. Each interview lasted approximately 15 minutes.

Results: A wide range of ages in the adolescent and young adult group were represented, with about half the sample from racial/ethnic minorities. Most participants lived at home with their parents. Most participants stated that their parents were fully (n = 6) or partially (n = 6) responsible for communicating their symptom concerns to clinicians. Only 3 patients claimed full responsibility in communicating with clinicians. Evaluation of the factors that may be related to these communication patterns will be shared.

Conclusion: These findings lay the groundwork for a detailed study of the communication patterns in the adolescent-parent-clinician triad in pediatric oncology. Additional qualitative methods for such a study (e.g., clinic observations and audio or video recordings of clinician encounters) should be employed. In addition, a study of clinicians’ delivery of symptom management recommendations to pediatric cancer patients and their parents is warranted. Although all participants were satisfied with partial or full parental involvement in symptom reporting, deleterious effects may be noted in adolescents’ ability to manage symptoms if symptom management advice is communicated solely to patients’ parents.

WEBLOGS OF PARENTS WITH A CHILD TREATED FOR CANCER: THEIR INTENTIONS AND EXPERIENCES

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Purpose: Weblogs are relatively new media and have become very popular in health communication. Nowadays, parents of children with cancer often create weblogs and regularly enter clinical information, personal events and pictures of their child. Our objective was to obtain an overall insight into their intentions and experiences with these personal messages, the possible links and the comments.

Method: All parents (n = 11) with a child in treatment at the moment of the study and who are maintaining a blog have been interviewed. The transcripts of all audiotaped semi-structured interviews are coded, using the software program NVivo 8.

Results: For parents, the main steps towards the creation of a blog are: the illness of their child combined with the burden of frequent phones of friends and family. Only a few start the blog as a way to escape from an isolated situation.

For a lot of parents the main goal is to inform friends and relatives and/or to communicate with them. They find it important to give information at first hand about their child’s condition. The blog is also a vent for feelings. As time passes other benefits occur: social and emotional support and exchange of information with peers. The blog also becomes a souvenir for their child once he has grown-up. The writing helps parents to cope with the situation.

Conclusion: From these preliminary results, we conclude that these parents experience the blog as a useful tool in communication and as a coping strategy. These results can contribute to the nurse’s body of knowledge. Further research is necessary to confirm the results.

INVESTIGATING THE EFFECT OF CHILDHOOD CANCER ON THE PARENTAL SUBSYSTEM RELATIONSHIP

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Purpose: The primary purpose of this study is to understand, from the perspectives of parents of children who have had cancer, the complexity of the effect that having undergone this experience had or continues to have on their relationship. A secondary purpose is to develop family focused, relational health care practices that address issues that may occur within the parental subsystem so that the relationship can be better supported in the care of families in pediatric oncology.

Method: This is a qualitative study, employing a sophisticated method of research well documented under the umbrella of phenomenological studies: hermeneutics. Hermeneutic inquiry is described as the practice and theory of interpretation and understanding in human contexts. It is a reflective inquiry concerned with understanding the world and the various forms which understanding is manifested.

Results: This study will be the focus of the first author’s PhD thesis. There have been some studies that have examined the effect of childhood cancer on the parental dyad, however the results of these studies are contradictory. It is not the intent of this study to determine “once and for all” whether childhood cancer experiences strengthen or challenge the relationships between parents, but to further understand this experience such that we might discover ways that pediatric cancer care can assist couples in mitigating the impact that having a child with cancer can have on their relationship.

Conclusion: It is well documented that the tone and quality of the parental relationship has profound effects on the physical, emotional, mental, and spiritual health of the child. A child’s relationship with parents is the often the most significant relationship influencing the child’s wellbeing. In this regard, attending to the parent’s relationship in whatever way is possible is indeed primary prevention in caring for the health of the child.

DIAGNOSIS AND TREATMENT OF PANCREATICODUODENAL TUMOR IN CHILDREN

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Purpose: Pancreaticoduodenal tumor are rare in children. It is necessary to analyze the clinical and pathological data to improve the diagnosis and treatment.

Method: The data of 34 cases with pancreaticoduodenal tumor enrolled from 2003 through 2009 were retrospectively analyzed. Male 20 and female 14, aged 4 months to 15 years. The cases included 16 with papillary and solid epithelioma, 9 with...
pancreatoblastoma, 1 with heterotopic pancreas in duodenum, 1 with pancreatic fibrohistiocytoma, 1 with simple pancreatic cyst, 1 with pancreaticoduodenal rest in pancreas, 1 with pancreatic PNET, 1 with islet cell adenoma, 1 with alveolus rhabdomyosarcoma and 1 with pseudocyst of pancreas. Results: Pancreatic papillary and solid epithelioma was the most common disease (16/34). Pancreatoduodenectomy was conducted in 2 of 5 cases with tumor on pancreatic head. Digging resection was done in 3 of 5 cases with complication of stress ulcer and pancreatic leakage. For tumor on body and tail of pancreas, pancreatectomy was the radical procedure. 5 of 10 procedures succeeded in preserving the spleen. Pancreatoblastoma was the second common disease (9/34). 5 cases had liver metastasis on diagnosis. 6 cases had preoperative chemotherapy, 4 cases underwent pancreaticoduodenectomy. 5 cases had pancreatic head and tail resection. 7 of 9 cases survived in the follow-up of 2 to 6 years. The youngest case who accepted pancreaticoduodenectomy was 4 month old patient with fibrohistiocytoma.

Conclusion: The most common pediatric pancreaticoduodenal tumor were pancreatic papillary and solid epithelioma and pancreatoblastoma. For tumors on pancreas on head and neck, pancreaticoduodenectomy was safe and suggested. Otherwise, digging resection had potential danger of relapse and pancreatic leakage. For tumor on pancreatic body and tail, pancreatectomy was recommended with strive to preserve the spleen. For other even rare disease, reasonable sequence must be set on diagnostic pathology, symptom control and radical treatment.

O094

SURGICAL AND CLINICAL CHARACTERISTICS OF PEDIATRIC PANCREATOBLASTOMA - REPORT OF THE EUROPEAN COOPERATIVE STUDY GROUP ON PEDIATRIC RARE TUMORS (EXPERT)

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Purpose: Pancreatoblastoma (PBL) is a challenging tumor. Aim of this report is to evaluate clinical findings and treatment in 19 patients (7 girls, 12 boys, age 1m-18 y, M = 4y), treated in France, United Kingdom, Germany, Italy and Poland (2000-2009). Method: Tumor sites were: head of pancreas 5, body 4, tail 3, multifocal tumor 5. Size exceeded 10cm in 10pts, was 5–10 cm in 6, and 2–5 in 3. Four patients were ST1, 5 STII, 4 STIII, 6 STIV. AFP was available in 15/19 pts and ranged from normal to 43000 ng/ml. Primary resections were undertaken in 8/19 and were complete in 7 (R0) and microscopically incomplete in 1 (R1). After chemotherapy, surgery was undertaken in 8 pts (R0/7, R2/1); three were not submitted to any curative resection. Chemotherapy was used in 17pts (based on PLADO in 12), and radiotherapy in 6. Results: 13pts are in CR (FU 10–88 months), 4 died of disease (3–77 months after diagnosis), 1 died of toxicity and 1 was lost from FU after relapse (22 months). Only 1pt who developed relapse is in second CR. Tumor size in survivors was > 10cm in 7, 5–10 in 5 and 2–5 in 1. In pts who died of disease (2STII, 2STIV), tumors were > 10 cm in 1 and 5–10 cm in 3. Thirteen pts in CR had all primary or secondary R0. All 4 patients who died never had complete surgery. Pancreas site seemed not correlated with results. Conclusion: Tumor size does not predict either outcome or resectability. Primary (6/13) or secondary complete surgery (7/13) remains the mainstay of therapy. Effectiveness of the PLADO-based chemotherapy seems to be confirmed by the high rate of secondary R0 resections on initially non-resectable tumors. Stages III and IV imply poor outcome, unless they become resectable after chemotherapy.

O095

MALIGNANT LIVER TUMORS IN CHILDREN - OUR 10-YEAR EXPERIENCE

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Purpose: This study reviews our institution’s experience with pediatric liver tumors in children, highlighting key differences between hepatoblastomas (HBs) and hepatocellular carcinomas (HCCs).

Method: With Institutional Review Board (IRB)’s approval, clinical charts from children treated for malignant liver tumors at KK Women’s and Children’s Hospital between January 1, 1997 and December 31, 2007 were reviewed. Data on demographics, clinical presentations, investigations, surgical procedures, histopathology findings, management and treatment outcomes were analyzed.

Results: Of the 27 children treated for primary malignant liver tumors, 21 (78%) had HBs while 6 (22%) had HCCs. Majority were local Chinese boys (52%). The median age of presentation for HB was 1.5 years (2 days – 6 years); compared to 9.7 years (6 years – 12.7 years) for HCC. Abdominal distension was the commonest presentation. Mean serum alpha-feto-protein (AFP) levels were higher in patients with HB (241649iu/L) than in those with HCC (37625ug/L). Only 2 patients with HB were hepatitis B carriers. Half of the HBs and 1 HCC were primarily resected. Three patients with HB and 4 with HCC had pre-therapy liver biopsies. One child was treated for presumed HB but the resected tumor revealed HCC. All but 2 patients with HBs received SIOPEN-based chemotherapy. The mean follow-up for HB patients was 7.6 years. Twelve (60%) had survived beyond 5 years from their initial diagnosis. The child who underwent primary resection for HCC was a hepatitis B carrier and had survived beyond 5 years. The remaining HCC patients survived an average of 6 months despite various therapies.

Conclusion: HCCs generally present in school-going children with moderately elevated AFP levels. Pre-therapy tissue diagnosis should be established in these situations. Unlike other Asian series, most of our pediatric HCCs did not arise in hepatitis B carriers. Regular surveillance in hepatitis B carriers allows early detection and best chance of survival.

O096

OUTCOMES OF RESECTION, RECONSTRUCTION AND REHABILITATION OF PEDIATRIC MANDIBLE AND MAXILLA TUMORS

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Purpose: Tumors of the mandible and maxilla in children are uncommon. Resection and especially reconstruction of these tumors remains a solemn technical challenge. In addition to the oncological comprehensiveness it is essential that special consideration be given to optimal restoration of function and cosmesis. We reviewed our institutional data on this complex area.

Method: Fifteen patients with tumors of the maxilla (5) and mandible (10) operated between August 2005 and February 2010 were included in this analysis. The histology included Ewing sarcoma (5), rhabdomyosarcoma (2), Osteosarcoma, (1) Epithelial sarcoma (1), synovial sarcoma (1), undifferentiated carcinoma (1), giant cell tumor (1), fibromatosi (1), hemangioma (1) and osteoblastoma (1). There were 9 males and 6 females with a median age of 9 years (range 3 – 16 years). Results: Hemimandibulectomy was performed in 5; extended hemimandibulectomy in 2; total maxillectomy in 3; posterior segmental mandibulectomy in 2; middle 3rd mandibulectomy, radical maxillectomy, structure maxillectomy in one each. Vascularized free fibular flaps were used in 9 patients; pectoralis major myocutaneous flaps were used in four and skin graft only were used to line the raw area after maxillectomy followed by a palatal obturator in two. There were two flap losses; one patient had skin edge necrosis. Two patients were lost to follow-up. Two patients have
undergone full dental rehabilitation and currently maintain a regular diet and deny pain with mastication or deglutition. The patients also deny pain at the donor site and do not have any restriction to recreational activity. All the 7 patients with fibrilar graft have gross facial symmetry and normal dental occlusion. Patients with PMMC flap have also good facial symmetry and no restriction of shoulder movements. Conclusion: Resection of jaw tumors remain a technical challenge in children. Several options for reconstructions are available, however free flap reconstruction though complex, offer good functional outcomes.

O097

ENDOSCOPIC SURGERY IN CHILDREN’S ONCOLOGY
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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 218, of which 112 were laparoscopic and 106 were thoracoscopic. Operation spectrum includes biopsies of large formations (56), lung resections (39), nephrectomies (46), adrenalectomies (14), kidney resections (1), gastric resections (1), hepatic resections (5), hemihepatectomies (6), retroperitoneal tumorectomies (9), mediastinal tumorectomies (24), operations performed on the organs of minor pelvis (5), appendectomies (1), splenectomies (1).
Operated children were aged form 2 months 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 adenrectomies) to 280 minutes (hemihepatectomies). Maximal blood loss was 400 ml in cases of hemihepatectomies.
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 thoracoscopic 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.

O098

DOT1L AND HISTONE 3 LYSINE 79 METHYLATION AS A THERAPEUTIC TARGET IN MIXED LINEAGE LEUKEMIA
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Purpose: Mixed Lineage Leukemia (MLL)-rearranged ALL continues to have a poor prognosis, despite intensive chemotherapy and/or stem cell transplant. More effective therapies are urgently needed. It was recently shown that the most common MLL-fusions, MLL-AF4, MLL-AF9, MLL-AF10 and MLL-ENL, interact with the histone methyl transferase DOT1L. DOT1L, by virtue of being an enzyme, is theoretically more amenable to drug targeting than MLL-fusion proteins. Increased methylation of Histone 3 Lysine 79 (H3K79) by DOT1L has been demonstrated on MLL-fusion target genes in MLL-AF4 leukemic patient samples. However, a direct and indispensable role for DOT1L in MLL-rearranged leukemias has so far not been shown.
Method: We analyzed the molecular and phenotypic consequences of sh-RNA mediated DOT1L suppression in a large panel of MLL-rearranged human leukemia cell lines, as well as non-MLL-rearranged control cells with a variety of other karyotypic abnormalities.
Results: We were able to demonstrate that suppression of DOT1L leads to loss of H3K79 methylation on known MLL target loci such as the 5’ HoxA cluster genes in the t(4;11) ALL cell lines SEMK2 and RS4;11. Decreased H3K79 methylation correlated with a decrease in expression of HoxA5 and HoxA9, which are central to MLL-mediated leukemogenesis. Phenotypically, suppression of DOT1L lead to cell cycle changes, a decrease in growth rate and cell numbers, and an increase in apoptosis in all MLL-rearranged cell lines. In contrast, several non-MLL-rearranged control cell lines were unaffected by DOT1L knock down. In vivo, we demonstrate that DOT1L suppression significantly increases the time to onset of leukemia in a xenograft mouse model for (4;11) ALL.
Conclusion: This study strongly suggests that MLL-rearranged leukemia cells are dependent on the presence of DOT1L, and that this enzyme may represent a promising therapeutic target for mixed lineage leukemia.

O099

ACCURATE PREDICTION OF NEUROBLASTOMA OUTCOME BASED ON MiRNA EXPRESSION PROFILES
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Purpose: Identification of new biomarkers and potential therapeutic targets is mandatory for improving risk stratification and survival rates of neuroblastoma patients. MicroRNA (miRNA) expression is deregulated in most cancers, including neuroblastoma. This study evaluated miRNAs as neuroblastoma biomarkers, and identified miRNAs important for neuroblastoma tumour biology and prognosis.
Method: MicroRNA expression was analysed by multiplex real-time PCR. Outcome was predicted using support vector machines (SVM), and actual survival times analysed in Cox regression-based models (CASPAR).
Results: Of the 430 miRNAs analysed in 69 primary neuroblastomas, 307 were readily detectable. Prediction of event-free survival (EFS) using SVM and actual survival times using CASPAR was highly accurate. EFS was predicted with 88.7% accuracy (95%CI: 88.5–88.8%) by SVM on the training set, and CASPAR predicted a 0.19 (95%CI: 0.05–0.38) 5y-EFS probability in the short survival group as compared to 0.78 (95%CI: 0.64–0.93) in the long survival group. Validation on an independent test set yielded accuracies of 94.74% (SVM) and 5y-EFS probabilities of 0.25 (95%CI: 0.0–0.55) for short vs 1 ± 0.0 for long survival (CASPAR). Kaplan-Meier analysis revealed that both classifiers effectively separated patients with adverse clinical course for EFS and OS (p < 0.001 on training and test sets). MYCN amplification was highly correlated with deregulated miRNA expression (p < 0.05, Mann-Whitney U-test), including the miR-17–92 cluster, miR-34a and miRNAs of the miR-181 family. Interestingly, 37 miRNAs correlated with TrkA expression, a marker of EFS. MYCN overexpression in vitro regulated 6 of 11 miRNAs analysed, suggesting a functional relationship. MiR-542-5p, which was significantly correlated with TrkA expression in vivo and induced by TrkA in vitro, was identified as a marker of EFS.
Conclusion: Neuroblastoma patient outcome prediction using miRNA expression is feasible and effective. Specific miRNAs, such as miR-542-5p, may be important in neuroblastoma tumour biology and qualify as potential therapeutic targets.

O100

TUMOR BIOLOGY OF ADULT AND PEDIATRIC MEDULLOBLASTOMA REQUIRES DISTINCT APPROACHES FOR MOLECULAR OUTCOME PREDICTION
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Purpose: The aim of this study was to compare the biology of adult and pediatric medulloblastomas (MBs).
Method: A total of 20 pediatric MBs and 15 adult MBs were included. The adult MBs were previously described. MBs were analyzed for genetic changes, microRNAs, protein expression, and clinical outcome.
Results: There were distinct differences in the genetic landscape between pediatric and adult MBs. Pediatric MBs had higher frequencies of mutations in chromatin modifiers and transcription factors, while adult MBs had higher frequencies of mutations in cell cycle, DNA repair, and tumor suppressor genes. MicroRNA expression was also different between the two groups, with some miRNAs being more highly expressed in pediatric MBs and others in adult MBs. Protein expression analysis revealed differences in the expression of several known medulloblastoma biomarkers.
Conclusion: The distinct biology of pediatric and adult MBs requires different approaches for molecular outcome prediction.
Leukaemia Group, CCLG. The delayed nephrectomy has not been systematically reported. The UKW3 trial rates of Wilms tumour (WT) in the setting of pre-operative chemotherapy followed by

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Purpose: Medulloblastoma is the most common malignant brain tumor in childhood, whereas low incidence is observed in adults. Genetic aberrations were investigated in 146 adult medulloblastomas and findings were compared with data obtained in pediatric medulloblastomas in order to pinpoint age-dependent differences in tumor biology and to refine risk stratification models.

Method: We prepared an integrative genomic analysis of pediatric and adult medulloblastoma samples including array-based comparative genomic hybridization (array-CGH), fluorescence in situ hybridization (FISH), genome-wide expression profiling (Agilent-44k), quantitative real-time PCR (QRT-PCR) and immunohistochemistry on tissue microarrays.

Results: Array-CGH identified several genomic imbalances as powerful markers for unfavorable outcome (CDK6 amplification, 17q gain, and 10q deletion) for adult medulloblastoma patients (n = 34). These findings were validated by FISH in an independent validation cohort of 112 medulloblastomas. Results were compared with a data set obtained from 404 pediatric medulloblastomas. Although MYC/MYCN oncogene amplifications are important biomarkers for high-risk medulloblastoma of childhood, they rarely occur in adult tumors. Surprisingly, adult tumors showing 6q deletion and consecutive WNT pathway activation do not share the excellent prognosis with their pediatric counterparts. In an integrative analysis, DNA copy-number changes are correlated with matching transcriptome data to fine-map genes targeted by these genomic imbalances and to determine age-specific differential gene expression. This transcriptome analysis was performed in 64 pediatric and adult medulloblastomas and then compared with an independent expression profiling study (n = 103). Candidate genes were validated by QRT-PCR and by immunohistochemistry on tissue microarrays. Notably, multivariate analyses revealed that genes associated with neuronal function (TAC1, CPLX3, NEF3) and the putative tumor suppressor gene ST18 showed a specific down-regulation in adult medulloblastomas compared to pediatric tumors.

Conclusion: In conclusion, adult medulloblastomas are distinct from pediatric tumors in terms of molecular background and its impact on clinical outcomes. Consequently, age-specific risk stratification models are required.

O102

CLINICAL PROGNOSTIC FACTORS IN HEPATOBLASTOMAS: THE SIOP EXPERIENCE

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Purpose: To identify factors relevant to long term outcome in newly diagnosed hepatoblastoma, and which stipulate risk stratification allowing treatment tailored to the individual patient and to identify subpopulations for clinical research on therapy.

Method: Between 1994 and 2006 the SIOPeL group conducted two clinical trials which established risk-adapted pre- and postoperative chemotherapy for hepatoblastoma patients. Patients were stratified into high-risk (HR: AFP < 100ng/ml and/or PRETEXT 4 and/or vascular invasion and/or extra-hepatic intra-abdominal disease (V/P/E) and/or metastatic) and standard-risk (SR: all others). The hierarchy of these factors plus multifocality. PRETEXT 2/3, high/low AFP (between 100 and 1000000, but not with multifocality, patient age and histology were further explored with multivariate Cox regression to refine the risk classification. The outcome measure was event-free survival (EFS, time from diagnosis to the first event of progression, relapse or death from any cause).

Results: In 541 patients, reduced EFS correlated significantly with small cell undifferentiated (SCU) histology (risk ratio [RR] 4.6, p = 0.0027), AFP < 100ng/ml (RR 2.8, p = 0.0012), metastatic disease (RR 2.4, p = 0.0003), PRETEXT 4 (RR 2.0, p = 0.054), PRETEXT 3 (RR 1.9, 0.023), age > 3 years (RR 2.0, p = 0.0068), AFP between 100 and 1000 or > 1000000 (RR 1.6, 0.042), but not with multifocality, platelet count or V/P/E. Three year EFS rates were 88% for SR and 59% for HR

O101

SHOULD BIOPSY INFLUENCE TUMOUR STAGING IN WILMS TUMOUR? THE UK EXPERIENCE

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Purpose: On behalf of the Renal Tumours Committee, Children’s Cancer and Leukaemia Group, CCLG. The influence of percutaneous biopsy on local recurrence rates of Wilms tumour (WT) in the setting of pre-operative chemotherapy followed by delayed nephrectomy has not been systematically reported. The UKW3 trial compared biopsy/pre-operative chemotherapy and immediate nephrectomy and affords the opportunity to examine this question.

Method: Data on treatment and outcome for 647 patients with unilateral WT (stage I-IV) registered in the UKW3 trial (1991–2001) were analysed. Metastatic and ‘inoperable’ tumours were electively biopsied, 39% of localised tumours were randomised; overall, 299 had biopsy and 348 immediate nephrectomy. Patients with metastatic disease (V/P/E) and/or PRETEXT 3 (RR 1.9, 0.023), age > 3 years (RR 2.0, p = 0.0068), AFP between 100 and 1000 or > 1000000 (RR 1.6, 0.042), but not with multifocality, platelet count or V/P/E. Three year EFS rates were 88% for SR and 59% for HR
patients. By using the above risk factors to stratify the population, we have identified three distinct prognostic groups: PRETEXT 1/2, and no other factors, have 3 year EFS of 92%, PRETEXT 3/4 and/or age > 3 years and/or high/low AFP have 3 year EFS of 79%, and SCU and/or AFP < 100ng/ml and/or metastatic have a 3 year EFS of 49%.

Conclusion: Previously used risk stratification may be refined by considering combinations of clinical and laboratory features readily available at diagnosis.

O103

ASSESSMENT OF TREATMENT PLANS AND THE DELINEATION OF TARGET VOLUMES AND ORGANS AT RISK FOR PAEDIATIC CASES

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Purpose: The “Swedish Workgroup for Paediatric Radiotherapy” was formed in 2000. We decided to perform a dummy run treatment planning study on a number of different patient cases. The aim was to quantify and identify differences in the segmentation of target volumes and organs at risk (OARs) as well as to analyse the treatment plans and dose distributions.

Method: Five cases were selected; PNET, Hodgkin’s disease, Wilms tumour, thalassemia with a chordoma of the skull base. The five participating centres received the same material, i.e. treatment planning CT, diagnostic information, patient charts and treatment protocols. Cases were introduced in the local treatment planning systems. Target volumes and OARs were delineated according to protocol and local practice and treatment plans were created by each centre. The complete cases were exported in Dicom-RT format to the study centre. The treatment plans were evaluated with the CERR software (Deasy et al. 2003). A number of volume and dose metrics were derived and compared. Reasons for the differences in target delineation were also analysed.

Results: Large variation in target segmentation was found for most cases. The PTV volumes varied typically with a factor of three to four with a concordance index in the range of 0.3–0.9. The segmentation of OARs showed good compliance. The treatment plans resulted in large variations in treated and irradiated volumes even though they in general showed good conformity to the PTVs.

Conclusion: Large variations in inter-physician target segmentation were found, leading to a spread in treated and irradiated volumes. Reasons are the considerations of the growing child, where experience and local practice varies, but also differences in interpretation of the radiotherapy information given in the treatment protocols. As a result, writing of national guidelines for the radiotherapy process of paediatric patients is now in progress.

O104

PREDICTORS OF INDEPENDENT LIVING AFTER CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Purpose: With increased success of treatments for pediatric cancers, attention has focused on functional outcomes of survivors. This study examines factors that predict independent living in adult survivors of childhood cancer.

Method: Adult survivors of childhood cancers (n = 6047) and siblings (n = 2326), all of whom were ≥ 25 years of age, completed a long-term follow-up questionnaire that assessed adaptive, neurocognitive, and psychological functioning, as well as demographic information and health status. Survivors were a mean age of 34.2 years (range 25–54) at study. Logistic regression models (expressed as odds ratio [OR] and 95% confidence interval [CI]) and structural equation modeling (SEM) were used to predict risk of dependent living based on demographic, neuropsychological, physical functioning and treatment variables.

Results: Compared to siblings, survivors were more than twice as likely to live independently (OR = 2.07, 95% CI 1.77–2.42), adjusted for age, gender and race. In multivariate logistic regression analyses, risk factors for dependent living among survivors included: racial/ethnic minority status (OR = 2.60, 95% CI 2.02–3.36), cranial radiation therapy in dose dependent fashion (OR > 0. U24 Gy OR = 1.35, 95% CI 1.11–1.60; ≥ 24 Gy OR = 3.63, 95% CI 2.82–4.68), attention and processing speed problems (OR = 1.89, 95% CI 1.57–3.33), depression (OR = 1.61, 95% CI 1.23–2.10), poor physical functioning (OR = 1.86, 95% CI 1.35–2.50), and use of neuroleptic, anticonvulsant, or psychostimulant medication (OR = 3.05, 95% CI 2.30–4.03). Structural equation modeling suggested poor neurocognitive functioning increased likelihood of dependent living through poor mental health, increased depression, increased somatization, and use of neurologically-directed medication (all p < 0.001).

Conclusion: Adult survivors of childhood cancer are less likely to live independently compared to siblings. Specific neurocognitive, medical and psychological late effects are strongly associated with extended dependency in adulthood. Findings are discussed in terms of reducing barriers to independent living and developing interventions to promote independence.

O105

HOSPITALIZATIONS AMONG CHILDREN OF SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER: A POPULATION-BASED COHORT STUDY

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Purpose: The continued rise in survival rates for childhood cancer, now about 80%, and the ability for survivors to have children of their own have highlighted the importance of evaluating the impact of cancer therapy on fertility, pregnancy and health of the growing number of children of cancer survivors. Curative but potentially mutagenic cancer therapy might lead to untoward disorders and increased hospitalization among the offspring of childhood cancer survivors.

Method: Hospitalizations in childhood were evaluated in a population-based cohort of 1,920 offspring of 3,963 childhood cancer survivors, 6,394 offspring of 5,657 siblings, and 9,594 population-based comparisons. The Danish Cancer Registry, Central Population Register, and National Hospital Register were used to identify study subjects and hospitalizations. The probability for children in the offspring cohort of being hospitalized before a given age was estimated using the Kaplan-Meier method. Hospitalization rate ratios (HRRs) were calculated using a Cox proportional hazards model with population comparisons as referent.

Results: Little differences in hospitalization histories were seen among offspring in the 3 cohorts. HRRs of overall hospitalization was 1.05 (95% CI 0.98–1.12) for offspring of survivors and 1.01 (95% CI 0.97–1.05) for offspring of siblings, neither of which was significantly different from that of population comparisons. No significant associations were seen for most of the main diagnostic groups of diseases including infections and perinatal disorders. A 6-fold excess risk of hospitalization for malignant tumors in survivors’ offspring, however, could largely be explained by hereditary cancer syndromes, and part of the 2-fold excess hospitalization for benign tumors might similarly be explained by underlying genetic susceptibility or by increased surveillance of children born to survivors.

Conclusion: Assuming that hospitalization is an indicator of multifactorial genetic disease, the findings provide further reassurance that cancer therapies do not confer a high risk of such conditions in offspring born after treatments.

O106

FATIGUE, VITALITY, SLEEP AND NEUROCognitive FUNCTIONING IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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Purpose: To examine the impact of fatigue, vitality, daytime sleepiness, and sleep quality on neurocognitive outcomes among adult survivors of childhood cancer.

Method: Neurocognitive outcomes were evaluated in 1,426 participants from the Childhood Cancer Survivor Study (CCSS) using the CCSS Neurocognitive Questionnaire (CCCS-NHQ). Relative risks for neurocognitive impairment were calculated using demographic and treatment factors, as well as survivors’ report on the FACT-Fatigue Scale, the Short Form-36 Vitality Scale (SF-36-V), the Pittsburgh Sleep Quality Index (PSQI), and the Epsworth Sleepiness Scale (ESS).

Results: Neurocognitive impairment was identified in over 20% of survivors, using sibling-based norms for comparison. Multivariable logistic regression models revealed that decreased vitality, (RR = 1.71, 95% CI 1.30–2.25), poor sleep quality (RR = 1.20, 95% CI 1.03–1.41), increased sleepiness (RR = 1.66, 95% CI 1.52–1.810), and fatigue (RR = 1.38, 95% CI 1.23–1.56) were all associated with impaired task efficiency. Decreased vitality increased the risk for emotional dysregulation (RR = 3.10, 95% CI 2.00–4.82), poor organization (RR = 1.68, 95% CI 1.22–2.32), and memory problems (RR = 2.01, 95% CI 1.42–2.86). Excessive daytime sleepiness was also associated with problems in these areas. Poor sleep quality was associated with an increased risk of impaired memory (RR = 1.44, 95% CI 1.21–1.73). The impact of fatigue, vitality, daytime sleepiness, and poor sleep quality on neurocognitive outcomes was independent of the significant effects of cranial radiation therapy, steroids, and antimitobolite chemotheraphy.

Conclusion: These findings suggest that neurocognitive function in long-term survivors of childhood cancer may be particularly vulnerable to the effects of fatigue and sleep disruption. This knowledge stresses the importance of good sleep hygiene in cancer survivors and may provide an additional avenue for interventions to improve neurocognitive outcomes.

Purpose: Advanced disease at diagnosis and poor survival characterize pediatric sarcomas in low income countries (LIC). We sought to investigate incidence, pattern of clinical presentation, adherence to treatment and physician’s perspectives on these solid tumors in Central American countries as a way to better understand the challenges faced when attempting to improve treatment outcomes.

Method: A questionnaire was distributed to pediatric oncologists in the region on clinical characteristics, treatment abandonment and refusal for osteosarcoma (OS), Ewing sarcoma (ES), rhabdomyosarcoma (RMS), and soft tissue sarcomas (STS) between 2000 and 2009 in 6 Central American countries were obtained and analyzed. Results: A total of 694 new cases of pediatric sarcoma were reported (234 OS, 135 ES, 225 RMS, and 100 STS). Thirty-five percent of children with osteosarcoma presented with metastases and 75% of patients with RMS had unrespectable or metastatic disease. Treatment abandonment rate for leukemia is reported as 4–8% in the region, but was much higher for sarcomas (19% OS, 13% ES, 23% RMS, 14% STS). Time to abandonment was shortest for OS and ES (mean 100 and 110 days, respectively vs 155 days for RMS and 188 for STS). Upfront refusal of treatment was highest for OS (12% vs 3% ES, 1.5% RMS, 6% STS). Amputation is the only modality available for local control of primary bone tumors of the extremity in 5 of the 6 countries. For all sarcomas except STS, abandonment is reported to occur most frequently at the time of surgery.

Conclusion: High tumor burden and high abandonment rates, particularly at the time of surgery, are likely important contributors to poor outcome for pediatric sarcomas in LIC. Initiatives for early diagnosis, family-oriented psychosocial support, and broader availability of limb sparing procedures are warranted to reduce abandonment and improve outcomes.
METHOD: The patients were treated in the high-risk-arm of the prospective multicenter study HB99 of the GPOH with 2 courses carboplatin/etoposide in conventional dose, 2 courses high-dose carboplatin/etoposide with peripheral stem cell rescue before delayed surgery or transplantation. We evaluated the subgroups with low AFP, lung metastases, involvement of the vena cava or the portal vein concerning chemotherapy response, resectability, event-free and overall survival.

RESULTS: 6 out of 51 high-risk patients had an AFP < 100 ng/ml. All 6 patients died. All other subgroups were evaluated within the 45 patients with an AFP > 100 ng/ml. In 13/45 the large vessels were involved. In 9/13 patients the tumour could be resected. The 3-y-EFS was significantly lower with 35% (OS 35%) compared to 68% (OS 87%) in patients without vessel involvement. But most of the patients with involvement of the vena cava also had lung metastases (8/7) and there was no significant difference in the OS in non-metastatic patients with or without vessel involvement. 25/45 patients had lung metastases, two died under therapy. In 21/24 patients the lung metastases showed good response to chemotherapy. The 3-y-EFS and OS was significantly lower with 44% (OS 58%) compared to 77% (OS 88%) in patients without metastases.

CONCLUSION: Patients with unresectable hepatoblastoma and low AFP and patients with metastases have a significant worse outcome compared to the other high risk patients. New risk stratification criteria can be discussed and there is the need for new treatment strategies especially for these “very high risk” patients.

O110 HIGH CURE RATE IN HIGH RISK HEPATOMBLASTOMA WITH DOSE INTENSIVE CISPLATIN BASED CHEMOTHERAPY - RESULTS OF THE SIOPEL-4 TRIAL

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Purpose: To test the efficacy of weekly cisplatin based chemotherapy in patients with high-risk hepatoblastoma (HR-HB).

Method: SIOPEL-4 was a single arm phase II trial (two-stage, endpoint: complete remission). Patients with tumour involving all 4 liver sectors (PRETEXT-IV) or extra-capsular growth were included. Stage and diagnosis was confirmed by radiological and pathological central review. Treatment consisted of 3 cycles of pre-operative chemotherapy (cisplatin 70 mg/m²/d, D1,8,15; doxorubicin 30 mg/m²/d, D8,9), tumor resection and post-operative chemotherapy (carboplatin AUC 6.6 mg/ml.min/d, D1,22,43; doxorubicin 25 mg/m²/d, D1,2,22,43,44). Patients whose tumor remained unresectable after the initial cycles received additional chemotherapy (carboplatin AUC 10.6 mg/ml.min/d, D1,22; doxorubicin 25 mg/m²/d D1,2,22,23,24) before surgery was attempted.

Results: In 4.5 years 62 eligible patients were enrolled (23 female, median age 20.1 months). Seventeen patients had PRETEXT-IV tumor, 40 had metastases, 5 presented with AFP < 100 ng/L. Overall response (CR + PR) to pre-operative chemotherapy was 87%. Response of lung metastases was 80% (17 CR, 15 PR). Complete resection of all tumor lesions was achieved in 46 patients (74%) including 12 who underwent liver transplantation. At the end of therapy 47 patients (76% (95% CI: 63%-86%)) were in complete remission. 2-y-EFS and OS were: 77% (65%-89%) and 84% (73%-95%). The 2-y-EFS of patients with metastasis was not inferior to that of patients without metastasis. Main toxicity was haematological: 93% of the patients experienced grade 3/4 haematological toxicity. In thirteen patients Brock-grade 1-4 ototoxicity is documented. One patient died of toxicity (fungal infection) due to delayed start of chemotherapy.

Conclusion: Weekly cisplatin with doxorubicin is a toxic but feasible treatment for HR-HB. Compared to previous results the SIOPEL-4 strategy has further improved the outcome of patients with HR-HB. More detailed analysis and longer follow up should elucidate which patients receive the most benefit of this intensive approach.

O111 OUTCOME OF HEPATOMBLASTOMA TREATED WITH THE JPLT2 PROTOCOL FROM THE EXPERIENCE OF JPLT (JAPANESE STUDY GROUP FOR PEDIATRIC LIVER TUMOR) STUDY

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Purpose: JPLT is running cooperative treatment studies on hepatoblastoma (HB) since 1991. JPLT-1 study evaluated the efficacy of cisplatin/pirarubicin (CITA) (J Pediatr Surg, 2002). JPLT-2 protocol was launched in 1999 to evaluate the cure rate of risk-stratified HB: standard risk (SR-HB) (a tumor involving three or fewer sectors of the liver) and high risk (HR-HB) (a tumor involving all sectors of the liver or with metastasis). In JPLT2, the CITA is kept as the first line and an ITEC (ifosfamide, etoposide, pirarubicin, and carboplatin) is the second line regimen. For the HR-HB cases, high dose chemotherapy with stem cell transplantation (HDC-SCT) was carried out. In this paper, we evaluated JPLT2.

Method: Among cases registered in JPLT-2 until 2008, 235 cases including 92 HR-HB cases (39%) had completed the protocol. All these cases were initially treated with the CITA, except for 12 SR-HB cases who underwent primary resection. Among them, an ITEC regimen was used in 79 cases and a HDC-SCT was used in 14 HR-HB cases.

Results: The 5-year OS and EFS of the SR-HB cases were 96% and 76% respectively, while those of the HR-HB cases were 54% and 34%. In the patients who were treated by the ITEC regimen, the 5-year OS rate was similar among SR-HB cases but that in the HR-HB cases was higher (67%). Among the 14 HR-HB cases who underwent the HDC-SCT, only 8 (57%) were cured. In addition, late phase complications included 3 malformations, 13 cardiac complications, 21 ototoxicity and 5 second malignancies.

Conclusion: As compared with other regimens, CITA regimens achieved similar or superior rates of survival among children with SR-HB. Second line ITEC regimens and the HDC-SCT regimen were effective in some HR-HB cases. More promising strategies including liver transplantation and new targeting drugs should be developed for HR-HB.

O112 SOMATIC COMPLAINTS IN PEDIATRIC CANCER SURVIVORS: THE ROLE OF MOTHER'S EMOTIONAL AWARENESS AND ACCEPTANCE

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Purpose: Survivors of childhood cancer show higher levels of somatic complaints than healthy peers. While this may in part reflect physiological-based symptoms that are due to late effects of cancer treatment, it may also reflect increased somatization seen in populations who have experienced trauma. Because of the life-threatening nature of this illness, parents are socialized to be hypervigilant to signs of relapse (e.g.,
fever, flu-like symptoms). This may result in parents (and subsequently children) focusing less on children’s emotional displays and more on their bodily symptoms and physical complaints, possibly at the expense of the child’s emotional growth and development. Previous research has found that how parents socialize children around emotional experience and expression is an important predictor of children’s psychosocial adjustment. When parents are more aware and accepting of their own and their children’s emotions, children show fewer internalizing and externalizing difficulties. The current study assessed whether mother’s awareness and acceptance of emotion explained links between the diagnosis of cancer and higher levels of somatic complaints in families with 7–12 year old Acute Lymphoblastic Leukemia survivors who were at least 2 years out of treatment as compared to healthy controls.

Method: Mother reports of children’s somatic complaints were measured using the Child Behavior Checklist. Meta-emotion interviews were also conducted with mothers to assess their awareness and acceptance of their own and their children’s fear and sadness.

Results: Survivors of childhood cancer had higher levels of somatic complaints than healthy controls. Specifically, survivors had significantly higher rates of somatic complaints compared to controls (F(2,49) = 9.78, p < .001).

Conclusion: Mothers’ discomfort around emotion may inadvertently reinforce children’s attention to somatic concerns. Mothers’ management of her own fears appears particularly important for child adjustment. Implications for intervention will be discussed.

O113
SOCIAL OUTCOMES AND QUALITY OF LIFE (QOL) OF CHILDHOOD CANCER SURVIVORS IN JAPAN: MARRIAGE, EDUCATION, EMPLOYMENT AND HEALTH RELATED QOL (SF-36)

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Purpose: To examine social outcome and quality of life (QOL) in childhood cancer survivors (CCS) compared to controls.

Method: We performed a cross-sectional survey with self-rating questionnaires on the social outcome and QOL of CCS and their siblings. One thousand general population (matched with age, gender, living area and work status to CCS) were recruited by web-based research using the same questionnaire. We estimated the prevalence of social outcomes and health related QOL among them. Adjusted odds ratios (OR) for interesting outcomes were estimated with logistic regression analysis.

Results: The questionnaires of 185 CCS (72% response rate) and 72 of their siblings (54% response rate) were analyzed. Median ages of CCS at diagnosis and survey are 8 years and 23 years, respectively. There was no difference in marriage rate for male among the 3 groups. The proportion of marriage is higher in female siblings (36%) but significantly lower than those of siblings in physical functioning (PF) (p = 0.002) and general health (GH) (p = 0.001), respectively. Poor PF scores were associated with recurrence (OR; 2.80, p = 0.041) and late effects (OR; 3.33, p = 0.010) and poor GH scores with late effects (OR; 2.81, p = 0.006). The proportion of medical job was high as 15% for female and 7% for male in CCS. Unemployment was significantly associated with poor QOL in physical subscales; part-time job and unemployment tended to be associated with poor QOL in mental subscales, respectively. Working ability and annual income were inversely correlated with poor physical subscale scores.

Conclusion: Our study revealed that CCS have made much efforts to get attained educational/vocational goal but significant proportion of CCS are at an increased risk of developing poor social outcome and QOL.

O114
PSYCHOMETRIC EVALUATION OF THE IMPACT OF CANCER (IOC-CS) SCALE FOR YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER

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Purpose: Psychosocial outcomes derived from standardized and disease-specific measures are often used in pediatric oncology; however, the reliability, validity and utility of these instruments in adult survivors of childhood cancer have yet to be established. The purpose of this work was to develop and evaluate a new instrument that assesses aspects of long-term survivorship not measured by existing tools.

Method: A deductive analysis of qualitative interviews with 64 young adult survivors of childhood cancer (aged 18–35) resulted in the derivation of 82 candidate items selected for inclusion in a mailed survey intended to examine the psychometric properties of the new instrument. These items, along with other standardized measures of health-related quality of life (HRQOL) and psychological distress, were then administered to a new sample of young adult survivors of childhood cancer. Psychometric evaluation involved a priori categorization of items by domains; exploratory factor analyses to test psychometric properties of hypothesized scales; item reduction; re-scaling and re-testing (factor analyses); and derivation and scoring of subscales. Subscales were evaluated for internal reliability, test-retest reliability, and internal and external validity.

Results: On average, respondents (n = 519) were age 26.7 years at study, 11.3 years at diagnosis, and 15.4 years post-diagnosis. Forty-two items comprising eight new specific subscales explaining 88% of common variance were identified: Life Challenges, Body/Health, Talking With Parents, Personal Growth, Thinking/Memory Problems, Health Literacy, Socializing and Financial Problems. Internal consistency measures for these subscales ranged from 0.70 to 0.86. Expected associations within and among the IOC-CS subscales and with standardized measures of HRQOL were observed, as were some unexpected findings.

Conclusion: Psychometric analyses indicated that this initial version of the IOC-CS measures distinct and relevant constructs for young adult survivors of childhood cancer. Future work is necessary to confirm the responsiveness and further validate the instruments in multiple and representative samples.

O115
PEDIATRIC ONCOLOGISTS’ PRACTICES OF PRESCRIBING SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI’S) FOR CHILDREN AND ADOLESCENTS WITH CANCER: A MULTI-SITE STUDY

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Purpose: Symptoms of depression and anxiety in patients are a common concern of pediatric oncologists, which may result in the use of pharmacologic interventions. The FDA issued a box warning in October 2004 regarding SSRIs and related agents, alerting prescribers to the risk of suicidal ideation in children and adolescents, and providing specific guidelines for monitoring patients on these agents. The purpose of this study was to survey pediatric oncologists in the U.S. regarding prescription of SSRIs for the treatment of depression and anxiety in children with cancer. Specifically, we sought to determine a) how many oncologists prescribed SSRIs; b) whether prescribing practices varied based on geography, size of the cancer center, or practice.

Method: Oncologists from 9 children’s cancer centers (N = 151) from across the U.S. were surveyed, responding to either on-line and paper versions of a questionnaire developed for this study.

Results: A majority of oncologists (71%) reported prescribing SSRI’s at least occasionally for their patients. Oncologists reported difficulties differentiating
symptoms of depression from aspects of cancer treatment. Mental health practitioners are consulted occasionally but not routinely, and oncologists reported a need for increased mental health resources. Approximately half of oncologists (51%) reported not being affected by the FDA guidelines. In addition, only 29% reported monitoring patients on SSRI’s at FDA recommended intervals, and only 9% indicated assessing for suicidality.

Conclusion: Prescription of SSRI’s is a common practice of pediatric oncologists, often without consultation with mental health professionals. Half of the prescribing clinicians report the box warning has not impacted their practice. Post-prescription monitoring appears to be suboptimal.

O116

ASSESSMENT OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN CHILDREN AND ADOLESCENTS WITH CANCER

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Purpose: Chemotherapy-induced nausea and vomiting (CINV) are the symptoms with most negative impact on the child’s quality of life during treatment. Very little attention has been paid to the problem. Existing guidelines for the prevention of CINV in children are inhibited by the lack of robust evidence. Children with high emetogenic attention has been paid to the problem. Existing guidelines for the prevention of CINV with most negative impact on the child

Chemotherapy-induced nausea and vomiting (CINV) are the symptoms that there was need for standardization of scoring nausea. There is also a shortage of satisfactory pediatric tools for assessment of CINV. The aim of this project is to find valid tools for assessment of CINV in children and adolescents with high emetogenic chemotherapy, regardless of age or language difficulties.

Method: We are using a diary designed by the Swedish Emesis Registry and have produced a face-ratings modified Wong-Baker scale indicating no nausea, mild, moderate and severe nausea. Registration is started from the time of the chemotherapy infusion and for 10 days post treatment. Episodes of vomiting and nausea as well as overall wellbeing are recorded by children (2–18 years) receiving moderately to highly emetogenic chemotherapy. Small children are assisted by their parents using the modified Wong-Baker scale.

Results: The tools have up to now been tested on approximately 20 children with 80 treatments cycles. One patient preferred interviews to a diary. Two patients did not experience any CINV and decided not to participate.

Conclusion: A diary combined with a modified Wong-Baker scale is a useful tool to assess CINV in children.

O117

IMPLEMENTATION OF A GUIDELINE FOR USE OF ANTIEMETICS IN A PEDIATRIC HEMATO-ONCOLOGY UNIT

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Purpose: Despite the advent of modern antiemetic agents, chemotherapy induced nausea and vomiting (CINV) remains a distressing side-effect in pediatric oncology. In 2008, we conducted a Drug Use Evaluation (DUE), in which the correlation of prescribed anti-emetics and the rate of emesis control were evaluated. One of the major findings was the lack of correlation between emetogenicity of the chemotherapy course and the concurrent choice of antiemetic medication. In addition, it was clear that there was need for standardization of scoring nausea.

The aim was to implement a clear, evidence-based guideline for prevention and treatment of CINV to obtain a higher degree of emesis control in all patients and to create a systematic approach for clinicians and nurses.

The introduction of a tool used by children to assess nausea intensity was a second objective.

Method: Based on literature, institutional experience and taking into account the results of the conducted DUE (2008), a new guideline was developed by a multidisciplinary team.

Results: Anti-emetics are prescribed according to the level of emetogenicity of the chemotherapy course. There are also specific instructions for the treatment of anticipatory, breakthrough and delayed CINV. In addition, the Pediatric Nausea Assessment Tool (PeNAT) for the evaluation of CINV is translated into Dutch and validated. This new guideline and the introduction of the PeNAT are implemented on the ward after intensive educational sessions for nurses and physicians. Continuous follow-up of the new established guideline and support for both physicians and nurses is necessary to ensure the appropriate use.

Conclusion: The guideline for CINV treatment was successfully implemented on the ward. We believe that the use of a validated tool is crucial for the clinical evaluation of interventions, in order to obtain a profound emesis control. A second DUE is ongoing to evaluate the value of the new guideline.

O118

EFFICACY OF GELCLAIR IN REDUCING THE PAIN OF ORAL MUCOSITIS

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Purpose: To conduct a prospective, open, uncontrolled pilot study to examine the feasibility and acceptability of Gelclair for use in children and young people experiencing pain with oral mucositis.

Method: Children and young people aged between 4–19 years, admitted to an in-patient unit following any chemotherapy anticipated to cause oral mucositis were recruited. Data were collected at baseline and at key defined points over a 48-hour period to record oral pain (faces scale), condition of the oral mucosa (oral assessment scale [OAG] and WHO scale), ability to eat and drink, pain medication taken, and acceptability of Gelclair. Data analysis were performed to indentify any possible relationship between patients’ mean and baseline pain scores, with the covariates; age, gender, baseline neutrophil count and the administration of opiate medication.

Results: Forty-eight were eligible for analysis. The median OAG score was 15 and the median WHO score was 3. 79.2% of the patients reported a lower pain score than at baseline at one of the assessment times post administration, and 60.4% of the patients reported their lowest pain score within the first 6 hours. 52.1% of patients showed an improvement in their ability to eat and drink over the study period with 17 patients showing improvement within the first 6 hours. At least 82.4% of the patients were assessed reported that their mouth felt nice and more than 50% of the patients reported that they liked the taste of Gelclair at every assessment time.

Conclusion: This study has found evidence that Gelclair is tolerable to children and young people who develop oral mucositis. Some patients had an improvement in their ability to eat and drink and most of the patients had some relief from pain. A randomised controlled trial is indicated to determine the efficacy of this agent.

O119

DIFFERENTIALLY EXPRESSED MICRORNAS IN CYTOGENETIC AND MOLECULAR SUBTYPES OF PEDIATRIC AML

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HIGH BRE EXPRESSION IN PEDIATRIC MLL-REARRANGED AML IS ASSOCIATED WITH FAVORABLE OUTCOME

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Purpose: Translocations involving the MLL-gene, localized at 11q23, frequently occur in pediatric acute myeloid leukemia (AML) and more than 60 translocation partners have been described. We recently reported differences in prognosis between pediatric AML with translocations to MLL-rearranged partners and other 245 pediatric AML patients and used quantitative RT-PCR and Western Blot experiments to validate expression levels. Methylation specific PCR (MSP) was used to investigate epigenetic regulation. The effect of the demethylating agent decitabine resulted in promoter demethylation and increased sensitivity for overexpression of BRE.

Results: Using these profiles, we were able to identify a specific gene expression signature for (t(9;11)(p22;q23)), and identified BRE (brain and reproductive organ-expressed) as one of the genes to be discriminative for (t(9;11)(p22;q23)) (p < 0.001) when compared with other MLL-subtypes. Patients with high BRE expression showed a significantly better outcome for 3-year relapse free survival (pRFS) (80 ± 13 vs. 30 ± 10%, p < 0.02) within MLL-rearranged AML cases. Moreover, multivariate analysis identified BRE overexpression as an independent favorable prognostic factor within pediatric AML for RFS (HR = 0.2 ± 0.03). No significant differences were identified for 3-year event free survival nor for 3-year overall survival. However, in vitro studies did not identify differences in cell proliferation, apoptosis or drug sensitivity for overexpression of BRE.

Conclusion: Recent, overexpression of BRE has been described in hepatocellular and oesophageal carcinomas. However, to the best of our knowledge, BRE had never been associated with hematological malignancies before. Our study shows that overexpression of BRE is predominantly found in MLL-rearranged AML with (t(9;11)(p22;q23)). Moreover, high BRE expression is an independent favorable prognostic factor due to a reduced relapse rate in remission. So far, we could not elucidate the exact underlying mechanism. Further research is warranted to explore this and to identify the link between MLL-AF9 and the transcription of BRE.
820 SIOP ABSTRACTS

Purpose: Childhood AML remains a disease with approximately 50% of pEFS, although some selected subtypes show a better outcome. Three consecutive BFM-based protocols for AML treatment were evaluated, for assessing the prognostic impact of cytogenetic/molecular features and response to induction.

Method: From Jan 1990 to Dec 2007, 353 children were admitted, being 266 (M:1455; F:121) of them evaluable. All patients were < 17 years of age and the most frequent FAB subtypes were M5 (64), M2 (55), M3 (51) and M4/M4Eo (30/14). Standard (SR) and High (HR) Risk groups were defined considering cytogenetic/molecular findings and response to treatment on day-15. In AML-90 (n = 90; evaluable = 60) and AML-95 (n = 72; evaluable = 62) this analysis was retrospectively performed, but in AML-99 (n = 189; evaluable = 144) patients were stratified prospectively according to these two prognostic factors.

Results: The SR/HR distribution of patients was AML-90: 25/35, AML-95: 41/21 and AML-99: 59/33. The response to treatment (AML-90/95/99) was: CR(%) : 53(80)/ 49(79)/ 119(83); deaths during induction (%): 10/15/011/17/20(13.8); null response: 3/25 cases. The observed events were (AML-90/95/99): Relapses: 21/24/38 cases; death in CR (%): 12/0/2/48; second malignancies: 2/0/0 cases. The pEFS(SE) for total/SR/HR groups was: AML-90: 35(6)/0/97/17(6)%; p-value SR/HR: 0.0002, AML-95: 38(6)/14(7)/29(9)% (p-value SR/HR: 0.1737) and AML-99: 50(4)/80(5)/ 34(6)% (p-value SR/HR: < 0.0001).

The pEFS(SE) according to cytogenetic/molecular subtypes was: t(8;21)/AML1-ETO (n = 42): 74(7)%; t(15;17)/PML-RAR (n = 49): 57(7)%; 11q23/MLL (n = 29): 42(9)%; inv(16)/CBFB-MYH11 (n = 9): 78(14)%; 7q7 (n = 8): 13(11)%; Normal (n = 45): 30(7)% and other abnormalities (n = 43): 27(7)% (p-value: 0.0002). The pEFS(SE) according to response on day-15 was 49(4)% for patients with < 5% blasts (n = 166) and 16(6)% for patients with > 5% blasts (n = 36) (p-value: < 0.0001).

Conclusion: 1- The pEFS of SR-AML has improved, especially in the last protocol. 2- Deaths during induction show a trend towards decreasing, although the rate is still high. 3- The correlation between pEFS with cytogenetic/molecular findings and response to treatment is good, confirming the important role of these parameters in AML risk group stratification.

O123

HIGH RISK OF OSTEONECROSIS REQUIRING TOTAL JOINT ARTHROPLASTY IN YOUNG PATIENTS TREATED FOR MYELOID LEUKAEMIAS - A NATIONWIDE, REGISTER-BASED STUDY

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Purpose: The risk of osteonecrosis (ON) requiring total joint arthroplasty (TJA) in patients treated for cancer in childhood or early adulthood was studied in a nationwide, population-based study.

Method: All Finnish patients diagnosed with cancer at 0–30 years in 1975–2000 and who survived at least two years after diagnosis were identified from the Finnish Cancer Registry (FCR). Non-melanoma skin cancers were excluded. The patients were linked to the databases on orthopaedic diagnoses and procedures in the National Hospital Discharge Register and the Finnish Arthroplasty Register for years 1980–2005.

Results: Of the 9903 patients, 25 had undergone TJA because of ON. The median time from diagnosis to TJA was 5 years (range 1–10 years). The proportion of ON requiring TJA was highest among patients treated for chronic myeloid leukaemia (6.25%, 6 out of 96) and for acute myeloid leukaemia (3.5%, 6 out of 172). TJA was required for a small proportion of patients with acute lymphoblastic leukaemia (ALL) (0.4%, 4 out of 990), Hodgkin lymphoma (HL) (0.4%, 4 out of 966) or non-Hodgkin lymphoma (NHL) (0.5%, 3 out of 570). Only two patients with any other cancer (1 colon carcinoma and 1 testicular cancer) had undergone TJA because of ON. Hip was the involved joint in 24 patients and knee in one patient.

Conclusion: Osteonecrosis requiring total hip arthroplasty is an important cancer-related complication in children and in young adults treated for myeloid leukemias. Also patients with ALL, HL or NHL have a risk of ON requiring TJA. The risk was very low in patients diagnosed with other cancers than leukemias and lymphomas.

O124

CLINICAL RELEVANCE OF CYTOGENETICS IN RELAPSED PEDIATRIC AML: RESULTS FROM THE INTERNATIONAL RANDOMISED PHASE III STUDY RELAPSED AML 2001/01

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Purpose: Study Relapsed AML 2001/01 enabled comparisons between cytogenetic abnormality and clinical and biological features and with outcome.

Method: Reinduction chemotherapy consisted of FLAG +/- liposomal daunorubicin (DNX), followed by FLAG and allo-SCT. Patients with AML M3 and those > 18 years of age at initial diagnosis were ineligible. In some cases molecular genetic data were used when karyotyping failed.

Results: A total of 569 patients were enrolled, with a median follow-up of 2.7 years. Cytogenetic abnormalities changed from diagnosis to relapse in 20% of patients. 422 patients had information on cytogenetics at relapse. Normal karyotype was seen in 25%. Other abnormalities in decreasing incidence were: MLL gene rearrangements in 15% (including t(9;11) in 4%), t(8;21) in 14%, inv(16) in 7%, t(8;21) in 7%, t(6;9) in 2%, and a wide range of other abnormalities each occurring in less than 1% of patients. Other aberrations not typical for AML were found in 28% of patients. Patients with a MLL gene rearrangement were more often below two years of age at relapse than other subgroups (23% vs 10%, p < 0.003). CBF-AML had a higher rate of good early treatment response (97% vs 72%, p < 0.001), a higher CR rate (90% vs 58%, p < 0.001), and a higher 4-yr pOS (67 SE 5% vs 31 SE 3%, p < 0.001) than other cytogenetic subtypes. Other cytogenetic subgroups did not seem to differ in clinical outcome. Overall survival for CBF-AML patients was significantly higher when liposomal daunorubicin had been added to FLAG. 4-yr pOS 82 SE 7% vs 57 SE 10%, p = 0.04.

Conclusion: Cytogenetics correlate with clinical and biological features in relapsed pediatric AML. CBF-AML has a favorable prognosis at relapse, albeit with the use of allo-SCT, and especially when DNX was added to FLAG. Patients with other abnormalities have a poor prognosis, and improvements in therapy should focus on that subgroup.
Purpose: The AIEOP-TW-2003 aimed at: reducing chemotherapy in stage I-II Wilms tumors (WT); improving the outlook for stage III and stage IV WT (balancing radiotherapy (RT) optimization and doxorubicin (D) dose reduction); significantly implementing tumour banking for protocol molecular studies and centrally reviewed diagnosis.

Method: Out of 398 newly-diagnosed kidney tumours (since 8/2003), the outcomes of 271 monolateral eligible WTs were analyzed. CT regimens as follows: stage I, 6-week vincristine (V) and actinomycin (A); stage II, 22-week VA; stage III, 34-week VAD + abdominal RT; stage IV, primary 6-week VAD, abdominal a/o metastatic site RT with a metastatic-response modulation, VAD. Stage II-IV anaplastic WT: alternating courses of ifosfamide/D and carboplatin/etoposide in an intensive schedule, + abdominal RT. Overall, 29% of non-metastatic patients received 4-week preoperative VA because referring surgeon choice.

Results: Centralized review of diagnosis: 81%; banked fresh tumor samples: 70%. For abdominal RT. Overall, 29% of non-metastatic patients received 4-week preoperative VA because referring surgeon choice.

Conclusion: Satisfactory results, both regarding patient outcome and protocol compliance of the participating Institutions, were reached. Further reduction of treatment for stage I-II non-anaplastic WT must face with the risk of methachromic contralateral tumour. The outlook for patients with anaplastic WT is remarkable.

O126 MANAGEMENT OF ADULTS WITH WILMS TUMOR: RECOMMENDATIONS BASED ON INTERNATIONAL CONSENSUS

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Purpose: Wilms tumor is exceedingly rare in adults, with only approximately 11 cases expected annually per 100 million population in Western Europe and North America. Most adult patients will be diagnosed unexpectedly following nephrectomy for presumed renal cell carcinoma. Due to its extreme rarity, no standard therapeutic recommendations are available so far. Population-based analyses show that outcome for adults with Wilms tumor is inferior compared to children, although better results are reported when treated within pediatric trials. While the reasons for this are multi-factorial, institutional experiences suggest that unfamiliarity of adult oncologists and pathologists with this childhood tumor delays in initiating chemotherapy and applying appropriate risk-adapted treatment are contributing factors.

Method: To improve outcome through standardized treatment an international consensus guideline for the management of adults with Wilms tumor is proposed. The guideline builds on discussions held during the SIOP 2003 congress in Cairo, where representatives of the renal tumors committees of SIOP and the Children’s Oncology Group (COG) were present and has been updated with a review of more recently published institutional and trial experience of adults treated on pediatric protocols.

Results: The proposed guidelines provide a critical evaluation of the current evidence for clinical decision making in the management of Wilms tumor in adults and propose details of how the current pediatric therapeutic recommendations should be adapted for use in adults. Moreover, we propose a prospective international registry to improve the evidence base.

Conclusion: A standardized approach to the diagnosis, staging and treatment of adults with Wilms tumor is proposed based on available literature and international expert consensus from the field of pediatric Wilms tumor. The aim is to limit treatment delay after surgery and encourage a uniform approach to the management of this very rare disease and thereby to improve survival.

O127 LATE RECURRENCES IN WILMS TUMOUR (WT) PATIENTS: AN UNDER-ESTIMATED PROBLEM? A RETROSPECTIVE COOPERATIVE PRELIMINARY VIEW ON AIEOP/SIOP/UKW PROTOCOLS

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Purpose: Approximately 95% of WT recurrences occur within 2 years of initial diagnosis. Recurrences beyond 5 years are extraordinarily rare. This study aimed to define the true incidence of late recurrences across large several clinical trials, to gain insights into the clinical behaviour of this subgroup of WTs displaying an unusual disease course.

Method: Available medical records on patients enrolled into SIOP-9301, AIEOP-CNR-92, UKW-1, -2 and -3 protocols were reviewed. Criteria for patient selection were: tumour recurrence > 5 years from initial diagnosis and with at least a further 5 years of follow-up.

Results: Twenty-nine (0.7%) out of 3905 WT patients experienced a first relapse > 5 years from initial diagnosis. No gender association was observed. Median time elapsing between initial WT diagnosis and first recurrence was 74 months (range, 62–
143. Median age at tumour recurrence was 121 months. Initial tumour characteristics were: stage I, 9 cases; stage II, 9; stage III, 2; stage IV, one; bilateral disease, 8; 7 cases were SIOP high-risk histology, 15 intermediate-risk (while 6 had high nephrogenic nephroblastoma, one nephroblastomatosis). 1529 children died of disease progression (6 had high-risk initial histology). All 6 patients developing contralateral metachronous tumour (4 had bilateral disease at origin) are alive without disease. Other known site of recurrence were: lung 5 cases, liver 2, pelvis 3, local + lung 1. Therapies administered at recurrence varied markedly between patients and centers, preventing any conclusion about the best salvage treatment.

Conclusion: First recurrences developing late in the WT course are a rare event, and do not justify regular monitoring diagnostic work-up. However, we believe that studying more deeply this population of patients might pin-point some WT biology insights, such as mechanisms underlying tumour cell dormancy or cancer stem cell maintenance. Considering the age at recurrence onset, a possible sex hormone-dependent tumour growth at puberty deserves further attention.

0128

REFINING RISK STRATIFICATION FOR PRETREATED LOCALISED WILMS TUMOURS: THE SIOP RENAL TUMOURS STUDY GROUP EXPERIENCE

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Purpose: The SIOP WT 2001 trial introduced a new ‘high risk’ entity: ‘blastemal type’ WT. However, the largest absolute number of relapses among localised tumours emanates from the ‘intermediate risk’ histology subgroup. We therefore investigated whether different thresholds for percentage necrosis/blastema might improve risk stratification based on pathological response to pre-operative chemotherapy.

Method: Data on 2,071 patients with localised unilateral WT treated with pre-operative chemotherapy in the SIOP 2001 trial (to Sept 2009) are analysed. Martingale plots of excess risk of relapse versus overall % necrosis or % blastema in the viable residue were interrogated for thresholds at which risk altered. Event free survival was analysed by Kaplan-Meier methods and subgroups compared by log rank.

Results: For the entire group, 2yr EFS was 88.2% (95% CI:86.6–89.8) and 5yr OS: 93.7% (95% CI:92.2–95.2). Histological risk group was a better discriminator of outcome than tumour stage (2yr EFS low risk:95.9%, intermediate risk:89.8% and high risk:76.9%, p < 0.001; 2yr EFS stage I:91.0%, stage II:87.8% and stage III:83.2%, p < 0.001). Martingale plots showed no threshold effect for necrosis but a reduced risk of relapse in those with < 20% blastema in the viable tumour, with a small but steadily increasing risk of relapse with > 50% blastema. For intermediate risk tumours, there was a significant decrease in EFS with increasing% blastema (comparing 0–10%, 10–90%, 90–100%). This persisted in the regressive subtype but was at the borderline for statistical significance in the mixed subtype (p = 0.05). The worst outcome group had 2 yr EFS of 79%.

Conclusion: Survival of blastema after pre-operative chemotherapy in Wilms tumour is a better prognostic factor than% necrosis. Improved definition of chemoreistant blastema requires molecular characterisation of the disrupted biological pathways to improve risk stratification and inform discussions of new therapeutic approaches for these higher risk tumours.

0129

FAILURE OF A PROSPECTIVE STUDY TO RESOLVE THE ISSUE ON THE ROLE OF CT-SCAN OF THE CHEST AT DIAGNOSIS IN CHILDREN WITH A RENAL TUMOUR

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Purpose: The significance of small lung lesions detected on CT-scan but not on chest X-ray (CXR) at the time of diagnosis (CT-only) in children with a renal tumour is still unclear. One subject of the SIOP-2001 study was to resolve this controversy by prospectively documenting patients with CT-only lesions, recommending treatment as localised disease and to compare their outcome with that of patients with localised disease of the same stage and histology.

It was hypothesised that the outcome of both groups of patients is the same.

Method: In the SIOP study 3583 patients were registered between November 2001 and November 2009. The data of all patients with localised disease, CXR negative and CT-positive (any size) lung lesions were reviewed and analysed in relation to treatment and outcome.

Results: Out of 3583 registered patients 367 (10.7%) were metastatic and 139 patients with localised disease were reported to have CT-only lesions. Of these patients 105 had unilateral Wilms’ tumour (WT), 14 had a Non-WT renal tumour, 12 had bilateral disease and 8 had unreported histotype. Preoperative treatment according to localised disease as prescribed by the protocol was given to 34 patients. Sixty-seven patients received treatment for metastatic disease; in 4 patients treatment was not reported. Doctor’s decision was the main reason for treatment deviation. In 3 patients a diameter of CT-detected lesions > 10 mm was the reason for stage IV treatment.

Preliminary survival analysis suggests that a different therapeutic regime does not translate in statistical significant differences in EFS or OS.

Conclusion: This study demonstrates how different opinions on the significance of type and size of lesions and clinicians’ preference for a more intensive treatment can compromise a prospective study protocol designed to resolve an important issue.

0130

SIGNIFICANCE OF LYMPH NODE INVOLVEMENT IN NEPHROBLASTOMA

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Purpose: Lymph node (LN) involvement at initial surgery for nephroblastoma has been identified as an adverse prognostic factor. The objective of this study is to compare the incidence and prognostic value of LN involvement in favorable histology nephroblastoma identified before or after initial chemotherapy. Method: Patients: Patients (pts) with delayed nephrectomy (DELAYED) included all study patients on the SIOP 93-01 and 2001 trials with localized unilateral favorable histology (non-anaplastic) disease aged at least 6 months treated with pre-nephrectomy chemotherapy. Patients with immediate nephrectomy (IMMEDIATE) included all study patients on the fifth NWTS with the same characteristics who underwent immediate nephrectomy prior to chemotherapy. Unknown lymph node status was considered negative in both groups. DELAYED stage III pts received 250 mg/m² doxorubicin versus 150 mg/m² for IMMEDIATE pts, as well as additional radiation dosage.

Results: Patients: Amongst DELAYED pts, there were 294/3560 (8.3%) with lymph node involvement (LN+) compared with 289/1655 (17.3%) IMMEDIATE pts. When only stage III pts were considered, 22/5643 (35%) DELAYED pts were LN+, compared with 273/538 (51%) IMMEDIATE pts. Considering only stage III pts with follow-up, in the DELAYED group, the five-year EFS for the 222 LN+ pts was 79.4% versus 84.3% for the 410 LN− pts (p = 0.02). For the IMMEDIATE group, the 5 yr EFS was 81% for LN+ (273 pts) and 89% for LN− (265 pts) (p = 0.0023).

Conclusion: Conclusions: LN+ is more than twice as common when assessed prior to chemotherapy, assuming equal degree of assessment. The worse outcome in the LN+
The immune response to two doses of novel influenza A (H1N1) vaccine is being studied. Children were recruited from the Royal Marsden Hospital, England, during November 2009. The vaccination schedule consisted of two doses of a split-virion, AS03B-adjuvanted vaccine given at days 0 and 21. Serological analysis was performed on blood samples taken at day 0 and day 42. Samples were tested at the Respiratory Virus Laboratory, Health Protection Agency. The primary immune end-point for seroprotection was an individual four-fold increase in haemagglutination-inhibition (HAI) titre after the second vaccine dose.

Results: 49 children with an age range from 1.4 to 16.6 years (median 6.3 years) received two doses of vaccine. A 4-fold increase in HAI titre by day 42 was achieved in 23/49 children (46.9%, 95% CI 33.0–60.9). Seroreponse rates were 9/26 (34.6%) in children with ALL, 4/9 (44.4%) in those with lymphoma/other leukemias, 6/8 (75.0%) in those with brain tumours and 4/6 (66.7%) in those with other solid tumours. Of children receiving ALL maintenance therapy, 4/14 (28.6%) achieved seroprotection. Only 4 children had baseline HAI titres ≥ 32, of which 3 achieved a 4-fold increase following vaccination.

Conclusion: These data suggest that two doses of novel influenza A (H1N1) vaccine can induce a protective immune response in the majority of children with solid tumours but that a much lower proportion of children with haematological malignancies achieve seroprotection. Lymphopoeisis does not appear to adversely affect serorespose rates.

**Role of Galactomannan Assay in Diagnosis of Invasive Aspergillosis in Children with Febrile Neutropenia**

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Purpose: Invasive aspergillosis (IA) is an important cause of morbidity and mortality in immunocompromised patients. Early diagnosis based on radiology and microbiological culture is difficult. Galactomannan (GM) antigen detection is a sensitive tool for the diagnosis of IA. Since pediatric data is sparse, we evaluated utility of a GM double sandwich Elisa assay in the diagnosis of IA in neutropenic pediatric patients. Method: A prospective study included children younger than 16 years of age with neutropenia (neutrophils < 500/mm^3) for more than 10 days and fever admitted in Pediatric Hematology Oncology from Oct 2006 to February 2010. Galactomannan assay (GA) was done twice weekly in each febrile episode. All new episodes of febrile neutropenia were recorded, GA > 1.0 was taken as positive. CT chest/sinus and broncho-alveolar lavage were performed as per protocol. IA was classified as proven, probable, possible and no fungus as per EORTC Guidelines. Results: 109 patients included were post hematopoietic stem cell transplantation (n = 10), ALL (n = 71), AML (n = 9), lymphoma (n = 5), inherited or acquired bone marrow failure (n = 10), others (n = 4). 109 (35%) out of 312 serum samples collected during 154 febrile episodes were positive. Thirteen patients had a single positive GA while 37 had 2 consecutive positive GA. Five children had proven IA, 17–probable IA, 3–possible IA and 84–no IA. The sensitivity and specificity of single positive GA for proven and probable IA group was 100% and 79% respectively. With two consecutive positive GA, the specificity increased to 88%. Sensitivity was 95%, positive predictive value 57% and negative predictive value 99%. GA was falsely positive in 2 patients with Candida septis, 2 with mucormycosis and 11 patients with no fungal infection. Conclusion: Serial GM assay > 1.0 is highly sensitive for the diagnosis of IA in neutropenic pediatric patients and has an excellent negative predictive value in ruling out IA.
Purpose: The experience of paediatric oncology patients and families may be improved with fewer unplanned hospitalizations. We set out to compare quality of life (QOL) between inpatient and outpatient IV antibiotic management of children and adolescents with low risk febrile neutropenia (LRFN).

Method: Randomized unblinded trial. Patients 1–21 years receiving low/moderate intensity chemotherapy, residing within 1 hour of hospital were pre-consented. Patients were eligible for randomization if presenting to ED with LRFN (no septic shock or significant comorbidities). Patients were randomized to IV cefepime 50 mg/kg (12hourly) outpatient or inpatient care. Outpatients received twice daily nurse visits. All patients continued antibiotics for at least 48 hours, until afebrile 24 hours and rising ANC ≥2000/mm³. A daily QOL questionnaire assessed patients and parents on a 10cm visual analog scale.

Results: 81 preconsented patients presented to ED with 159 episodes of fever. 37 febrile neutropenia presentations involving 27 patients were randomized to inpatient (18) and outpatient (19) management. QOL combined mean scores for parent variables were higher for outpatients than inpatients on day 3 (n = 33, 7.4 vs 4.7 p < 0.01) and day 4 (n = 24, 7.6 vs 4.7 p < 0.01). Mean scores for 3 parent variables were higher among outpatients than inpatients (keeping up with household tasks 6.4 vs 0.9 p < 0.01, time spent with partner 6.1 vs 0.7 p < 0.01, time spent with other children 6.7 vs 1.3 p < 0.01). There was no difference in parent confidence/satisfaction in care between groups. Parent well-being scores scored better in outpatient group without reaching significance. Mean length of fever was equivalent. 6/18 outpatients were readmitted for persistent fever or medical comorbidities. There were no serious adverse events attributable to cephalosporin or outpatient care.

Conclusion: Low risk hospitalization for low risk febrile neutropenia episodes provided significant benefit to families by several measures of quality of life, and appeared to be a feasible alternative.

O135

KNOWLEDGE AND UNDERSTANDING OF THE INFORMED CONSENT PROCESS AMONG PARENTS OF CHILDREN ENROLLED ON CANCER CLINICAL TRIALS

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Purpose: Clinical trials are central to pediatric oncology, yet the process and outcomes of informed consent are poorly understood. We evaluated correlates of understanding among parents of pediatric trial participants, and explored differences in the informed consent process and outcome between parents and a comparison group of adult participants.

Method: We administered the Quality of Informed Consent (QIC) to parents of children who were newly enrolled onto a cancer clinical trial, and to a contemporaneous group of adult patients. We identified independent correlates of knowledge among parents, and compared parents’ knowledge to that of adult trial participants, using multiple linear regression models.

Results: Parents (n = 47) were less likely than adult participants (n = 204) to report having enough time to learn about the trial (64% vs. 87%, p < 0.001) or sufficient opportunity for questions (79% vs. 93%, p = 0.01), and reported lower overall satisfaction with the consent process (71% vs. 90%, p = 0.002). The mean parental knowledge score was 73.6 (95% confidence interval [CI] 69.5–77.8, theoretical maximum 100). In multivariate analysis, two predictors were significantly associated with higher parental knowledge scores: consent sought by the study investigator (increment 13.6, CI 2.7–24.6) and physician-reported poor prognosis (increment 13.8, 95% CI 5.4–22.1). Although we observed no significant difference in objective knowledge scores between parents and adult participants, parents’ subjective assessment of their knowledge was lower than that of adults (median self-assessment scores 79.5 vs. 87.8, p < 0.0001).

Conclusion: Parents of pediatric cancer patients report greater difficulty than their adult counterparts with the informed consent process for clinical trials, likely due to contextual differences between pediatric and adult trials. Parents’ knowledge of their trials is imperfect, and may be influenced by clinical and situational factors. Although parents’ knowledge of their children’s trials is objectively similar to that of adults, parents view themselves as less well-informed.

O136

LOW-DOSE GCSF PROPHYLAXIS IS AS EFFECTIVE AS STANDARD-DOSE IN PEDIATRIC CANCER PATIENTS RECEIVING MYELOSUPPRESSIVE CHEMOTHERAPY A PROSPECTIVE RANDOMIZED OPEN LABELED PARALLEL GROUP PHASE III STUDY

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Purpose: G-CSF administered prophylactically after chemotherapy reduces the duration and severity of neutropenia. The dose and duration required to gain maximum clinical and economic benefit has not been fully investigated. This randomized study was designed to assess whether a lower dose of G-CSF is as effective as a standard dose of 5 microgram/kg daily.

Method: Patients who received standard-dose chemotherapy regimens expected to cause neutropenia received G-CSF (Filgrastim) that started the day after chemotherapy for 14 days or until the absolute neutrophil count (ANC) recovered to greater than 5 x 10^9/L. The filgrastim dose was randomly allocated to be 2.5 or 5 microgram/kg daily in the first cycle of chemotherapy. The study was designed to accrue 172 assessable patients to provide a power of 90% to detect a difference in duration of grade IV neutropenia/ANC > or = 0.5 x 10^9/L of 1 day.

Results: 172 patients were randomized to treatment and 167 patients completed the planned therapy. Both standard (n=85) and low-dose Filgrastim (n=89) resulted in a similar mean duration of grade IV neutropenia (4.05 vs. 4.65 days, P = 0.2) and incidence [62/79(80%) vs 66/87(80%), P = 0.6]. Also, incidence of febrile neutropenia [35/44(79%) vs 37/42(88%), p = 0.9] and duration (4.35 vs 4.5P = 0.8) were similar. Furthermore, there was no difference in the depth of neutrophil nadir (0.19 vs 0.15P = 0.6) and incidence of fever (79% vs 86%, P = 0.80, duration of neutropenia (5.14 vs 5.98, P = 0.1) as well as duration of growth factor usage (8.91 vs 8.92) in 2 arms. There was also no significant difference in blood product support. The total cost of G-CSF (cost/drug x duration of administration) was significantly lower in patients who received low dose filgrastim.

Conclusion: A low-dose of Filgrastim is as safe and effective as standard dose Filgrastim and pharmaco-economically more beneficial in children receiving myelosuppressive chemotherapy.

O137

MYOCARDIAL PERFORMANCE INDEX IN THE PREDICTION OF EARLY ANTHRACYCLINE INDUCED CARDIOTOXICITY IN CHILDREN

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Purpose: Anthracycline induced cardiotoxicity causes significant delay or breaks in chemotherapy. Investigations currently employed identify it only after significant and usually non reversible cardiac damage has occurred. These tests are often invasive and expensive. The Myocardial performance index (MPI) is a non invasive and reproducible Doppler echocardiographic measurement of myocardial efficiency which is independent of the heart rate and blood pressure. We have studied the role of MPI in predicting early anthracycline induced cardiotoxicity in children.

Method: Newly diagnosed children with acute lymphoblastic leukemia and undergoing standard chemotherapy (MCP ±41 protocol) were enrolled. After clinical examination, Color Doppler echocardiography was done by a single observer at four different stages of therapy i.e. at initiation, at the end of induction (II), re-intensification (RII) and during the third maintenance cycle (M3), corresponding to cumulative anthracycline dosages of > 100 mg/m², > 200 mg/m² and > 300 mg/m² respectively. The standard parameters of cardiac toxicity (abnormal fractional shortening (FS) and ejection fraction (EF) were measured and compared statistically with the MPI in each group and the children were followed up.

Results: Forty two children, aged between 13 to 156 months with a MF ratio of 2:1 were studied. Forty one, thirty and eleven received 100 mg/kg, > 200 mg/kg and > 300 mg/kg of anthracycline cumulatively, of which zero, four and three children were identified to have MPI significantly lower in patients who received low dose filgrastim.

Conclusion: A low-dose of Filgrastim is as safe and effective as standard dose Filgrastim and pharmaco-economically more beneficial in children receiving myelosuppressive chemotherapy.
more abnormal at lower cumulative dosages. A number of these children, especially in the first group who were found normal by EF and FS, then went on to develop cardiotoxicity (with abnormal EF and FS) later in the study, suggesting earlier detection of cardiotoxicity by the MPI.

Conclusion: MPI appears a better parameter to identify early anthracycline induced cardiotoxicity than the traditional echocardiographic measurements.

O138

METABOLIC SYNDROME AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION DURING CHILDHOOD AND ADOLESCENCE IN CHILE

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Purpose: Our purpose was to determine the frequency, characteristics and risk factors of metabolic syndrome (MS) in patients undergoing hematopoietic progenitor cells transplantation (HSCT).

Method: Descriptive, prospective and transversal that included 69 patients, age > 6 years old, with at least 1 year post HSCT. In all, we calculated the body mass index (BMI), pubertal development was assessed, waist circumference, blood pressure (BP) and triglyceridemia was measured in addition, HDL cholesterol and fasting glucose. The diagnosis of MS children took at least three of the following criteria: waist circumference > 95th percentile for age and sex, BP values > 90th percentile, triglyceridemia > 100 mg/dL; HDL cholesterol < 50 mg/dL or glucose > 100 mg/dL.

For diagnosis in over 20 years used the criteria of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) as amended by the American Heart Association (AHA). For statistical analysis used Chi square or Fisher’s exact as appropriate.

Results: The MS was present in 32% of patients and parameters abdominal obesity were more prevalent (73%), hypertriglyceridemia (91%) and low HDL cholesterol levels (96%). As a risk factor for all patients we found, having received steroids before HSCT (p < 0.01) and in patients undergoing allogeneic HSCT using steroids during the first year post transplant (p < 0.03). The finding of abdominal obesity, hypertriglyceridemia, low HDL cholesterol and blood glucose > 100 mg/dL were significantly associated with the presence of MS (P < 0.04).

Conclusion: MS is 3.5 times more frequent after HSCT. MS increases risk of cardiovascular disease, is essential to prevent and treat early to improve the quality of life of patients and prevent premature death.

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CARDIOVASCULAR RISK FACTORS IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBlastic LEUKEMIA – A REPORT FROM THE SJLIFE STUDY

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Purpose: Survivors of childhood acute lymphoblastic leukemia (ALL) have been shown in small studies to have an increased risk of metabolic syndrome (MS), obesity, and heart disease risk. Recipients of cranial radiotherapy (CRT) are especially at risk. We compared the prevalence of these factors in a large population of adult survivors of ALL to the general U.S. population to verify these findings.

Method: The St. Jude Life (SJLIFE) study is a cross-sectional cohort of survivors of pediatric malignancies treated at St. Jude Children’s Research Hospital. 318 adult survivors of ALL (mean age, 35 years; range 20 to 50 years) underwent comprehensive evaluation and screening for MS, and heart disease risk by physical exam, laboratory evaluation, anthropometrics, and medical record abstraction. Comparisons were made to a matched cohort from the 2005–2006 National Health and Nutrition Examination Survey (NHANES) using multiple regression models.

Results: Mean survival time was 30 years. Compared to the NHANES control population matched on age, gender, and race, ALL survivors were significantly more likely to have three or more components of MS than controls (37.26% vs. 28.70%, p = 0.03). They were also more likely to have BMI > 30 kg/m2 (51.26% vs. 30.85%, p < 0.001). After adjusting for age and gender, those survivors who were treated with CRT were 2.35 times (95% CI 1.14–4.83) more likely to meet criteria for MS, and 2.39 times (95% CI 1.29–4.41) more likely to have BMI > 30 kg/m2.

Conclusion: This large study of adult ALL survivors confirms previous findings that there is a higher prevalence of metabolic syndrome, obesity, and heart disease risk, particularly in recipients of CRT, compared with the general population necessitating intensified screening and aggressive reduction of modifiable risks.

O140

CARDIOVASCULAR SEQUELAE IN LONG TERM SURVIVORS OF CHILDHOOD CANCER

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Purpose: We aimed to examine incidence of cardiovascular sequelae within a cohort of long-term survivors of paediatric and adolescent cancer.

Method: Inpatient hospital admissions were linked to the Yorkshire Specialist Register of Cancer in Children and Young People. Eligible subjects were those diagnosed aged < 30 years between 1974–2005 and survived for at least five years. Cardiovascular sequelae were identified from diagnosis and procedures codes recorded in national hospital episode statistics (1996–2006). Patients with an event post-diagnosis were compared to those without; likelihood of having an event was modelled using logistic regression adjusting for diagnostic group, sex, age, year of diagnosis, ethnicity and deprivation.

Results: A total of 1939 patients were included in the analysis, of which 7% (n = 144) had a cardiovascular related hospital admission, 40% of which occurred exclusively post-diagnosis. We observed an excess of leukaemia (26.4%; n = 38) and lymphoma (25.9%; n = 36) patients with cardiovascular episodes compared to those without (19.8% and 20.8% respectively). Cardiac episodes were 33% less likely among other solid tumours than haematological malignancies (OR = 0.67; 95% CI 0.47–0.94). There was 5% less chance of a cardiac episode for every single year increase in year of diagnosis. Gender, age, ethnicity and deprivation were not significantly associated with cardiovascular sequelae in survivors. The five most common cardiac episodes observed post-diagnosis were essential hypertension (30%), complications and ill-defined descriptions of heart disease (10%), hypertensive renal disease (9.5%), cardiomyopathy (6.2%) and heart failure (5.5%).

Conclusion: Our data showed some indication of increased incidence of cardiovascular events amongst haematological malignancies compared to other tumours. Future work will involve expanding the study to include England as a whole and will include outpatient hospital data with the aim of capturing a more comprehensive population of patients with cardiovascular sequelae.

O141

PULMONARY HYPERTENSION AFTER TREATMENT FOR CHILDHOOD CANCER. A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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COMPONENTS OF THE METABOLIC SYNDROME IN 500 ADULT LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Purpose: Adult survivors of childhood cancer have been reported to have an increased risk of late sequel. A cluster of abnormalities that contribute to the metabolic syndrome may be expressed at a higher level and therefore result in an increased risk for diabetes mellitus and cardiovascular diseases.

Method: We investigated a single centre cohort of 500 adult survivors (228 females) of childhood cancer, median age 28 years (range 18–59 years) and median follow-up time 19 years (range 6–49 years). This cohort included 146 acute lymphoblastic leukaemia (ALL) survivors (75 females). We measured total cholesterol, high-density lipoprotein (HDL)-cholesterol, systolic and diastolic blood pressure, body mass index and the prevalence of diabetes mellitus. Data from the Dutch epidemiologic MORGEn-study were used to calculate standard deviation scores as normative values.

Results: The criteria of the metabolic syndrome were met in 13% of the total cohort. ALL survivors treated with cranial irradiation (CRT) had an increased risk of developing the metabolic syndrome compared with ALL survivors not treated with CRT (23% vs. 7%, P = 0.011). ALL survivors who received CRT had higher total cholesterol levels compared with ALL survivors who did not (mean SDS 0.38 vs. mean SDS = 0.05, P = 0.027), whereas their HDL levels did not differ. Also, ALL survivors treated with CRT were more often hypertensive compared with ALL survivors not treated with CRT (22% vs. 10%, P = 0.036) and more often overweight (59% vs. 34%, P = 0.003), however they were not more often obese (12% vs. 9%, ns).

Conclusion: Adult survivors of childhood cancer, especially ALL survivors treated with CRT, are at increased risk of developing the metabolic syndrome. This increased risk is probably determined by higher prevalence of hypertension and hypercholesterolemia in these survivors.

INTEGRATING DIVERSITY-ORIENTED SYNTHESIS AND EXPRESSION-BASED SCREENING TO IDENTIFY NEW INDUCERS OF NEOBLASTOMA DIFFERENTIATION

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Purpose: Long-term survival for patients with high-stage neuroblastomas remains poor despite intensive cytotoxic therapy. One alternative treatment strategy is tumor differentiation. Although 13-cis-retinoic acid differentiation therapy has been incorporated into treatment of patients with minimal residual disease, efforts to identify new differentiation agents have been hampered. There is minimal industry interest in leading such efforts, a lack of high-throughput phenotypic assays to measure neuroblast maturation, and limited chemical diversity in current combinatorial libraries. We sought to overcome these challenges by integrating screening of a structurally diverse small molecule library with a gene expression-based differentiation assay.

Method: Gene Expression-based High-throughput Screening (GE-HTS) uses the expression pattern of a defined set of genes to represent a biological state. We identified a 59-gene neuroblastoma differentiation signature and adapted this signature to a high-throughput assay using ligation-mediated amplification and detection of amplicons with fluorescent beads. We screened a library of 3,840 molecules including bioactives and diversity-oriented synthesis (DOS) compounds. DOS is a library synthesis approach yielding compounds rich in stereochemical and structural complexity, accessing chemical space unoccupied by the products of standard combinatorial chemistry.

Results: A top hit was BRD-K53308430, a DOS molecule containing a 9-membered ring core, a chromatin-biasing element, and defined stereochemistry at three positions. Interestingly, other known chromatin modulators have been reported to induce neuroblast differentiation. We next used GE-HTS to rapidly evaluate structure-activity relationship (SAR) of 13 BRD-K53308430 analogues, exploiting the “poised for optimization” nature of DOS molecules. The chromatin-biasing ortho-amino amide element proved to be necessary but not sufficient for the observed activity, and both skeletal and stereochemical alterations were used to optimize activity.

Conclusion: Ongoing efforts focus on the application of SILAC (stable isotope labeling by amino acids in cell culture) to reveal the protein targets of the optimized BRD-K53308430 analogue with the expectation of identifying novel therapeutic differentiation targets in neuroblastoma.
putative tumor suppressive microRNAs, miR-542-5p and miR-628, were expressed in favorable neuroblastomas and virtually absent from the transcriptomes of unfavorable neuroblastomas. Various miRNA species were strongly expressed, and correlation of expression of the miRNA to the respective miRNA* varied markedly. In-depth sequence analysis revealed extensive post-transcriptional miRNA editing. Of 13 identified novel miRNAs, three were further analyzed with stem-loop RT-qPCR, and expression was confirmed in a cohort of 70 primary neuroblastomas.

Conclusion: Next-generation sequencing is a valid tool to explore the quantitative and qualitative differences in the small RNA transcriptomes of primary tumors. Principle differences exist in the small RNA transcriptomes of favorable and unfavorable neuroblastomas.

O145
HIGH EXPRESSION OF THE ALK RECEPTOR TYROSINE KINASE PRECEDES MUTATION AS A DETERMINING FACTOR OF UNFAVOURABLE PHENOTYPE IN PRIMARY NEUROBLASTOMA

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Purpose: Amplification and activating mutations of the anaplastic lymphoma kinase (ALK) have been postulated to contribute to the pathogenesis of neuroblastoma. This study aimed to determine the contribution of genomic ALK alterations and ALK expression to the clinical phenotype of neuroblastoma.

Method: The genomic status and mRNA expression levels of ALK were determined by sequencing, quantitative PCR, and oligonucleotide-microarray analysis in 263 primary neuroblastomas. Allele-specific ALK expression was determined by cloning and sequencing of cDNA fragments, and validated using allele-specific quantitative PCR. ALK protein expression levels were examined in western blots. The association of genomic ALK alterations and ALK expression levels with survival were determined using log-rank tests and in Cox regression models.

Results: Amplifications and non-synonymous mutations of ALK were detected in 2/263 and 2/263 neuroblastomas, respectively. Tumors with mutated ALK had significantly higher ALK mRNA and protein expression, and were associated with unfavorable patients outcome. Unexpectedly, the mutated allele was not the predominantly expressed form in many tumors with ALK mutations. In neuroblastomas without ALK mutations, ALK overexpression was strongly associated with prognostic markers of adverse outcome and with poor survival. The clinical course was highly similar for patients with mutated or wild-type ALK which had comparable ALK transcript levels. In multivariate analysis, ALK expression, but not ALK mutation, was an independent factor of adverse outcome (EFS, ALK expression level p < 0.001, HR 4.26, CI 1.95–9.27; ALK mutation, p = 0.359; OS, ALK expression level p < 0.001, HR 8.70, CI 3.11–24.32; ALK mutation, p = 0.269). Gene expression patterns revealed by microarray analysis correlated with ALK expression levels rather than with ALK mutational status.

Conclusion: High ALK expression precedes ALK mutation as a determining factor of clinical course in neuroblastoma, suggesting that elevated ALK expression, in general, should be considered as a specific target for novel therapeutic strategies.

O146
TOXICITY AND EFFICACY OF HDC WITH BU/MEl AND HSCT IN HIGH RISK NEUROBLASTOMA PATIENTS: A SINGLE CENTER STUDY.

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Purpose: The impact of high dose chemotherapy (HDC) and hematopoietic stem cell transplantation (HSCT) in improving the survival of high-risk neuroblastoma patients has been well established. We previously presented the positive impact of the Busulfan-Melphalan (BuMel) regimen in these patients. In this study, we analysed the toxicity and survival of a large cohort of patients treated with BuMel at the Pediatric Department, Institut Gustave Roussy.

Method: We evaluated comprehensive data prospectively collected between 1980 and 2008 concerning all patients aged more than one year treated with HDC and SCT for high-risk neuroblastoma. Patients enrolled on the HR-NBL1/ESHO protocol were excluded.

Results: From October 1980 to December 2008, 209 patients aged more than one year were treated with BuMel and autologous HSCT for high-risk neuroblastoma. The median age at diagnosis was 40 months (range 12–218), the sex ratio M/F was 1.4 and 88% of patients had an abdominal primary tumor. Bone marrow involvement was detected in 80% of cases and N-MYC amplification was present in 30% of tumors. HSCT consisted of bone marrow, peripheral stem cells and both in 50%, 46% and 4% of the patients respectively. Mean duration of hospitalization and neutropenia was 48 and 18 days respectively (range 15–143 and 3–66 days). Grade 3/4 mucositis occurred in 75% of patients and veno-occlusive disease complicated 40% of grafts. Overall, treatment related toxicity significantly decreased with time. The 5-year EFS and OS post-diagnosis was 50% and 44% respectively, with a median follow-up of 41 months (range 5–231).

Conclusion: Analysis of this large series is encouraging with an improved EFS at 5 years compared to the cohort published by our team in 1999 (O. Hartmann et al.). BuMel is currently being compared to the CEM combination in the ongoing HR-NBL1 European protocol.

O147
USE OF DIETARY SUPPLEMENTS AMONG CHILDREN WITH CANCER IN GUATEMALA

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Purpose: International surveys demonstrate children with cancer are significant consumers of traditional and complementary/alternative medicine (TCAM). Dietary supplements are often the most common type of TCAM in use with conventional treatment. Utilization of dietary supplements and its consequent impact on the decision for conventional treatment and survival among children with cancer in Guatemala have yet to be explored.

Method: Institutional review board approval was obtained for a survey of TCAM use and its associations in children with cancer at the Unidad Nacional de Oncologia Pediatrica, Guatemala. A random, cross-sectional sample of 78 parents was interviewed in person from May 2008-February 2010 after obtaining consent. Demographic data, dietary supplements used, and referral and communication about use were collected.

Results: Median age 10 years (1–18). Gender: 49 male/29 female. Diagnoses include leukemia (60%), lymphoma (18%), solid tumors (13%), and other (9%). 24% were Mayan, 86% attended religious services regularly, and 62% lived > 2 hours from the clinic. 52 (67%) patients reported dietary supplementation use. 46% used herbal supplements, 31% juicing, 28% addition of specific fruit/vegetable, and 5% snake/scorpion venom. Reasons for dietary supplementation were to provide immune support (34%), overall strength/wellbeing (30%), improve hemoglobin (15%), cure (11%), nutrition (3%), weight gain/loss of appetite (3%), gastrointestinal relief (2%), and relaxation (2%). Quilete (20%), alfafa (14%), noni (10%), bulls tea (6%), and macay (8%) were the most common types of herbal supplements used. The majority of dietary supplements were described as very effective (68%) and were referred by family/community members (55%). 49% of all reported dietary supplements were not disclosed to their physician.

Conclusion: Use of dietary supplements was quite common among this sample of pediatric oncology patients. As there are concerns about the potential for adverse interactions, educational and research initiatives on the safety and efficacy of dietary supplements are needed.

O148
DELINEATION OF FOUR NOVEL TUMOR PREDISPOSITION SYNDROMES IN PATIENTS WITH CHILDHOOD CANCER AND IDENTIFICATION OF UNDERLYING MOLECULAR EFFECTS, A PILOT STUDY
828 SIOP ABSTRACTS

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Purpose:
Background: Genetic syndromes can be associated with an increased risk for tumor development. Previous studies in our center showed a significantly increased incidence of morphological abnormalities and high prevalence of syndromes in a cohort of 1,073 childhood cancer patients compared to 1,007 schoolchildren. Furthermore, we described four new statistically significant patterns of co-occurring morphological abnormalities indicating new tumor predisposition syndromes.

Purpose of Study: Further delineation of four new syndromes in childhood cancer patients and identification of their associated molecular genetic defects.

Method: In forty-nine patients previously designated as showing one of four new tumor predisposition syndromes morphological examination was redone, to investigate if the phenotypes in these candidates were consistent 5 to 9 years after the initial examination. 3D analysis of facial morphology was performed. Karyotyping was done to identify balanced translocations. Copy number variation (CNV) analysis for detecting microdeletions and –duplications was performed using SNP array on genomic DNA. FISH and Q-PCR was performed in order to validate the events identified in cytogenetic and CNV analysis.

Results: The new syndromes were confirmed in 45 patients (92%). In 3D analysis, facial differences between patients and controls were colour coded. Facial features were quantified using anatomical landmarks. Cytogenetic analysis showed an inversion on chromosome 15(q25–q26.2). Currently, the proximal and distal breaking points are being characterized using FISH. CNV analysis revealed 155 copy number variation events, of which 76 gains (duplications) and 79 losses (deletions). We defined a set of distinct event characteristics to come to a selection of 16 events eligible for validation experiments using BAC-FISH and Q-PCR.

Conclusion: The phenotypes in the new tumor predisposition syndrome candidates were consistent. 3D photography is a suitable technique to objectify facial features. Cytogenetic analysis showed an inversion in one patient. CNV analysis revealed 16 events, for which validation experiments are pending.

O149

IMMUNOTHERAPY OF RECURRENT OR RESISTANT HIGH-GRADE PEDIATRIC GLIOMAS USING REPETITIVE INTRATHECAL INJECTIONS OF ALLOGENIC FAMILIAL DONOR IMMUNOCOMPETENT CELLS IN COMBINATION WITH DENDRITIC VACCINES.

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Purpose: Basing on preclinical data we hypothesized that repeat i.t. injections of allogeneic lymphocytes with KIR receptor disparity across blood brain barrier may potentially provide antitumor effect in poor prognosis high-grade gliomas.

Method: Eight pts with a median age of 6.8 (1–19) years (glioblastoma GB) - 3, anaplastic astrocytoma (AA)-3 and diffuse brainstem glioma-2 were enrolled in this protocol since 2006. All pts have been previously treated with at least 2nd line of CT and RT. Median interval to relapse was 3 (1–7) mo. Disease status was: PD-1, 1st relapse-2, 2nd relapse-4 and 3rd-1 pt. Protocol included collection of immunocompetent cells (IC) from familial donors (HLA disparity were 3/6 in 7 and 1/2

6 in 1 pt) for i.t. therapy. Leukapheresis product was proceeded in order to get 20 doses of cells. Dendritic vaccines (DC) were prepared using pt’s dendritic cells and tumor cells obtained during surgery. Pts scheduled to receive 18 i.t. injections of donor IC and 15 DC during 1st year of treatment. In case of positive response treatment was continued for the next 12 mo.

Results: Pts received a median number of 19 (2–40) IC with a median number of 2.2 (1.6–3.5) CD16/56 and 10.3 (4.2–22) CD3x108/injection and 16 doses of (2–30) DC. Five pts progressed under treatment in 1 to 3 mo (median 5 IC, 5 DC). Three pts (2 AA, 1 resistant GB in 3rd relapse) completed protocol (median 26 IC and 21 DC). We observed a tumor reduction in up to 40% and disappearance of seizures 3–4 mo after treatment start. All 3 pts are alive without disease progression 29, 33 and 46 mo after the beginning and 2, 9 and 19 mo after the end of therapy.

Conclusion: We can speculate that both cytotoxic T-cells and NK cells can potentially provide an antitumor effect.

O150

CHILDHOOD DIFFUSE BRAIN STEM TUMORS. RISK FACTORS OTHER THAN HISTOLOGY

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Purpose: Despite progress in pediatric neurooncology treatment results of brainstem tumors remain poor, with diffuse tumors having the worst prognosis. The most common tumors in this site are gliomas. Localization and infiltrating character of these tumors often enable to perform biopsy without risk of complications so as a result more than half of these patients are treated without pathological diagnosis. The aim of our study was to: define prognostic factors other than tumor histology in diffuse brainstem tumors, characterize risk groups and establish risk based treatment.

Method: Retrospective analysis of 107 medical records of children with brainstem tumors treated with radiotherapy alone or pre-irradiation chemotherapy, radiotherapy and maintenance chemotherapy was performed. Statistical analysis of: gender, age, symptoms and it’s duration, MRI tumor images (size, contrast enhancement, intra or peritumoral cysts), chemotherapy, radiotherapy, response to treatment and it’s influence on 1 and 5 year overall survival (OS) was performed. Risk groups were defined based on prognostic factors identified with Cox multivariate analysis.

Treatment based on risk groups is proposed.

Results: 1 and 5 yrs OS of patients with brainstem tumors was 54 and 16.7% respectively. Multivariate analysis showed that duration of symptoms, fully expressed brainstem syndrome, type of contrast enhancement and response to pre-irradiation chemotherapy statistically influenced outcome. Low intermediate and high risk groups were identified with 5 years OS – 76%, 14.4% and 0% respectively.

Conclusion: Detailed description of proposed treatment strategies will be presented.

O151

10-YEAR EXPERIENCE OF HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS PERIPHERAL STEM CELL TRANSPLANTATION ADMINISTRATION IN CHILDREN WITH MEDULLOBLASTOMA

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Purpose: We evaluated the usefulness of a treatment regimen that included high-dose chemotherapy with autologous stem-cell rescue in patients with newly diagnosed medulloblastoma.

Method: 103 untreated children with morphologically verified diagnosis of medulloblastoma, both standard and high risk groups, received treatment including: 4 courses of chemotherapy (Vincristin 1.5 mg/m2 d, VP-16 100 – ß-OH/C223–1–3 d, Cyclophosphamid 1000 – ß-OH/C4–2–3 d, Carboplatin 500 – ß-OH/C223–1 d or Cisplatin 100 – ß-OH/C223–1 d). Then standard risk patients received craniospinal radiotherapy. Patients of high risk group were given high dose chemotherapy with autologous peripheral stem cell transplantation followed by craniospinal radiotherapy.
Children under 4 years of age were administered high dose chemotherapy with autologous peripheral stem cell transplantation without radiotherapy.

**Results:** Children of standard risk group have reached 10-year EFS 0.84, 40,08, respectively, (p < 0.041). 10-year EFS was 0.64, 15 in children under 4 years of age. Toxicity of the protocol was tolerable.

**Conclusion:** Introduction of this treatment modality provides rather high efficacy against disease recurrence in the standard and high risk group patients.

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**O152**

TREATMENT OF PEDIATRIC GLIOMAS WITH IRINOTECAN AND CISPLATIN

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**Purpose:** After a pilot-study suggesting that Irinotecan/Cisplatin (IC) may be effective for pediatric spinal-cord Astrocytomas (Mora et al, Neuro-Oncol-2007), we initiated a phase-II trial for pediatric-High-risk gliomas, with the aim of assess IC safety and efficacy.

**Method:** Pediatric-patients without prior IC and high-risk (HR) gliomas (cohort-1 = HGG, cohort-2 = DIPG, cohort-3 = HR-low-grade-glioma) were eligible for this Phase-II trial. Therapy consisted of 8-weekly-iv-cycles of C(30 mg/m²) and I (50 mg/m²).

**Results:** Since 2003, 55 patients received this outpatient-based-regimen, aged 3m 16y (median 6,9 y). For 18 patients (pt) (8-DIPG, 10-OPG, 1 spinal NF1) no biopsy was performed. The distribution among treatment cohorts was: HGG 16 pt, HR-LGG 31 pt (10 without biopsy) and DIPG 8 pt patients. At this time, 12 patients have died of disease (10 HGG or DIPG). Objective response using conventional radiological/ophthalmological measurements were found in 8 patients (1-HGG, 7-LGG). SD in 29, PD in 12. 5 non-evaluable, one-still on treatment. OS/PFS for each cohort group is: HGG: 60%/70%, DIPG-OS = 12.5%, HR-LGG = 94%/90%, median follow-up 116 m(3-93m). No grade 3–4-toxicities were observed, vomiting being the most common side effect, easily controlled. All but DIPG or relapsed-HGG patients completed the protocol, with no documented otoxic, renal, or GI side effects on follow-up. Radiation was avoided in all HR-LGG patients.

**Conclusion:** The IC regimen is well tolerated and allows outpatient treatment of HR-gliomas. Objective clinical or radiological responses show clinical benefit in 78% of cases. Further studies are ongoing using MRI/volumetric/DTI-analysis, tumor–metabolic-changes (Methionine-PET), and biological profiling (MGMT-promoter-methylation/MSI1/) to better define IC response.

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**O153**

METRONOMIC ANTIANGIOGENIC THERAPY IN CHILDREN WITH RECURRENT BRAIN TUMORS OF DIFFERENT HISTOLOGIES

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**Purpose:** Patients with relapsed malignant brain tumors have a poor prognosis despite intensive treatment including high-dose chemotherapy with stem cell rescue. We report on our experience with an antiangiogenic metronomic chemotherapy for patients with recurrent CNS tumors of different histologies.

**Method:** 22 patients (median age: 11 years; range: 2-24) with recurrent brain tumors (medulloblastoma n = 6, CNS PNET n = 3, pilocytoma n = 1, ATRT n = 1, CNS germ cell tumor n = 2, pilocytic astrocytoma n = 1, pilomyxoid astrocytoma n = 1, malignant peripheral nerve sheath tumor (MPNST) n = 2, anaplastic ependymoma n = 2, choroid plexus carcinoma n = 1, spinal epithelioid sarcoma n = 1, and meningioma n = 1) received daily oral thalidomide 3 mg/kg, twice daily oral celecoxib 100-400mg, daily oral fenofibrate 70 mg/m², and alternating 21-day cycles of daily oral etoposide 10–50 mg/m² and cyclophosphamide 0.5–2.5 mg/kg, augmented with biweekly intravenous bevacizumab 10 mg/kg plus/minus intrathecal chemotherapy.

**Results:** OS at 6 months was 94.7 ± 5.1%, and PFS 81.8 ± 8.2%. OS at 12 months was 83.6 ± 8.7% and PFS 72.2 ± 9.7%. OS at 24 months was 83.6 ± 8.7% and PFS 56.1 ± 12.5%. Overall, therapy was well tolerated. No intratumoral hemorrhage occurred in any of the patients. Side effects included lymphopenia in 2022 patients, severe pneumonia in 7/22 patients, peripheral neuropathy requiring dose reduction of thalidomide in 7/22 patients, proteinuria in 4/22 patients, venous thrombosis in 2/22 patients, bradycardia in 2/22 patients, hypertonia grade III in 1/22 patients, necessity of immunoglobulin substitution in 5/22 patients and new onset hypothyroidism in 1/12 patients. Quality of life was considered better by all patients compared to prior conventional chemotherapy.

**Conclusion:** Antiangiogenic metronomic chemotherapy has clinical activity in recurrent malignant brain tumors and may present a promising therapeutic option for heavily pretreated patients.

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**O154**

OUTCOME IN PROGRESSIVE HIGH GRADE GLIOM (HGG) TREATED WITH COMBINATION OF BEVACIZUMAB AND IRINOTECAN

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**Purpose:** Recurrent HGG in children have a dismal prognosis with minimal improvements in survival seen following currently available salvage therapy. Method: We evaluated prospectively the results of treatment 22 patients (pts) with progressive HGG, who enrolled in the study from February 2008 till October 2009. Age 12.5 yrs (range – 5.7 – 17 yrs). Resection of the tumor followed by RT with parallel Temozolomide and monochemotherapy of Temozolomide was the first standard scheme of treatment. Relapse was detected by CT/MR/PET. Median of follow-up until PD was 6 months (range – 2 – 17 mths). In 19 pts (86.3%) the glioblastoma (GB) was histologically verified, in 3 pts (13.7%) – anaplastic astrocytoma (AA). All pts received 6-weeks cycles of combined therapy: Bevacizumab 5 mg/kg i.v. 1, 15 and 29 days + Irinotecan 125 mg/m² in (pts receiving anticovulant – 340 mg/m²/ d) 1, 8, 22, 29 days. Median of follow up was 6 mths (range – 1–18 mths). Median of number of cycles for patient was 3 (range 1–10).

**Results:** CR and PR observed in 10 pts (45.5%), SD in 6 pts, PD also in 6 pts (27.3%). 6-months PFS/OS in all pts with HGG was 0,40;0,60, 12-months – 0,19;0,24, 18-months – 0,10;0,24 respectively. For the analyzed moment 9 pts are still alive (40,9%), 13 – died (59,1%); 1 pt with CR died in remission in 1.5 month after finishing therapy from leukoencephalopathy. In pts with GB 18-months PFS/OS was 0,11;0,28. Objective response observed in 15 pts (78,9%), PD – in 4 pts (21,1%). Median of OS/PFS was 10 and 5 mths. In 3 pts with AA PD observed in all 3 pts, 7-months PFS and 12-months OS were 0. Median of OS/PFS was 10 and 7 mths.

**Conclusion:** In relapsed GB pts Bevacizumab in combination with Irinotecan is an effective strategy. PFS in this group is higher than in pts with AA.

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**O155**

TRANSITIONING TO EVERYDAY LIFE: ADOLESCENT LEUKEMIA PATIENTS LIVED EXPERIENCE, A PILOTSTUDY GENERATING IMPLICATIONS FOR NURSING CARE IN AN OUT PATIENT CLINIC

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Purpose: The purpose of this study is to examine what kind of care the adolescent leukemia patient might need subsequent to treatment for leukemia in an outpatient clinic. In the survey six seventeen to twenty-one year old patients are asked about their experience with returning to everyday life and how they cope with being a survivor after a long treatment for a serious disease.

Method: The methodology is chosen from a phenomenological, hermeneutical frame of reference, and the method is a semistructured email interview. The data is analyzed based on Steinar Kvæle’s, professor of Aarhus University, idea of hermeneutical interpretation.

Conclusion: The adolescents need a network to support them when returning to a normal life. They need support in coping with the concerns and the emotional strain the treatment can create in the subsequent period, in a way that is adapted to adolescents’ personal development. Finally the adolescents wish to be met in the oncology outpatient clinic with the special needs adolescents have.
SIOP ABSTRACTS 831

PEDIATRIC OSTEOSARCOMA IN LOW-INCOME COUNTRIES (LIC): EXPERIENCE OF THE CENTRAL AMERICAN ASSOCIATION OF PEDIATRIC HEMATOLOGY-ONCOLOGY (AHOPCA)

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Purpose: In 1998 the Central American Association of Pediatric Hemato-Oncology (AHOPCA) was created with the participation of specialists from five Central American nations (Guatemala, Honduras, El Salvador, Nicaragua and Costa Rica). A study was developed to evaluate the feasibility to provide a multicenter collaborative treatment protocol for children with osteosarcoma.

Method: Patients aged 0–18 years with newly diagnosed osteosarcoma of the extremities were included. Treatment consisted of three alternating cycles of presurgical chemotherapy with doxorubicin/cisplatin and ifosfamide/etoposide, followed by amputation on week 9. Post surgical treatment consisted of 5 additional alternating cycles of chemotherapy.

Results: A total of 154 cases of osteosarcoma (50 males) were diagnosed from January 1999 through June 2007. A total of 110 patients met the eligibility criteria. Median age at diagnosis was 13 years (6–17 yrs). Metastatic disease was present in 29% of patients. Abandonment rate or early interruption of treatment occurred 23% of the patients.

The 3-yr overall survival estimates considering abandonment as event or censored were 32% ± 5% and 47% ± 7% respectively. Three year EFS considering abandonment as event was 29% ± 5 and 41% ± 6 with abandonment censored.

Conclusion: Although the prognosis for patients with nonmetastatic osteosarcoma has improved considerably in developed countries, in LIC the treatment of osteosarcoma represents a major challenge. The advanced stages in which patients are diagnosed, with large tumors, and high percentage of metastatic disease, along with a high rate of abandonment of therapy due to refusal of amputation represent important causes of treatment failure. The results of the first collaborative treatment protocol in Central America demonstrate the need to implement early diagnosis strategies and twinning programs with centers in developed nations to promote training and develop regional limb salvage programs, as a strategy to reduce abandonment of therapy and improve outcomes.

O162

ACCRUENT PREDICTION OF CHEMOTHERAPY RESPONSE IN Ewing’s SARCOMA BY (18)F-FUORODEOXY-D-GLUCOSE POSTERION EMISSION TOMOGRAPHY (FDG-PET).

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Purpose: The prevalence of submicroscopic bone marrow (BM) minimal disseminated disease (MDD) at diagnosis and its clinical significance in Ewing Sarcoma patients treated at SCMC was retrospectively analyzed.

Method: Multiparameter flow cytometry (MPPC) was used for the evaluation of minimal disease involvement in bone marrow samples of 46 Ewing Sarcoma patients at diagnosis. CD99+/CD90+CD45- cells differentiate malignant cells from normal hematopoietic progenitors defined by CD3/14/16/19/45. In addition CD56 (a neuroectodermal marker) was evaluated on the CD99+/CD90+/CD45- cell population.

Results: The sensitivity of the method was evaluated by spiking of known quantities of MHHES ES cell line into control normal peripheral blood mononuclear cells. Sensitivity and specificity were 1 in 100,000 cells. The Ewing sarcoma markers CD99/CD90 and CD56 were defined positive at a cut point of above 0.003% and 21%, respectively. We retrospectively analyzed bone marrow samples of 46 Ewing sarcoma patients: 11 with metastatic disease and 35 with localized disease at diagnosis, median age was 15.8 years. There were no statistical differences in the overall and event free survival (OS, EFS respectively) between patients with either positive or negative MDD (CD99+/CD90+CD45- cells) at diagnosis. CD56 was evaluated on the CD99+/CD90+/CD45- cells in BM samples of 38/46 Ewing sarcoma patients. Overall survival was better for patients with CD56 positive cells below the cutoff (21%) having 5y OS of 100% vs. 74% in patients with CD56+ cells above the cutoff, (p < 0.05). The 5y EFS was 87% Vs. 50% in patients with CD56+/CD99+/CD45- and CD56-CD99+/CD45- respectively (p < 0.05).

Conclusion: Multiparameter flow cytometry is a rapid, feasible and sensitive method for detection of Ewing sarcoma cells in BM. We could show for the first time that the presence of CD56 positive cells above the threshold in the BM significantly correlated with worse prognosis.
Purpose: Response to neoadjuvant chemotherapy is a significant prognostic factor for the Ewing sarcoma (ESFTs). FDG-PET is a noninvasive imaging modality that accurately predicts histopathologic response. To determine its predictive value in ESFTs, we reviewed the Tata Memorial Hospital experience.

Method: 58 patients with osseous ESFT were evaluated by FDG-PET. All patients received standard neoadjuvant chemotherapy. FDG PET standard uptake values before (SUV1) and after (SUV2) chemotherapy were correlated with chemotherapy response assessed by histopathology. Good FDG PET response was defined as SUV2 < 2.5 or SUV2:1 < or = 0.5. Data was also analyzed for patients with > 90% necrosis (favourable response), and < 90% necrosis (unfavourable response).

Results: The study included 58 patients (M:F:2:1; mean: 15.3 years) The site of primary disease was axial in 18 patients and appendicular in 40 patients. The mean SUV 1 in subset A (necrosis > 90%) was 5.60 (range 2.2–17) and in subset B (necrosis < 90%) was 6.06 (range 2–14.9). The mean reduction in SUV was 92.2% in subset A, while it was 62.4% in subset B (P < 0.05). Both SUV2 and the ratio of SUV2 to SUV1 (SUV2:SUV1) significantly correlated with histologic response (P = 0.01 for both comparisons). FDG PET response by SUV2 or SUV2:1 was discordant with histologic response in 85% and 88% of patients, respectively.

Conclusion: FDG PET evaluation of Ewing’s sarcoma demonstrates significant alteration in response to neoadjuvant chemotherapy with higher SUV reduction in patients with favourable response. SUV2 and SUV2:SUV1 ratio correlates with histopathologic response and potentially could be used as a noninvasive surrogate to predict response in Ewing’s sarcoma.

O163

**ADOLESCENT’S EATING EXPERIENCES DURING BONE MARROW TRANSPLANT RECOVERY**

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Purpose: High dose chemotherapy and total body irradiation required before bone marrow transplantation (BMT) can cause severe gastrointestinal (GI) side effects that can result in poor oral intake and inadequate nutrition. The GI symptoms and interventions to improve nutrition during BMT hospitalization have been well identified; however, there is limited information of ongoing issues beyond the hospitalization. Symptom experiences and management strategies need long term investigation. This study allowed adolescents an opportunity to share eating experiences and eating strategies in their own words during the first 100 days post BMT.

Method: An interpretive phenomenological design was used for the study, guided by Martin Heidegger’s philosophical underpinnings. Information was obtained from individual interviews at 50 days and 100 days post BMT among 13 adolescents using a purposeful sampling method. Limitations of the study included single institution sampling and interviewing only the adolescents. Data were analyzed using the hermeneutic method, and rigor of the study was supported by establishing credibility, dependability, and confirmability.

Results: Five themes were derived from the interviews. Adolescents discussed a slow return of eating: “It Just Takes Awhile”, barriers that affected their eating: “Every Time I Eat, Something Goes Wrong”, personal eating strategies: “Working Your Way Up”, a return to normalization: “Getting Back to Normal”, and supportive advice to others: “Just Don’t Worry”.

Conclusion: Nurses need to have an awareness of eating issues throughout BMT recovery. Eating strategies and the fact that eating provided a return of normalization should be shared with other BMT patients to provide encouragement during recovery. With information from this study, nurses can educate future patients about potential eating issues and recommend eating strategies that will allow patients to make effective choices to enhance their eating.

O164

**PARENTS AND CARERS PERSPECTIVES OF NUTRITIONAL CONCERNS DURING THEIR CHILD’S TREATMENT FOR CANCER**

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Purpose: It is reported that up to 48% of children will experience the problem of weight loss as a consequence of reduced oral intake while receiving treatment for cancer. There is a paucity of studies exploring parental worries, concerns and informational needs from the perspective of parents. In order to empower parents to manage more effectively their child’s nutritional needs, it is crucial from the outset of treatment that the needs of parents are assessed, identified, explored and addressed.

Identifying parent’s perspectives of the nutritional challenges faced whilst their child receives chemotherapy can help to identify and implement appropriate intervention strategies. The aims of this study were: to identify parental concerns and problems regarding nutritional management; describe parents informational needs including specific information they would like to receive; investigate how beneficial parents found the information they received; identify the most suitable person to supply nutritional information.

Method: This qualitative study employed a grounded theory approach, utilising focus groups for data collection. A total of 9 parents were recruited into 3 focus groups. Parents were recruited based on their experience of dealing with nutritional challenges. Focus groups were recorded and transcribed verbatim.

Results: Four main themes emerged that were connected by significant subcategories: information needs- general concerns; parental worries- general concerns and maintaining child’s physical well being; consequence of treatment; change to treatment patterns. A common theme to all focus groups related to a lack of teaching and information being offered regarding the management of treatment related side effects and also parents need to have a nutritional talk.

Conclusion: Health care professionals who educate parents regarding nutritional concerns need to develop and utilise a variety of approaches to meet parent’s needs. A lack of written information and a nutritional talk were key themes in this study and should be the primary focus of educational materials.

O165

**DEVELOPING A CONSENSUS DOCUMENT TO ADDRESS THE NUTRITIONAL NEEDS OF PAEDIATRIC ONCOLOGY PATIENTS**

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Purpose: Good nutritional intake is vital for the child undergoing treatment for cancer as inadequate nutrition can lead to reduced tolerance of treatment, potential infectious complications and a potential poorer outcome. A survey of nutritional practice in the Children’s Cancer and Leukaemia Centres in the United Kingdom showed an inconsistent approach to both nutritional support and advice given to children and their families. Following this survey it was felt that a document looking at nutritional assessment and support would be beneficial to practice.

Method: A multidisciplinary team of nurses, dieticians and doctors met together with the aim of developing a consensus document to address the nutritional needs of paediatric oncology patients. Any available evidence to support practice was considered and included in the document. A draft was developed and distributed to a wider group of professionals for review.

Results: Following review the following issues were included in the final document: importance of nutrition, organisational issues, hospital food provision and management of nutrition.

Conclusion: A document has been established to address the nutritional needs of children with cancer which is available for all the Children’s Cancer and leukaemia centres. It has however highlighted several areas where there is lack of evidence and research to support nutritional assessment and support where further work will be required in the future. There will also be a need to re-survey nutritional practice to look at the impact the document has had in the future.

O166

**LATE RECURRENT OF CHILDHOOD T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA FREQUENTLY REPRESENTS A SECOND LEUKEMIA RATHER THAN A RELAPSE: FIRST EVIDENCE FOR GENETIC PREDISPOSITION**

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Purpose: The current study reports the case of a 15-year-old boy suffering from T-cell acute lymphoblastic leukemia (T-ALL) who presented with a late recurrence of his disease, which was very difficult to treat. The blasts were immunophenotypically similar to the patient’s previous lymphoblastic neoplastic disease. However, the cytogenetic analysis revealed four aberrations that were not present in the primary leukemia. These aberrations were two sets of trisomy 8, 15 and 20, and a deletion of 20q11.21-q13.1. The patient was treated with chemotherapy and immunotherapy. The patient received 8 cycles of carboplatin, vincristine, dexamethasone, cytarbazine, high-dose methylprednisolone, and rituximab and received a bone marrow transplant. The patient was in remission for 21 months. He is alive with disease but still in remission.

Conclusion: The patient presented with a late recurrence of his disease, which was very difficult to treat. The blasts were immunophenotypically similar to the patient’s previous lymphoblastic neoplastic disease. However, the cytogenetic analysis revealed four aberrations that were not present in the primary leukemia. These aberrations were two sets of trisomy 8, 15 and 20, and a deletion of 20q11.21-q13.1. The patient was treated with chemotherapy and immunotherapy. The patient received 8 cycles of carboplatin, vincristine, dexamethasone, cytarbazine, high-dose methylprednisolone, and rituximab and received a bone marrow transplant. The patient was in remission for 21 months. He is alive with disease but still in remission.

References:


Of discordant twin set 1, the patient was treated on the EPhA1 protocol, inclusive of imatinib mesylate. She was a Slow Early Responder (SER) and had high MRD at the end of induction. She received an allogeneic stem cell transplant, but unfortunately relapsed 6 months later and died of progressive disease. SNP array analysis demonstrated deletion of IKAROS, CDKN2A, and PAX5. The healthy co-twin had, in blood, a BCR-ABL1 positive clone (at ~10^-4) lacking IKAROS deletion. Blood spots of the two twins shared the same BCR-ABL1 genomic sequence.

Conclusion: This data indicates prenatal origin of BCR-ABL1 fusion and subsequent - presumed post-natal - loss of IKAROS and is compatible with the notion that the malignancy and poor outcome of Ph+ p190 BCR-ABL1 ALL is driven in some measure by IKAROS deletion.

O168

BREAKPOINTS OF BTG1 DELETIONS IN PEDIATRIC PRECURSOR-B ACUTE LYMPHOBLASTIC LEUKEMIA CLUSTER TIGHTLY AND GIVE RISE TO A TRUNCATED BTG1 PROTEIN

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Purpose: Recent genomic profiling studies by our group and others have revealed that pediatric precursor B-cell acute lymphoblastic leukemias (ALLs) exhibit recurrent micro-deletions encompassing genes acting in cell cycle regulation (CDKN2A), B-cell differentiation (PAX5, EBF1, IKZF1) and growth arrest (BTG1).

Method: To gain insight into the role of BTG1 in leukemogenesis, we have studied the occurrence and nature of BTG1 deletions in ALL using both targeted and whole genome profiling assays.

Results: Through a locus-specific MLPA procedure, 26 novel micro-deletions were detected in an unselected cohort of 305 precursor B-ALLs (8.5%). High resolution genome-wide copy number and homozygosity profiling of 22 BTG1 deletion-positive samples revealed that concurrent deletions in IKZF1 and CDKN2A were particularly frequent in these cases. All BTG1 deletions were focal in nature, varying in size from 104 kb to 1.4 Mb. Quantitative PCR-mediated fine mapping and sequencing of the deletion boundaries revealed that all telomeric breakpoints cluster in exon 2 of the BTG1 gene, leaving the promoter and exon 1 intact. At the centromeric side of the deletions, four distinct breakpoint clusters could be identified. As a consequence, all deletions appear to result in the expression of truncated BTG1 proteins.

Conclusion: In conclusion, our data indicate that BTG1 deletions represent a frequent and highly uniform abnormality in precursor B-ALL. Expression of the truncated protein may result in loss or gain-of-function or dominant-negative effects. These alternative scenarios are currently under investigation.

O169

COMBINED USE OF MINIMAL RESIDUAL DISEASE CLASSIFICATION AND IKZF1 MUTATION STATUS GREATLY IMPROVES RELAPSE PREDICTION IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: The pathogenesis of childhood Acute Lymphoblastic Leukemia (ALL) is presumed to follow a 2-hit model. The transcription factor IKAROS (IKZF1) is deleted in the majority of BCR-ABL1 ALL. This suggests that loss of IKAROS function is an important event in the development of BCR-ABL1 ALL. The sequence of cooperating oncogenic events in BCR-ABL1 ALL is currently unknown.

Method: We performed extensive genomic analysis of two pairs of monozygotic, monochorionic twins, one pair discordant the other discordant for Ph+ - ALL.

Results: The discordant twins received identical treatment (AIEOP-BFM ALL 2000) but followed a different clinical course. Twin 1 was a good prednisone responder and followed a different clinical course. Twin 2. BCR-ABL1 fusion breakpoint sequence was shared between the discordant twins.
Purpose: Despite major improvements in treatment over the last decades, relapses still occur in more than 20% of patients with pediatric acute lymphoblastic leukemia, of whom a major proportion is treated in non-high-risk-stratified subgroups. To improve risk stratification, we have retrospectively analyzed the prognostic value of minimal residual disease (MRD) and IKZF1 mutation status in an uniformly treated cohort of 131 patients enrolled in the dexamethasone-based Dutch Childhood Oncology Group treatment protocol ALL9.

Method: MRD levels were determined at 42 and 84 days after treatment initiation using PCR-based detection of Ig/TCR rearrangements. Patients were classified as MRD-Low (MRD negative at both time points), MRD-High (MRD $>5x10^{-4}$ at second time point) or MRD-Medium (all other patients). IKZF1 mutation status at diagnosis was determined using multiplex ligation-dependent probe amplification and genomic sequencing.

Results: Both MRD classification and IKZF1 mutation status were associated with relapse and were strong independent prognostic markers for relapse free survival (RFS), both in the entire cohort as well as in the high-risk and non-high-risk treatment arms separately. Whereas the good RFS rates of MRD-Low patients (98%) and poor RFS rates of MRD-High patients (31%) were independent of IKZF1 mutation status, this latter marker was strongly associated with poor RFS rates in the large MRD-Medium group (8-year RFS IKZF1 WT 96% versus IKZF1 DEL 36%, P < 0.001). MRD/IKZF1-based stratification correctly predicted 14 of 18 (78%) relapses with a specificity of 92%.

Conclusion: In conclusion, both MRD and IKZF1 status show a strong prognostic value in a group of uniformly treated patients. More importantly, both factors supplement each other and can identify patients at risk of relapse development with high sensitivity and specificity. Consequently, the combined use of MRD classification and IKZF1 deletion status has a high potential for future risk stratification.

ABSENCE OF BIALLELIC TCR$\gamma$-LOCUS DELETIONS PREDICTS EARLY TREATMENT FAILURE IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: Despite remarkable advances in the treatment of T-cell acute lymphoblastic leukemia (T-ALL), four to ten percent of patients fail to respond to initial induction therapy and do not achieve complete remission. Patients who fail induction are currently indistinguishable from the majority of patients at diagnosis, and the purpose of this study was to identify them based on DNA copy number analysis of leukemia samples obtained at diagnosis, at a time when major treatment changes can be instituted.

Method: Array comparative genomic hybridization (CGH) was performed on genomic DNA extracted from diagnostic lymphoblasts from 47 children with T-ALL treated on Children’s Oncology Group Study P9404 or Dana-Farber Cancer Institute Protocol 00-01. These samples represented 9 patients who failed to achieve an initial complete remission, 13 who relapsed, and 25 who became long-term event-free survivors. The findings were confirmed in an independent cohort of patients by quantitative DNA-PCR, an assay that is well-suited for clinical application.

Results: Analysis of the CGH findings in induction failure cases compared with those in which induction chemotherapy was successful identified the absence of biallelic TCR$\gamma$-locus deletion (ABD), indicative of an early thymocyte precursor prior to VDJ recombination, as the most robust predictor of induction failure (P = 0.0002). This feature was also associated with markedly inferior event-free and overall survival rates (P = 0.002 and P = 0.0002, respectively). Using a rapid and inexpensive quantitative DNA PCR assay, we validated ABD as a predictor of a poor response to induction chemotherapy in an independent series of cases.

Conclusion: Lymphoblasts from children with T-ALL should be evaluated at diagnosis for deletion within the TCR$\gamma$ locus. Patients lacking biallelic deletion, which confers a very high probability of induction failure with contemporary therapy, should be assigned to alternative therapy in the context of a prospective clinical trial.

DETECTION OF MINIMAL RESIDUAL DISEASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED ACCORDING TO THE ALL IC-BFM-2002 PROTOCOL

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Purpose: Although the enormous progress in the therapy of acute lymphoblastic leukemia (ALL) has been made, still around 15% of children will eventually relapse. Hence, new and more precise outcome indicators are needed in order to improve outcome of those group of patient. Sequential monitoring of MRD (minimal residual disease) in a set time points during induction therapy in ALL proves to be a powerful and independent indicator of treatment outcome. Thus, we aim to define prognostically relevant measurement time points and crucial level of MRD, that the best estimate the hazard of treatment failure. We also assess correlation between level of MRD in bone marrow (BM) and peripheral blood (PB), and relation between MRD and standard risk factors.

Method: From May 2005 to January 2008 among 78 patients with ALL treated in Oncology/Hematology Department, Children’s University Hospital according to ALL-IC-BFM-2002 protocol, 68 were enrolled in minimal residual disease study. 50 patients were eligible for evaluation (32 boys and 18 girls; 42 common B-ALL, 2 pro-B-ALL, 6 T-ALL). For MRD detection 4-colour flow cytometry was used.

Results: Positive level of MRD (< 0.01%) at all time points of the study in BM and PB was prognostically important. However the most important for the prognosis was level of MRD at day 15 in PB and at day 78 in BM. Children with MRD level at day 15 > 0.1% in PB or at day 78 higher than 0.008% were at highest risk of treatment failure. We also have shown statistically important correlation between presence of gene BCR/ABL and high level of MRD (p = 0.023).

Conclusion: Our results show that detection of MRD is strongly associated with relapse, and limited panel of antibodies used in the study allows defining leukemic phenotypes and monitoring levels of MRD at set time points.

SKELETAL MUSCLE PRECURSOR CELLS SERVE AS A CANCER CELL-OF-ORIGIN IN A NEW, KRAS-DRIVEN IN VIVO MODEL OF EMBRYONAL Rhabdomyosarcoma

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Purpose: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children and adolescents, but its developmental origin has remained unclear. Given that RMS morphologically resembles an aberrant stage of normal skeletal muscle development, it has been proposed that RMS arises as a consequence of dysregulation of muscle growth and maintenance which, in normal skeletal muscle, is mediated by muscle satellite cells. In order to investigate the cellular origins of RMS, we have developed a new mouse model of embryonal RMS based on the ex vivo genetic manipulation of freshly isolated mouse muscle satellite cells.

Method: Satellite cells represent a heterogeneous pool of cells retained beneath the basal lamina of mature muscle fibers. We have isolated distinct subsets of satellite cells, including the subpopulation of highly myogenic skeletal muscle precursor cells,
from CKN2A-/- mice using combinatorial analyses of multiple cell surface markers and fluorescence-activated cell sorting (FACS). The isolated cells were transduced with kras(G12v) in a lentiviral vector and orthotopically seeded into the extremity muscles of NOD/SCID mice within 48 hours after cell isolation.

Results: Kras(G12v)-infected CDKN2A-/- skeletal muscle precursor cells gave rise to tumors with short latency (19–71 days), and the tumors could be propagated in secondary recipients with high efficiency. We show that these engineered sarcomas resemble human embryonal RMS and express myogenic markers, such as MyoD and Myogenin.

Conclusion: Our data establish that genetic alterations introduced specifically into mouse muscle satellite cells can give rise to embryonal RMS tumors, thereby providing strong evidence in support of a muscle origin of these tumors. Moreover, this new mouse model of RMS provides a powerful platform for future applications, aimed at preclinical drug discovery and testing.

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ARE WEIGHT/BMI AT DIAGNOSIS OR WEIGHT CHANGE ON THERAPY PREDICTIVE OF TOXICITY IN INTERMEDIATE RISK RHABDOMYOSARCOMA? CHILDREN'S ONCOLOGY GROUP REPORT

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Purpose: To determine the prevalence of weight loss, a known morbidity of cancer therapy, in intermediate risk rhabdomyosarcoma (IRMS) patients treated on COG protocol D9803 and to determine if an association exists between baseline weight/BMI and/or weight change early in therapy and number of grade 3/4 toxicities.

Method: 471 patients with IRMS age ≥2 and <21 years treated on D9803 had height, weight and toxicity information available. Separate regression models were used to determine if change from baseline at 12 and 24 weeks for four measures of weight/BMI (Percent weight change, BMI centile, BMI percent, and BMI z-score) predicted number of grade 3/4 toxicities, hospital days or infections per phase per patient at 24 and 42 weeks, respectively, after adjusting for race, risk stratum and baseline weight/BMI measurement.

Results: 33% and 37% of patients had >5% weight loss at 12 and 24 weeks, respectively, while 9% and 17% had >10% weight loss. No weight/BMI change parameters were predictive of number of hospital days, grade 3/4 toxicity or days hospitalized. Increased infection was demonstrated in overweight patients (BMI > 95 percentile) at week 12 (p = 0.03).

Conclusion: Although nearly 1 in 5 IRMS patients experienced >10% weight loss half way through therapy, we did not detect a significant increase in number of hospital days, grade 3/4 toxicities or infections in these patients after adjusting for race, risk stratum and baseline BMI. Similarly, baseline weight status did not predict outcome. Future studies might elucidate whether the extent/sverity of weight loss in IRMS patients is modifiable by aggressive nutritional intervention.

O174

RHABDOMYOSARCOMA IN ADOLESCENTS. A REPORT FROM THE AIEOP SOFT TISSUE SARCOMA COMMITTEE (STSC)

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Purpose: The progress in survival obtained in adolescents with cancer has been estimated inferior with respect to the improvement obtained in younger patients. Many factors contribute to these unsatisfactory results including tumor biology, psychological and social environment, pattern of referral, accrual in clinical trials.

Studies on the different tumors are limited we analyzed a population of adolescents with rhabdomyosarcoma (RMS) included in STSC trials from 1988 to 2005.

Method: 643 registered patients: 567 children (0–14 years old) and 76 adolescents (15–19 years old). Histology was centrally reviewed and data prospectively collected and reviewed for the purpose of this study.

Results: A median of 4 adolescents/year was registered (range 1–8). The observed/expected ratio was 0.27. The following differences were evident comparing adolescents to children: sex distribution: M/F = 2.3 vs. 1.4; interval from initial symptoms to diagnosis: 8.4 vs. 4.8 weeks; nodal infiltration: 39% vs. 23.3%; metastasis at diagnosis: 30.7% vs. 17.8%; tumor site: more GU non VP (36.8%), less orbit (2.6%) and other site (17%) in adolescents.

A similar number of patients in the two groups had tumor resection or received radiotherapy. No significant differences resulted in the 5-year progression free survival (PFS): 61.2% in children vs. 52.8% in adolescents (p = 0.1), with 67.9% and 67.0% in localized tumors.

On multivariate analysis tumor site, nodal involvement and presence of metastases resulted significant factors for both overall and PFS. Age (0–15 vs. 15–20) was significant for survival only.

Conclusion: The number of adolescents with RMS enrolled in Italian pediatric protocol is unsatisfactory. The results obtained in the registered patients appear satisfying, especially in patients with localized disease, and support the inclusion of adolescents in pediatric protocol, tailoring the treatment on tumor characteristics.

SIOPT ABSTRACTS 835
836 SIOP ABSTRACTS

Method: The overall study population consisted of 304 group III patients < 21 years treated between 1980 and 2005 with multi-modal therapy including chemotherapy (given to all but 9 patients), radiotherapy (given to 162 cases) and delayed surgery (performed in 146 cases).

Results: Synovial sarcoma (35%) and malignant peripheral nerve sheath tumor (MPNST) (23%) were the most frequent histotypes. Across all diagnoses, initial chemotherapy achieved a major response (RC or PR > 50%) in 41% and a minor response in a further 16% of cases. Overall Survival (OS) was 60.0% and 51% at 5 and 10 years, respectively. Univariate analysis for OS showed a relationship to patient age, histological subtype, tumor site, tumor size. MPNST was the tumor type with the worst chemotherapy response rate and the worst outcome (5year OS 31%). Multivariable Cox model analysis showed that survival was significantly better for those patients who had a major response to chemotherapy, and was strongly influenced by the extent of delayed surgical resection (complete > incomplete > no surgery) and the use of radiotherapy. Noteworthy, no any survival improvement was observed over the 25-year period.

Conclusion: In locally-advanced NRSTS patients, radiotherapy and delayed surgery are of crucial importance. Chemotherapy may have a relatively limited efficacy in term of response rate, but, when effective, it plays an important role in term of survival. Intensive multimodal treatment approaches as well as novel strategies are warranted in this group of patients.

O176 LOCALIZED RHABDOMYOSARCOMA IN CHILDREN: A COMPARISON BETWEEN ITALIAN SOFT TISSUE SARCOMA COMMITTEE (STSC) PROTOCOLS RMS 88 AND 96

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Purpose: In this study we analyzed the results obtained in the two most recent STSC protocols addressed to in patients with localized Rhabdomyosarcoma (RMS). Method: We analyzed the 5-year overall (OS) and progression free survival (PFS) obtained in 509 children less then 19 years old: 218 treated according to RMS88 [1.88 \(\pm\) 10.2005] and 291 according to RMS96 [1.96 – 10.2005]. The treatment has been modulated on the risk group (low, standard and high) assigned according to a new risk classification. OS and PFS were not significantly different in the two studies, being 78.5% and 67.6% in the RMS 96 and 73.8% and 65.6% in the RMS 88. Subgroup analysis showed an improvement in children with RMS located in orbit (PFS: 56.5% in RMS88 vs 84.8% in RMS96, p = 0.02) and limbs (PFS: 33.3% in RMS88 vs 53.1% in RMS96, p = 0.03). Unfortunately less satisfying results were evident in bladder-prostate RMS (PFS: 84.6% in RMS88 vs 64.3% in RMS96, p = 0.06). These results are mainly explained with differences in the aggressiveness of local treatment: in the RMS 96 study more children with orbit primary were irradiated but less children with bladder-prostate RMS received aggressive surgery.

Conclusion: No major differences in the outcome of patients are evident when the results of the two most recent STSC protocols are analyzed. The 78% OS obtained in the whole population of patients with localized RMS appear satisfactory.

O177 PROGNOSTIC FACTORS AFTER RELAPSE IN NON-METASTATIC Rhabdomyosarcoma: WHO CAN BE SALVAGED?

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Purpose: Previous studies suggest poor outcome in children with relapsed rhabdomyosarcoma. A better understanding is needed of which patients can be salvaged after first relapse. The purpose of this study was to determine which factors, known at the time of first relapse of localised rhabdomyosarcoma, predict outcome following relapse.

Method: The analysis included children enrolled in the SIOP MMT 84, 89 and 95 studies. Patients with relapsed rhabdomyosarcoma and embryonal sarcoma were included if they had localised disease at first presentation, achieved disease control with initial treatment and follow up data were available for at least 3 years from the time of the last event. The clinical features and initial treatment characteristics were correlated with survival in univariate and multivariate analyses.

Results: 474 eligible patients were identified for the study. At 3 years from the last event, 176 (37%) were alive (“cured”). In a full model multivariate analysis the factors identified at first relapse that mostly strongly associated with poor outcome were metastatic relapse (OR = 4.19 95%CI = 2.11–8.97), prior radiotherapy treatment (OR= 3.64 95%CI = 2.99–6.50), initial tumour size > 5cm (OR = 2.53 95%CI = 1.56–4.15) and time of relapse < 18 months from diagnosis (OR = 2.20 95%CI = 1.35–3.63). Un favourable primary disease site; nodal involvement at diagnosis; alveolar histology and previous 3 or 6-drug chemotherapy were also independently associated with poor outcome. A nomogram was developed, allowing for different weighting of these significant factors, in order to predict chance of cure for individual patients.

Conclusion: Some children with relapsed rhabdomyosarcoma remain curable. It is now possible to predict the chance of salvage for individual children in order to tailor therapy appropriately towards cure, use of experimental therapies and/or palliation.

O178 LIFE SATISFACTION IN ADULT SURVIVORS OF CANCER WITH ONSET DURING ADOLESCENCE

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Purpose: Previous studies revealed that the quality of life (QoL) of survivors of pediatric cancer is not negatively affected by the aftermath of the cancer experience. However, up to now no study systematically investigated the latter life satisfaction (LS). The aim of this study therefore was to determine the general and health-related LS of long-term survivors of adolescent cancer, to compare it to a community sample and to identify risk factors associated with an impaired satisfaction with life.

Method: LS of 820 Survivors (age M = 30.4 ± 6.0 years; time since diagnosis M = 13.7 ± 6.0 years) was assessed with the Questions on Life Satisfaction (FLZM) and compared to an age- and sex-matched community sample. The effects of medical, psychological and socio-demographical factors on the survivors’ general and health-related LS were investigated by means of multiple regression analyses.

Results: Survivors were significantly less satisfied than the comparison group in terms of both their general (p < .001; d = 0.35) and health-related (p < .001; d = 0.47) life. The largest discrepancy was revealed for ‘health’ as the most negatively affected part of the general LS (p < .001; d = 0.75). Somatic late-effects, symptoms of depression and anxiety, and less posttraumatic growth were associated with impaired general and health-related LS. Moreover, being married contributed significantly to a higher general LS.

Conclusion: Adult survivors of cancer with onset during adolescence are experiencing less LS than the general population. Psychological distress as well as somatic late effects and absence or only little posttraumatic growth increase the risk of an impaired satisfaction with life. Long-term routine-follow up visits are recommended to identify persisting psychological effects of cancer and provide support for those with special needs.

Acknowledgement of Funding: Funded by the Deutsche Krebshilfe e.V.

O179 POSTTRAUMATIC STRESS, DEPRESSION, AND ANXIETY AMONG ADULT LONG TER M SURVIVORS OF CANCER IN ADOLESCENCE

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Purpose: To determine the prevalence of posttraumatic stress, depression, and anxiety in adults who have survived cancer (≥5 years) diagnosed in adolescence, as compared to healthy controls.

Method: 820 survivors of cancer during adolescence (age M = 30.4 ± 6.0 years; M = 13.7 ± 6.0 years since diagnosis) and 1027 matched controls without history of cancer (age M = 31.5 ± 6.9 years) completed standardized questionnaires measuring posttraumatic stress, depression and anxiety. Additionally, sub-groups of 202 survivors and 140 controls with elevated scores received structured interviews to ascertain DSM-IV-diagnoses.

Results: 22.4% of the survivors reported clinically relevant symptoms of posttraumatic stress, anxiety, and/or depression compared to 14.0% of the controls (OR 1.77; 95% CI 1.39–2.26). The odds of posttraumatic stress symptoms in male (OR 3.92, 95% CI 1.80–8.51) and female (OR 3.83, 95% CI 2.54–5.76) survivors were more than twice those in the controls. However, only female survivors reported symptoms of depression and anxiety significantly more often (respectively: OR 2.12; 95% CI 1.16–3.85; and OR 1.86; 95% CI 1.33–2.59) than the controls. 24.3% of the survivors met DSM-IV criteria for at least one mental disorder compared to 15.3% of the controls.

Conclusion: Survivors of cancer during adolescence show an elevated risk of presenting symptoms of posttraumatic stress, anxiety and depression during adulthood which is also reflected in a greater number of DSM-IV diagnoses when compared to controls. Comprehensive follow-up assessments should include examination of possible psychological late effects of a cancer diagnosis in adolescence in order to identify survivors needing psychosocial interventions even years after completion of successful medical treatment.

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EMOTIONAL, BEHAVIORAL AND SCHOOL DIFFICULTIES FOR SIBLINGS OF CHILDREN WITH CANCER: A COMPARISON WITH MATCHED CLASSMATES

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Purpose: A recent literature review (Alderfer et al., in press) suggests that siblings of children with cancer are at risk for problems within two years of cancer diagnosis; current research evidence, however, is methodologically weak. This study provides a carefully controlled investigation of emotional, behavioral and school difficulties of siblings of children with cancer.

Method: Siblings (aged 8-15) of children diagnosed with cancer (M = 17 months post-diagnosis) were recruited along with comparison classmates matched on gender, ethnicity/race and age. Sixty-two children (31 siblings) completed measures of depression (Child Depression Inventory-Short Form) and anxiety (Revised Children’s Manifest Anxiety Scale) and their parents (one per child, 95% mothers) completed the Child Behavior Checklist. Directional paired t-tests were used to assess between-group differences.

Results: Compared to matched classmates, siblings of children with cancer reported more symptoms of depression (M’s = 50 vs. 45; t[30] = 2.24, p < .05) and anxiety (M’s = 52 vs. 47; t[30] = 2.79, p < .01). No comparison children fell into clinical ranges on these measures whereas 2 siblings (6.5%) did so for depression and four (13%) did so for anxiety. Parents of siblings reported more emotional and behavioral problems for their children than did the parents of classmates (Total Problems: M’s = 52 vs. 48; t[30] = 1.98, p < .05) including greater anxiety/depression, withdrawal/depression, somatic complaints, thought problems, rule breaking and attention problems (p’s < .05). Eight siblings (26%) versus one comparison child (3%) fell into the clinical range for Total Problems. The difference between groups on Total Social Competence yielded a trend toward significance (M’s = 48 vs. 52; t[30] = 1.41, p < .09). Significant differences were noted in school performance (p < .05).

Conclusion: Siblings of children diagnosed with cancer within the past two years experience poorer parent-reported school performance and more symptoms of depression, anxiety, somatic complaints, attention problems, thought problems, and rule breaking than carefully matched classmates. Siblings of children with cancer may need greater support in meeting emotional, behavioral and school-based needs.

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STRESS RELATED QUALITY OF LIFE DOMAINS IN CHILDHOOD CANCER: A MULTIDIMENSIONAL ANALYSIS

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Purpose: As treatment for childhood cancer improves, the need to supplement overall survival endpoints with patient-centered outcomes evaluating well-being and quality of life has become apparent. In contrast to the questionnaire or proxy-rater methodologies typically used in such investigations, the present study employed a multivariate approach to identify health-related stressors experienced by adolescents undergoing cancer treatment.

Method: The overall sample consisted of 21 mixed-diagnosis cancer patients (11–21 years old) under treatment at an NCI-designated comprehensive cancer center. Participants responded to a focus statement (“Lots of things make a person’s life difficult. Tell me all the things that make your life bad”). Subject responses were combined and edited to eliminate redundancies, resulting in 74 items. Participants first sorted the responses into groups of similar items, and then rated each item on a five-point scale in terms of its impact on their quality of life and their degree of control over the stressor. Subject sorts were then analyzed using multidimensional scaling and cluster analysis to identify stress-related quality of life domains.

Results: Subjects generated 74 items that were grouped into 5 stressor clusters (Phii = .028). The stress domains included Emotional Impact; Self; Emotional Impact: Interpersonal; Disease Impact: Physical; Disease Impact: Functional; and School Related Impact. Strikingly, subjects rated the stress domains as significantly impacting their quality of life (mean = 3.7), but rated their control over these domains markedly lower (mean = 2.9). Although ratings identified the Disease Impact: Physical stress cluster as having the most influence on quality of life, it was rated as the least controllable; while stressors related to functional status were rated as most controllable.

Conclusion: The multivariate methodology employed herein resulted in a conceptually rich yet empirically derived mapping of treatment-related stress domains underlying quality of life that can be used to develop targeted stress-management interventions in this critical population.

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QLOLP: THE BRNO QUALITY OF LIFE LONGITUDINAL STUDY OF PEDIATRIC ONCOLOGY PATIENTS. INTERIM REPORT OF THE PROJECT

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Purpose: We report an interim report for the third year of the project the purpose of which is to establish a longitudinal study of the quality of life in children surviving cancer.

Method: Identification of target areas is based on a comparison of three study populations – children with cancer, children with chronic diseases other than cancer and healthy children.

Results: Since 11/2006 until 12/2009 202 childhood cancer survivors, 155 children and adolescents with chronic diseases and 869 matched controls entered the study. Analyses to date suggest the following conclusions: 1) the quality of life of former cancer patients is not significantly reduced in comparison with the control populations; 2) while former patients participate less in social and leisure-time activities, the quality of their relationships with parents is higher (warmth and consistency of upbringing); 3) former patients of higher age score higher on emotional well-being; 4) former patients attach greater importance to the values of “attending school” and “participation in leisure-time activities” and are more content with their “state of health”, “faith”, “school attendance” and “looks”; 5) while detailed
analysis of the quality of life of individual diagnostic groups it is not as yet possible, it is children with brain tumours who seem to have most problems; 6) a special analysis has been carried out to study the post-traumatic growth in parents of sick children.

Conclusion: We give an overview of current results. We expect use of the research conclusions in the preparation of preventive and interventional strategies and programmes improving the quality of life in children treated for cancer and in the preparation of information and educational materials for child patients and their parents in the Czech republic.

The project’s website: http://qgdp.eu.

Supported by the Grant Agency of the Czech Republic 06/07/1384 and 406/09/1255.

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CHALLENGES FOR SOLID TUMOUR DIAGNOSIS IN A RESOURCE-LIMITED SETTING

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Purpose: Late diagnosis of solid tumours in developing countries is common. South Africa, after the democratic change in 1994, has introduced several public health interventions to strengthen primary health care and improve child health. The aim was to compare the type and stage of solid tumours during two time periods after the establishment of a pediatric oncology unit (POU) in a resource limited setting in 1993 and indirectly whether introduced primary health care interventions since 2001 had an impact.

Method: The two time periods chosen was 1993 till 2000 (1st period), which was the POU establishment period and 2001 till 2008 (2nd period). More than 90% of the patients were African. During the 2nd period junior doctors in South Africa started doing a compulsory community service year in resource-constraint peripheral hospitals.

Results: There were 44% more patients diagnosed with a solid tumour in the 2nd period versus the 1st period (280 versus 156 patients), which is probably due to an increased recognition of cancer by peripheral hospitals. Advanced disease was predominant in both periods with 56% and 64% respectively. The stage was known for all patients in the 2nd period (100%) while in 14% of patients in the 1st period the stage was not known. The predominant solid tumour was nephroblastoma in 27%, followed by retinoblastoma in 23%. Brain tumours were rare (5%). The overall survival was 34% (excluding patients lost to follow up) for the 1st period, which improved for the 2nd study period to 50%.

Conclusion: Childhood solid tumours are still diagnosed late, which negatively impacts on overall survival. The most common solid tumour was nephroblastoma, while brain tumours were uncommon. Public health interventions in primary health care did not translated into early diagnosis. Different strategies need to be developed to improve early diagnosis.

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CAN WE HELP? NURSING RESPONSES TO PATIENT RELATED CALLS IN A CHILDREN’S CANCER CENTRE

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Purpose: To develop a profile of calls received by a children’s cancer centre. Further, to utilise this information in the development of risk stratified management algorithms that will standardise telephone triaging. Present guidelines are that family members and health professionals are encouraged to call the primary care centre if they have concerns regarding a child being treated for cancer. Calls are frequently received by a variety of clinical areas and health professionals (often nurses) within a children’s cancer service. Further, callers concerns can cover a wide range of urgent and non-urgent clinical and non-clinical issues. Whilst anecdotally aware of the variety of calls received, this major paediatric oncology unit was lacking evidence that mapped these calls.

Method: A prospective audit tool was utilised to record details about all calls received in the unit for a 3-week period. Data was entered into Microsoft Excel for descriptive analysis to identify caller concerns in relation to frequency, time, location, and evidence of documentation.

Results: Analysis revealed key information regarding peaks in the time and types of caller concerns that influence allocation of resources and development of family education/informational material. Initial caller concern grouping revealed a myriad of issues (24). The research team themed these into 10 key groups of caller concerns. Telephone response algorithms, for each of the 10 themes, were developed with reference to current literature, clinical practice guidelines and in conjunction with other multidisciplinary team members.

Conclusion: Profiling calls to a children’s cancer centre enabled the development of telephone triage tools to facilitate evidence-based and consistent telephone advice. Further auditing will evaluate the impact of this initiative. Although the research team recognises the role of standardised telephone triage guidelines, caution is needed with strict protocolisation that can lead to diminished response to individual issues and impose limits upon nursing experience and judgment.

O185

ONCOLOGY COMMUNITY OUTREACH PROGRAM

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Purpose: Pediatric oncology patients and their families are faced with many challenges upon the diagnosis of cancer. One of the greatest challenges faced is providing the necessary care for the child at home as they transition back into the community.

Method: Recognizing that the care of the child does not cease upon discharge, and in an effort provide the best possible care, Dana-Farber/Children’s Hospital Cancer Care (DFCHCC) Program created the Pediatric Oncology Community Outreach Program in 2006. This program encompasses Hospital to Home, Back to School, Call Back and Nursing Agency Education Programs. Hospital to Home provides a home visit by the DFCHCC nurse to newly diagnosed oncology and stem cell transplant patients post discharge to reinforce patient/family education, identify issues, and to review the plan of care with the caregivers and homecare nurses.

Results: In 2009, visits were expanded to newly diagnosed neuro oncology and end of life patients. Last year, more than fifty percent of home visits required an intervention from the DFCHCC nurse. Interventions included clarification of discharge instructions, reinforcement of medication teaching, central line care and troubleshooting supply issues. For example, during one visit, the parent was found to have drawn up a 10 fold dose of oral cyclosporine with an incorrect syringe. The error was discovered after two incorrect doses, the incorrect supplies were discarded, and reeducation related to correct administration was provided. Currently, we are participating in multicenter Home Medication Errors Study that will help to understand reasons for administration errors.

Conclusion: Based on results, we will develop interventions to improve medication administration practices in the home. Patient satisfaction, interventions and outcomes demonstrate the need for the Oncology Community Outreach program and ensuring safe care across the continuum.

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HOSPITAL-BASED HOME CARE FOR CHILDREN WITH CANCER

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Purpose: Hospital-based home care for children with cancer is widely used but controlled studies are relatively rare and the evidence base is limited. This prospective
non-randomized controlled intervention study aimed to evaluate hospital-based home care for children with cancer in relation to parents’ satisfaction with the care, incidence of adverse events, and costs.

**Method:** A hospital-based home care program was conducted August 2008–December 2009. Participants were children with cancer and their parents. The intervention group received part of their therapy, such as intravenous chemotherapy and antibiotics, as home care by a hospital-based home care nurse with paediatric oncology experience. Children in the control group received all their treatment at the hospital. The outcome measures are quality of life, satisfaction with care and preference of place of treatment, incidence of adverse events, rate of infections, and costs. The outcomes were evaluated by quantitative and qualitative methods.

**Results:** Fifty-two children between 0 and 16 years were included in the home care program, and 72 children were included in the control group. After each home visit the parents answered a questionnaire. The results from 655 questionnaires showed that 100% were ‘very satisfied’ or ‘satisfied’ with home care and all would choose home care again, if offered as an option. There were no deaths or adverse effects of intravenous chemotherapy or antibiotics. A cost analysis based on the expenses associated with home care in correlation with standard cost of inpatient admissions and outpatient visits in 2008 indicated that the hospital-based home care program was economically equal. Further analyses are being conducted on the families’ quality of life, infections, hospital admissions, and costs and will be presented at the conference.

**Conclusion:** The results indicate that the hospital-based home care program is safe, economically neutral and the parents’ satisfaction with the program is major.

**O187**

**EVALUATION OF PLACE OF CARE AT TIME OF DEATH AT ONE UNITED KINGDOM PRINCIPAL TREATMENT CENTRE FOR CHILDREN WITH CANCER**

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**Purpose:** We review the success of a specialist Children and Young People’s Oncology Outreach and Symptom Care Nursing Service (CYPOONS) in determining place of death for children with cancer treated at one United Kingdom Principal Treatment Centre (PTC). The service includes proactive provision of individualised symptom guidelines, blood product support and an emergency box in the home and coordination of local services.

**Method:** A prospectively maintained database containing demographic information, cancer diagnosis, cause and place of death has been maintained for all NHS patients aged between 1 year and 18 years with a confirmed cancer diagnosis referred to one PTC since January 2000. All deaths occurring over an 8 year period were reviewed by a Paediatric Oncologist and categorised as ‘expected’ (child receiving palliative care dying of underlying disease progression or complications thereof) or ‘unexpected’ (child receiving treatment of curative-intent who died of acute complications of treatment or the tumour itself). All deaths in the period could be confidently assigned to one or other category.

**Results:** Between 1.1.2000–31.12.07, 272 patients died, at age 18 months–20 years. The underlying cancer diagnosis was leukaemia/lymphoma in 66, primary brain tumour in 103 and extracranial solid tumour in 103 patients. 234 deaths (86%) were expected. The underlying cancer diagnosis was leukaemia/lymphoma in 66, primary brain tumour in 38 (14%) and 34 (14.5%) in a hospice. Where death was expected, the underlying cancer diagnosis, cause and place of death has been maintained for all NHS patients.

**O188**

**LATE GASTROINTESTINAL SEQUELAE IN SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY**

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**Results:** Survivors of childhood cancer who participated in the Childhood Cancer Survivor Study, a retrospective cohort study of five-year survivors of childhood cancer diagnosed between 1970 and 1986. A randomly selected group of siblings of these survivors served for comparison. Rates of ‘late’ GI complications, problems occurring 5 or more years after the childhood cancer diagnosis, were evaluated in association with survivors’ clinical characteristics and cancer treatments, adjusting for age, sex, and race. These were compared to siblings’ rates of GI complications. Poison regression was used to estimate rate ratios for these associations.

**Results:** Median age at diagnosis was 6.8 years (0–21.0). Median age at outcome assessment was 23.2 years (5.6–48.9) for survivors and 26.6 years (1.8–56.2) for siblings. Chemotherapy was utilized in 80.5% of survivors, abdominal radiation in 30.1% and abdominal surgery in 30.3%. Compared with siblings, survivors were at elevated risk for late onset upper GI complications (Rate Ratio (RR) 1.8; 95%CI 1.6–2.0), liver complications (RR 2.1; 1.8–2.5) and lower GI complications (RR 1.9; 1.7–2.2). The rate ratios for requiring colostomy/ileostomy, liver biopsy, and for developing liver cirrhosis were increased at 5.6 (2.4–13.1), 24.1 (7.5–77.8), 8.9 (2.0–40.0), respectively, relative to siblings. Older age at diagnosis, intensified therapy with high dose alkylating agents, abdominal radiation, abdominal surgery or TBI, and relapse increased the risk of certain hepatic, upper and lower GI complications.

**Conclusion:** Survivors of childhood cancer are at increased risk for late GI complications. Clinicians providing care for this population should be aware of these risks.

**O189**

**SLOWER PROCESSING SPEED AFTER TREATMENT FOR PEDIATRIC BRAIN TUMOR AND ALL**

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**Purpose:** CNS-directed treatment for pediatric cancer is associated with IQ declines. It remains unclear the extent to which these lower scores represent global cognitive decline versus domain-specific impairment. The objectives of this study are: 1) to examine discrepancies between processing speed and estimated IQ scores, and 2) to identify clinical characteristics associated with score discrepancies in a sample of pediatric ALL and brain tumor (BT) survivors.

**Method:** Data were collected on 100 survivors (50 ALL, 50 BT), ages 12–17. An estimated IQ score was derived from the WASI Vocabulary and Matrix Reasoning subtests. A Processing Speed Index (PSI) score was obtained from the WISC-IV or WAIS-III according to participant age.

**Results:** Survivors’ PSI scores (M = 88.7) were lower than their IQ scores (M = 101.4), t(97) = 8.95, p < .001, and were lower than the test population mean of 100, t(97) = 7.9, p < .001. Survivors treated with M = 84.9 had lower PSI scores than those without irradiation (M = 91.7), t(96) = 2.40, p < .05, while IQ scores did not differ by irradiation group. PSI scores (but not IQ scores) were lower for BT survivors who received chemotherapy (M = 80.60) than for BT survivors who did not (M = 92.70), t(46) = 2.9, p < .01. A negative correlation was identified between PSI scores and time since treatment for ALL survivors only, r = –.03, p < .05.

**Conclusion:** Many pediatric BT and ALL survivors exhibit slower processing speed than expected for their age while general intellectual reasoning ability remains largely intact. Clinical risk factors associated with larger IQ-PSI discrepancies included cranial irradiation, chemotherapy (BT only), and longer time since treatment (ALL only). Describing post-treatment cognitive declines by way of IQ scores alone is likely to provide an incomplete characterization of the quality of cognitive late effects exhibited in this population. A global measure of general intellectual ability might
underestimate dysfunction or fail to isolate the specific underlying deficits contributing to impairment.

O190
DIFFERENCES IN HOSPITAL INPATIENT PATTERNS BETWEEN ATTENDEES AND NON-ATTENDEES AT A PAEDIATRIC AND ADOLESCENT LONG-TERM FOLLOW-UP CLINIC IN YORKSHIRE, UK

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Purpose: We aimed to examine hospital activity among a cohort of young people, comparing differences between attendees and non-attendees at a paediatric and adolescent long-term follow-up (LTFU) clinic.

Method: Hospital admissions were linked to the Yorkshire Specialist Register of Cancer in Children and Young People. Eligible subjects were those who survived to at least five years post completion of active treatment, diagnosed under the age of 21, between 1974-2002. Hospital admissions of LTFU attendees and non-attendees were compared and factors affecting the probability of attendance at the LTFU clinic were assessed using logistic regression and reported using odds ratios (OR).

Results: 731 eligible long-term survivors were identified from the register, of whom 368 (50.3%) attended the LTFU clinic and 363 (49.7%) did not. Of those that attended the clinic, 38% were diagnosed with leukaemia, 16% with lymphoma, 10% with a CNS tumour and 37% with other solid tumours. This compared to non-attendee figures of 20%, 19%, 31% and 30% respectively. Both reason for admission and procedures undergone during inpatient stay varied between diagnostic group. Age group (OR 0.06–15 vs. 0–14), year of diagnosis (OR 1.09) and diagnostic group were shown to have a significant effect on the probability of a patient attending the clinic. LTFU attendees accounted for 60% of hospital admissions, with a median number of admissions of 19 per patient, compared to 9 for non-attendees. The median number of admissions per patient ranged from 1 to 26 and 1 to 33.5 for attendees and non-attendees respectively across diagnostic groups.

Conclusion: Our data showed clear differences in the distribution of cancers, number of admissions and reasons for admission between attendees and non-attendees of a LTFU clinic. We were able to identify patient groups who are currently under represented in the long-term follow-up clinic.

O191
PERI- AND NEONATAL OUTCOMES AMONG OFFSPRING OF FEMALE CANCER SURVIVORS

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Purpose: To explore peri- and neonatal outcomes following cancer, we studied the deliveries of female cancer survivors and female siblings in Finland.

Method: Nationwide cancer and population registries were merged to identify 5135 survivors. However, the risk of stillbirth (OR 0.77, 95% (CI) 0.33–1.78) or early death (early neonatal 1.13, 95% CI 0.64–1.99; neonatal 1.15, 95% CI 0.69–1.94; infant 0.89, 95% CI 0.56–1.41) in the offspring of cancer survivors was not elevated compared to siblings offspring.

Conclusion: Although offspring of female cancer survivors are more likely to experience certain adverse perinatal health outcomes, they are not at increased risk of stillbirth, neonatal or infant death. While reassuring, the results indicate a need for close prenatal surveillance and heightened observation of deliveries of cancer survivors.

O192
A SURVEY ON HEALTH STATUS AND HEALTH RELATED QUALITY OF LIFE OF CHILDHOOD CANCER SURVIVORS IN HONG KONG

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Purpose: To explore the health status, health behaviours, health-related quality of life (HRQOL), and psychological distress of adolescent and young adult survivors of childhood cancer.

Method: Subjects fulfilled following criteria were recruited: had diagnosis of childhood cancer prior to age 19, off-treatment for 2 years or more and survival of at least 5 years from the time of diagnosis. A telephone survey was adopted to study the health status of the subjects and aim at a sample of 600 eligible survivors. Study instrument was SF-36 questionnaire and the Baseline Questionnaire developed by the Childhood Cancer Survivor Study (CCSS) of University of Minnesota. Main outcome measure and analysis include Health status, Health behavior and HRQOL.

Results: Preliminary findings of 250 subjects were reported. 62% subjects were male and 50% were < 21 years, 32% 21–25 years, 14% 26-20 year and 4% > 30 years. 44% had leukemia and 10% had relapse of cancer. SF36 showed that HRQOL was good, with highest score in physical functioning scale (m = 92, SD = 13.8) and lowest score in general health scale (m = 60, SD = 18.8). Younger subjects (age < 21) appeared to have less bodily pain (p < .05) and higher vitality (p <.01). 92% of subjects did not smoke, around 55% of them had regular body check and dental check. Only 23% had medical insurance, 21% with life insurance and their role physical scale (p <.01) and role emotional scale (p <.001) were higher than those without insurance coverage. Subjects who had excellent self–perception of health (p <.01) had higher scores in all subscales of SF36 (HRQOL).

Conclusion: Childhood cancer survivors in Hong Kong had satisfactory HRQOL and active health seeking behaviors. Those who had poor self-perception of health, older in age, and without medical and life insurance coverage were at risk of poorer health status and poorer HRQOL.

O193
TRACKWELL: A NEUROCOGNITIVE SCREEN TO MONITOR COGNITIVE DEVELOPMENT IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: Significant cognitive late-effects are reported in survivors of childhood Acute Lymphoblastic Leukemia (ALL). Despite the known impact of some CNS-directed treatments (CRT and Methotrexate), the factors influencing individual vulnerability to neurocognitive late effects are not well understood. As most centres have limited neuropsychological services, an efficient, targeted neurocognitive screening protocol may be warranted. The aim of this study was to: (i) Assess the feasibility of using a neurocognitive screen with ALL survivors &; (ii) Determine rates of neurocognitive impairment in ALL survivors.
Method: A brief screen (“Trackwell”) adapted from a battery used at Texas Children’s Hospital, and aimed at identifying neurocognitive ‘risk’ was administered to 83 ALL survivors (51 female; aged 3–18 years) who received treatment with MTX or CRT 2–6 years ago at the Royal Children’s Hospital, Melbourne. The screen included measures of selective attention, processing speed, working memory, visuo-motor integration and academic skills. Impairment was identified as a score one or more standard deviations below the mean.

Results: Study participation rates (70%), questionnaire feedback from participants and prevalence of deficits suggest a neurocognitive screening protocol is feasible. Impairment in visuo-motor integration skills was most prevalent (42%), followed by deficits in selective attention skills (25.6%), processing speed (18.3%) and working memory abilities (17.1%). Approximately one quarter of the sample also displayed impairment in one or more academic areas, with reduced numeracy skills most prevalent (26.8%). Performance on academic tasks was significantly correlated with cognitive abilities (r = .51 to .32), except for visuo-motor integration. Higher treatment intensity was associated with poorer selective attention, visuo-motor integration and spelling skills.

Conclusion: A neurocognitive screen may be a feasible approach to monitor neurocognitive outcomes in ALL survivors. A significant proportion of ALL survivors exhibited cognitive difficulties warranting further assessment and/or intervention. Treatment intensity explained some of the variance in outcomes.

A CASE-CONTROL STUDY ASSESSING THE RELATIONSHIP OF GST POLYMORPHISMS AND THE RISK OF DEVELOPMENT OF HEPATOPATHY ON NATIONAL WILMS TUMOR STUDY-5 (NWTS-5).

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Purpose: The polymorphic glutathione-S-transferases (GSTT1 and GSTM1) potentially determine the cytotoxicity of acyclovir and/or doxorubicin in Wilm tumor (WT). Phenotypic absence of enzyme activity is determined by the GSTT1 null genotype (15% of US population) and the GSTM1 null genotype (50%). We postulate that these null genotypes are associated with hepatotoxicity (grade 3-5) in NWTS-5 WT patients.

Method: Patients with banked DNA treated on NWTS-5 frontline therapy for WT who developed grade 3, 4 or 5 hepatotoxicity were eligible. GST genotyping was performed using the fluorescent PCR-based allelic discrimination (TaqMan) assay using the ABI Applied Biosystems 7200 Sequence Detection System. Detection of specific probe hybridization to its target was accomplished by the analysis of the fluorescence of a specific reporter dye.

Results: 52 NWTS-5 WT patients experienced hepatopathy. DNA samples were not available for 11 cases. For the remaining 41 cases, controls were chosen matched by treatment regimen, race, disease type [unilateral, same side; bilateral], similar duration of follow up and age. 8 cases were excluded from the final analysis because of inadequate samples, indeterminate results, lack of controls or coding error. Thirty-four (34) of the 66 remaining paired samples (52%) were positive for GSTM. GSTM was positive in 15/33 (45%) with hepatopathy and in 19/33 (58%) without hepatopathy (p = 0.46). Fifty-four (54) of the 66 samples (82%) were positive for GSTT. GSTT was positive in 28/33 (85%) with hepatopathy and 26/33 (79%) without hepatopathy (p = 0.75). We found considerable variability in GST polymorphisms based on reported ethnicity: GSTM positive [White 18/42 [43%], Black 0/10 [0%], Asian 2/4 [50%], Hispanic 4/10 [40%]]. GSTT positive [White 33/42 [79%], Black 8/10 [80%], Asian 3/4 [75%], Hispanic 0/10 [0%].

Conclusion: We found no evidence that GST1 or GSTM1 homozygous mutations predispose WT patients to grade 3-5 hepatopathy. We confirm ethnicity-related differences in the frequency of the GSTT1 and MI mutations.

SPINDLE CHECKPOINT GENES EXPRESSION IN CHILDHOOD ADRENOCORTICAL TUMORS (ACT): AURKB IS ASSOCIATED WITH METASTATIC DISEASE AND POOR SURVIVAL

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Purpose: 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. Spindle checkpoint genes are important for chromosome segregation during mitosis and dysfunction of these genes is implicated in the development of many cancers, but their expression in ACT remains undetermined. The aim of this study was to analyze the expression profile of the spindle checkpoints genes in consecutive pediatric adrenocortical tumors of different stages classification.

Method: The levels of mRNA expression of the genes AURKA, AURKB, BUB and BUBR1 were analyzed by quantitative real-time PCR in consecutive microdissected tumor samples obtained from 57 children with diagnosis of adrenocortical tumors (31 classified as stage I, 11 as stage II, 3 as stage III and 10 as stage IV) and 11 non-neoplastic adrenal samples. Mann-Whitney and Fisher exact tests were used to assess the correlation between gene expression and clinical/biological variables. Overall survival was analyzed by Kaplan-Meier and log-rank test. Values of gene expression higher than median were considered as overexpressed.

Results: The 5 years-EFS was 79.3% for the overall group of patients analyzed (90.1% to stage I/II versus 32.3% to III/IV, p < 0.0001). TP53 mutation R337H was found in 48/57 patients (84.2%). In ACT overexpression was observed when compared with non-neoplastic adrenal to genes BUB (P = 0.0001) and BUBR1 (P = 0.001). TP53 R337H mutation was associated with overexpression of BUBR1 (P = 0.005) and AURKA (P = 0.03). Overexpression of AURKB was associated with metastatic disease (P = 0.02) and unfavorable event (P = 0.02). Patients with expression values higher than median to AURKB presented a significant lower overall survival (64.6 versus 95%; P = 0.02).

Conclusion: Our results suggest that spindle checkpoints genes may be related to pediatric adrenocortical tumors and more aggressive disease and could be potential targets to therapy in these tumors.
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primarily a parental one in 14/25; one did not specify. The reasons for not enrolling on the observation only study are (multiple selections possible): a. EE4A chemotherapy better option - Parents (n = 10)/Physicians (n = 4); b. Observation too experimental - Parents (n = 6)/Physicians (n = 4); c. Concern about salvage intensity - Parents (n = 5)/Physicians (n = 2); d. Intensity of CT monitoring too high - Parents (n = 6)/Physicians (n = 1); e. Central line already placed- Parents (n = 1)/Physicians (n = 2); f. Staging uncertainty - Parents (n = 0)/Physicians (n = 6). 19 patients received EE4A therapy (Vincristine and actinomycin D) and 5 patients observation alone. There were no relapses or deaths. Conclusion: Almost half of eligible VLR patients do not enroll driven by parental and physician concerns that observation alone is insufficient or that planned salvage therapy for relapse is too intense. Future study design of reduced intensity should take these findings into consideration.

O197 SONOGRAPHIC ASPECTS OF EARLY DIAGNOSIS OF WILMS' TUMOR

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Purpose: Analysis cases with early diagnosis of Wilms' tumor in infants. Method: We analysed of the data on 13 patients of both sexes under the age of one year (median - 7 months) with morphologically diagnosed Wilms' tumor in stage I-II. All children were of the group of the 20 patients with Wilms' tumor, admitted for examination and treatment to our Center from 1999 to 2009 with stages I-V of the disease.

Results: In the all of patients there was no suspicious medical history concerning tumor of the kidney during the prenatal U.S. Ultrasonography (U.S.) - was the method of primary visualization of the tumor in general clinical network in all patients. Minimum tumor size in greatest dimension by U.S. was 4 cm, maximum - 14 cm (86 ± 30 mm) at average volume of 292 ± 323 ml (M ± SD). Time the moment of birth to diagnosis of the tumor ranged from the third to eleventh months of life (238 ± 76 days). There was no correlation between age of patients and of the volume tumor. The number of tumor-doubling of estimated visualization volume of reference (1 m1) to diagnosed volume - was 7.8 ± 1.6. Given the minimal period of doubling of Wilms' tumor (11 days), assuming a linear growth rate, the time tumor growth may be 66–101 days.

Conclusion: Thus U.S. is the method of first choice for primary diagnosis of Wilms' tumor in infant. Diagnosis of tumor of the kidney is made at volume of the tumor significantly higher than the minimal diagnosis volume. By planning screening programs for postnatal Wilms' tumor the interval between inspections should not exceed 2–3 months.

O198 HOW DO PAEDIATRIC RENAL TUMOURS PRESENT? A RETROSPECTIVE REVIEW FROM A SINGLE CENTRE OVER A 10 YEAR PERIOD

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Purpose: While Nephroblastoma (Wilms Tumor) is the most common renal tumour seen in childhood, there is a large differential. As part of SIOP, our strategy is to treat renal tumours based on clinical findings and imaging. Biopsies are performed where clinically indicated. There is little in the literature on clinical findings at presentation and their impact on outcome in these tumours.

Method: We performed a retrospective, single centre study of all children who presented to Institute Gustave Roussy between January 2000 and December 2009 with a renal mass, to determine the clinical features at presentation of renal tumours and their impact on outcome.

Results: 187 children (48% female), aged 2 days to 21.56 years (median 2.81 years) presented with a renal tumour during this period. 47% were left sided, 45% right sided, 7% bilateral and 1 ectopic kidney tumour. Pain was the main presenting cause in 23%, symptoms of fever/infection in 14%, haematuria in 13%, abdominal distension in 12%, a mass found incidentally by a parent in 14%, in 8% the child had a scheduled medical examination and in 4% the child was under surveillance due to an increased risk of developing a renal tumour. 40% of children were hypertensive at presentation, with 53% of these requiring anti-hypertensive medication. At presentation 32% were febrile and 28% in pain. 15% had metastatic disease at and 11% locoregional extension (tumoral thrombus or nodal extension). 14 children had a biopsy (4 of whom were febrile): 9 were nephroblastomas, 4 non-nephroblastoma malignant tumours and 1 abscess.

Conclusion: Diagnosis in 86% was Nephroblastoma, another malignant tumour in 12% and 2% had a benign condition. 83% received pre-operative chemotherapy, 10% a primary nephrectomy.

O199 WHY WILMS TUMOUR DIAGNOSED IN CHILDREN < 24 MONTHS OF AGE HAVE A BETTER PROGNOSIS? AN EVALUATION FROM THE ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA (AIEOP) WT WORKING GROUP

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Purpose: To investigate whether the better prognosis reported for children < 24 months of age (infants) with Wilms tumour (WT) could be related to a precocious subclinical diagnosis in this age group compared with older patients.

Method: Results from AIEOP-TW-2003 protocol show that infants have a trend toward better 4-year DFS (94% ± 3) compared with older children (80% ± 3) (p<0.01). A specific questionnaire was delivered to AIEOP centers, mainly focusing on the modality of WT diagnosis, trying to distinguish between symptomatic and incidental diagnosis.

Results: Medical records and the results of the questionnaires were available for 100 WT infants. Fifty-five were males; mean age was 21.5 months, 14 cases had bilateral disease, 42 right-sided, 42 left-sided, 2 not known; 4 patients had multifocal tumours. Noteworthy, 18 patients had malformations associated. The diagnosis of a renal mass was incidentally made in 20/85 fully evaluable infants (7 stage I, 6 stage II, 3 stage III, 4 stage V); they all displayed unifocal disease, and the mean tumour weight was 207.3 g (mean tumour diameters 5.57, 5.5, 4.95 cm). Overall 65 patients had WT diagnosis based on clinical revealing signs/symptoms (26 stage I, 19 stage II, 5 stage III, 5 stage 4, 10 stage V); mean tumour weight resulted 350 g (mean tumour diameters 10, 8.5, 7.5 cm). The median tumour weight for all eligible WTs in AIEOP-TW-2003 was 345 g.

Conclusion: Approximately 25% of infant WT patients had an incidental renal mass diagnosed during diagnostic check-up performed for other reasons. They all presented with non-metastatic smaller tumour at diagnosis and a rate of malformations higher than in older patients (69%). This might represents one of the factors influencing the better outcome in the children < 24 months. Adjunctive possible risk factors, like a different tumour LOH pattern between age groups, are under evaluation.
Purpose: The purpose of the study was to evaluate child characteristics and clinical factors (i.e., disease and treatment) that may be related to outcomes of a social skills group intervention program for survivors of childhood brain tumors.

Method: Participants were 46 survivors (24 males, 22 females) aged 7 to 18 years and of stable health. The intervention consisted of 8 2-hour weekly sessions. Social skills training included: Friendship Making. Survivors and parents completed the Social Skills Rating System (SSRS; Gresham & Elliot, 1990) and Pediatric Quality of Life Inventory (PedsQL4.0; Varni, Seid & Rode, 1999) at pre- and post-intervention. Child characteristics (e.g., gender, age, IQ) and clinical variables (e.g., diagnosis, tumor location, time since treatment) were examined as potential related factors.

Results: Change scores were calculated for pre- and post-intervention. Pearson and Spearman rank correlations were conducted to identify relationships between change scores and covariates. Parent reported PedsQL was related to age (r = -.42, p < .05) and time off treatment (r = -.42, p < .05). Based on bivariate correlations, a multiple regression analysis was conducted including age, time off treatment, and tumor location as predictor variables and the change score for parent reported PedsQL as the criterion variable. The overall model was significant (F = 3.98, p < .05). Age emerged as a significant predictor (b = -2.09, p = .05) indicating that older participants showed more improvement than younger participants in quality of life.

Conclusion: Younger children who have received finished medical treatment are the ideal candidates for the social skills intervention program for childhood brain tumor survivors. Future research should explore the specific range of time following treatment that is most conducive to intervention efforts.

O201

GENETIC KNOWLEDGE AND ATTITUDES TOWARDS GENOMIC RESEARCH: COMPARISON OF VIEWS OF YOUNG ADULT SURVIVORS WITH HEREDITARY CANCER ETIOLOGY AND WITHOUT HEREDITARY CANCER ETIOLOGY

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Purpose: In 21st century genetic medicine, pediatric cancer survivors are increasingly asked to participate in genomic research. We sought to ascertain survivors’ genetic knowledge, concern about hereditary cancer and future cancer risks to themselves and their children, attitudes towards participation in genomic research, and interest in targeted educational interventions about genetics for survivors. We compared findings for survivors with and without hereditary etiology of their disease.

Method: 40 young adult survivors of pediatric cancer from the Dana-Farber Cancer Institute in Boston and The Hospital for Sick Children in Toronto were sent mail questionnaires and interviewed via telephone about genetics and genomic research. Survivors with physician-assigned known or suspected hereditary cancer etiology (H group; n = 16) were matched by age, gender and diagnosis to survivors without hereditary etiology (NH group; n = 24).

Results: While hereditary etiology subjects knew more about cancer genetics, both groups had significant knowledge gaps and exhibited much remaining concern (average 14.3 years post-diagnosis) about “Why did I get cancer?” and about risks to offspring. Hereditary cancer subjects demonstrated confusion about whether they had had cancer (4/16 thought not) and whether the cause was heredity (only 25% H attributed cancer to heredity vs. 8% NH). Worry about future cancer was higher among hereditary cases (81% v. 25%). Both groups showed high interest in participating in genomic research and identified the media as a common source for genetic information. Little worry was voiced about possible loss of insurance or inclusion of genetic test results in medical charts and accuracy and utility of test results for prevention or treatment of late effects were valued more highly in decisions about participation. Subjects endorsed the value of targeted genetic information as a resource for pediatric survivors.

Conclusion: There is need for and interest in development of a targeted genetic information resource for pediatric cancer survivors.
SIOP ABSTRACTS

Results: Since 2003, 42 training workshops were attended by 4520 CHWs. Of the 1129 patients diagnosed from 2003 to 2009, 272 (24%) were referred directly by CHWs. Early death occurred in 139/1968 (7.1%) of all patients, 86/839 (10.2%) during the earlier period versus 53/1129 (4.7%) during the later period (p = 0.001). Early death decreased from 11.6% to 5.5% in acute lymphoblastic leukemia (n = 613, p = 0.005), from 17.4% to 9.5% in AML (n = 197, p = 0.006), and from 8.0% to 3.6% in patients with other cancers (n = 1158, p = 0.003). When early death was defined as that within 2 weeks of diagnosis, results were similar. Five-year EFS increased from 49% to 62% (p < 0.001).

Conclusion: In Northeast Brazil, education of CHWs and improved access to tertiary care were associated with reduced early death and improved 5-year EFS. Oncologists in similar regions must expand community involvement and access to tertiary care to improve survival.

O204

COPIING IN ETHNICALLY DIVERSE ADOLESCENTS WITH CANCER: AN OPTIMISTIC PERSPECTIVE

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Purpose: Historically, pediatric psycho-oncology research has focused on a deficit model of coping. More recently, interest has burgeoned in adopting a positive psychology approach to studying the adjustment of children with cancer. Research in adult psycho-oncology indicates that optimists have unique coping styles which influence better quality of life (QOL). Preliminary data suggest that children and adolescents with cancer are psychologically resilient; however, little is known about how minority adolescents cope with cancer. The current study investigated optimism in adolescents with cancer, and how it is related to coping style, QOL and health-related QOL (HRQOL).

Method: Eligible patients had any type of cancer and were between 13 and 21 years old. Assessment measures included The Life Orientation Test, Revised, The KIDCOPE, and The Pediatric Quality of Life Inventory, Generic Core Scale and Cancer Module.

Results: The mean age of the final 46 participants was 16; the majority were male. Participants were predominantly Hispanic (50%); 24% Black, 19% White, 7% Other). Eighty-two percent of the adolescents were actively receiving chemotherapy at the time of their participation. This sample was highly optimistic and used more positive-approach than negative-avoidant coping strategies. Optimism was significantly related to greater use of cognitive restructuring and positive emotion regulation. Adolescents with higher use of negative avoidant coping (e.g. resignation, social withdrawal) reported significantly lower psychological and overall QOL. There was a trend for Hispanic and African American adolescents to report lower HRQOL in the communication domain (e.g. they have difficulty communicating with physicians) than Caucasians. Qualitative analysis of the stressors generated in the KIDCOPE revealed that this sample of adolescents was capable of tremendous psychological growth, a finding consistent with existing data on Latino adolescent cancer survivors.

Conclusion: Further research should assess whether interventions that increase optimism and positive-approach coping lead to greater QOL in this population.

O205

HEALTH-RELATED HINDRANCE OF PERSONAL GOAL PURSUIT: COMPARISON OF ADOLESCENTS WITH CANCER AND HEALTHY CONTROLS AND ASSOCIATED RISK AND RESILIENCE FACTORS

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Purpose: The impact of health on self-identified goals is referred to as health-related hindrance (HRH). Assessing HRH of adolescents with cancer is important given that: (1) critical developmental processes may be compromised when cancer impedes goal pursuit during adolescence and (2) the perceived impact of health on personal goals during adolescence may be an important risk factor for the later adverse psychological outcomes and delays in achievement of developmental milestones experienced by some young adult survivors. The current study aimed to: (1) compare HRH of adolescents with cancer and healthy controls and (2) identify disease-related risk factors and psychosocial resilience factors related to HRH in adolescents with cancer.

Method: Adolescents (ages 13–19) with cancer (n = 102) and without cancer (n = 96) completed measures of HRH (rating the impact of pain, fatigue, other physical symptoms, and taking care of their health on their ability to pursue personal self-identified goals) and well-being and family functioning.

Results: HRH was significantly (p < .0001) higher in adolescents with cancer compared to healthy adolescents. Pain was the only significant disease-related correlate of HRH. In particular, HRH correlated with current pain severity (r = .28, p = .00) and severity in the last 4 weeks (r = .52, p = .00), and pain frequency in the last 4 weeks (r = .49, p = .00). In terms of psychosocial factors, HRH related to self-blame (r = .31, p = .003). HRH was not related to social support, parenting, family functioning, self-efficacy, or dispositional hope among the adolescents with cancer.

Conclusion: HRH is a significant problem for adolescents with cancer, especially those with pain. That there were few other correlates of HRH indicates that the predictive factors of HRH are yet to be known and require further study. Given the importance of goal pursuit and achievement for adolescent development, well-being, and successful transition to adulthood, interventions to reduce HRH are needed.

O206

MULTIPROFESSIONAL COLLABORATION IN CHILDREN’S CANCER CARE: THE ECCO PROJECT CONCLUDED

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Purpose: Collaborative working, where care is delivered through teams of professionals working together, has become a central characteristic of services within children and young people’s cancer care. In cancer care we might all agree that collaboration is in fact a ‘good thing’. But clearly collaboration and multiprofessional working is less than straightforward. It would be naïve to think that collaborative ways of working develop spontaneously or through good will alone.

Method: Funding from ECCO, the European CanCer Organisation, has supported teams of nurses and doctors from European countries to meet over the course of three years. Eleven teams have been working on individual projects in their own clinical units, supported by mentors at a distance and attendance at 4 weekend seminars. Appraciative Inquiry was adopted as an approach to embrace organisational change. Collaboration through the implementation of clinical projects was explored in the seminars, as well as through written reports from teams and in dialogue with mentors. Evaluation methods were informal, and concluded with a final recorded interview with 6 of the teams.

Results: The projects were varied and included examples such as, collaboration between doctors and nurses in providing information to the patients and their families during the course of treatment; improving phone communication with parents; implementation of a weekly multi-professional round to improve sharing of information relevant to patient care; and implementation of a paediatric pain protocol.

Conclusion: Although there were challenges along the way, much has been learnt in terms of multiprofessional working, alongside the benefits of learning and sharing with professionals from other countries. This presentation will focus on detailing the project, sharing some examples of the projects and introduce delegates to a DVD available to implement this approach in their own workplace.

O207

COMMUNICATION BETWEEN DOCTORS AND NURSES IN A PEDIATRIC HEMATOLOGY AND ONCOLOGY DEPARTMENT IN POLAND

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Purpose: Good communication between doctors and nurses in the oncology setting has been shown to reduce the risk of human error, improve patient safety, and reduce patient distress. This study aimed to explore communication between doctors and nurses in a Polish oncology setting.

Method: A mixed-methods approach was used, including a survey of doctors and nurses, interviews with key stakeholders, and the analysis of video recordings of interactions. The survey was anonymous and voluntary, and included questions on communication practices, challenges, and training needs.

Results: The survey was completed by 60 doctors and 80 nurses. The most commonly reported communication barriers were time constraints, workload, and communication styles. The majority of respondents believed that communication training was necessary.

Conclusion: The study highlights the importance of communication training in oncology settings, and identifies areas for improvement. Further research is needed to develop effective training programs.
Purpose: A three-year (2007–2009) program inspired by SIOP, EONS, ECCO was carried out to investigate the possibilities of improving communication between physicians and nurses at a Department of Pediatrics, Hematology and Oncology in Poland.

Method: Two rounds of a survey were undertaken. In May 2007, an initial survey was conducted among both professional groups. Closed-ended questions were intended to evaluate communication within the Department, while open-ended questions were included to provide space for each professional group to have an opportunity to comment. Based on an analysis of open-ended questions a joint decision was taken to launch the following initiatives: delivering a series of monthly lectures in pediatric oncology for nurses (topics to be suggested by nurses) given by doctors; altering the organization of medical visits in the Department; and two project meetings were held for the Department. In December 2009, the survey was repeated to measure change.

Results: In the initial survey, the overall team communication rating awarded by 38 nurses was 3.0 on a 1–5 scale, whereas 16 physicians graded it 3.31. Results of detailed questions were analyzed statistically. In the repeat survey, communication between the two professional groups in the Department was awarded an average rating of 3.67 by 30 nurses and of 3.63 by 16 physicians. An analysis of detailed closed-ended questions confirmed that communication between physicians and nurses at the Department had been improved. The improvement was most significant in nurses' opinions.

Conclusion: Methods employed successfully helped improve communication between physicians and nurses. Even though the overburdened staff were originally very reluctant to participate in the project, thanks to emphasizing the importance of communication, the situation improved as soon as it was launched. This presentation will focus on the methods employed to improve communication and the results of two rounds of a survey.

O208

MID-LEVEL PRACTITIONER-PHYSICIAN COLLABORATION IN PEDIATRIC BLOOD AND MARROW TRANSPLANTATION PROGRAMS

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Purpose: Mid-level practitioners (MLP’s) are utilized in the inpatient and ambulatory care settings in many pediatric Blood and marrow transplantation (BMT) programs. While strict guidelines exist surrounding the training of resident physicians and fellows, practice guidelines for MLP’s are less well defined and vary by state or provincial regulations. In an effort to enhance the MLP-Physician collaborative relationship, we designed a brief survey to determine how MLP’s and physicians perceive the MLP-Physician relationship.

Method: On-line surveys were sent to 75 Pediatric Blood and Marrow Transplant Consortium centers (PBMTCT). Thirty-six MLP’s and 25 physicians participated in the survey. The survey asked the MLP’s and physicians to define the MLP clinical role.

Results: Results showed that physicians had an excellent understanding of the MLP role. The physicians acknowledged that the MLP’s play a role in resident/fellow and nursing education. There was significant agreement between MLP’s and physicians with respect to autonomy, scope of practice, communication, and feedback. Both MLP’s and Physicians felt that MLP’s were not compensated fairly. Physicians tended to underestimate the MLP workload and do not fully appreciate the physical and emotional demands of the MLP role. There were also misperceptions about how MLP’s spend their time.

Conclusion: This initial survey suggests that MLP’s and physicians have a strong collaborative relationship. These responses show that physicians and MLP’s need to develop strategies for regular structured feedback. If publishing manuscripts, conducting research or taking leadership roles in teaching are desired, then more protected time needs to be provided to the MLP. Physicians should also recognize that there is a significant physical and emotional aspect to the MLP role. This survey will provide a foundation for future research into optimizing the MLP-Physician collaboration.
ICCP0003

THE BENEFITS OF GROUP PSYCHOSOCIAL ACTIVITIES FOR SIBLINGS OF CANCER PATIENTS: RESULTS OF A 7 YEAR QUALITATIVE STUDY
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Purpose: The purpose of this qualitative study was to determine common themes and emotions expressed by children who had a brother or sister with cancer during group activities that were part of the Dana Farber Cancer Institute’s Annual Sibling Week. While existing research has illuminated sibling issues, there has been little systematic investigation of these factors within a group setting.

Method: A variety of group psychosocial activities were provided to siblings of patients during the Annual Sibling Program weekly event in April of each year. Qualitative data was collected over a 7 year period. These activities were designed to elicit thoughts and emotions related specifically to the sibling experience. Three of the psychosocial activities were repeated for two years and one activity for one year. Each day different groups of siblings participated. The total number of siblings participating was approximately 245. The age range of the participants was 5–12 years.

The activities were as follows:
1. “Tips for Sibs”
2. “Sibling Wishing Well”
3. “Sibling Road Map” (adapted from the Sibling Journey designed for clinicians by Supersibs!)
4. “Sibling Emotion Ocean” (formulated by Supersibs!)

Results: The results reveal common themes expressed when siblings are afforded the opportunity to meet in a group format and are provided with a psychosocial activity led by a clinician. The profile of thoughts and emotions that emerged involved feelings of sadness and loneliness, guilt and anger, worry and anxiety, concerns about school and, importantly, suggestions by siblings on how to cope as well as hope for the future.

Conclusion: The findings of this study are consistent with and support the findings observed in current research. The findings also illuminate the substantial benefits of a group activity format. This format not only facilitated expression of thoughts and emotions specific to the sibling experience, but also provided for therapeutic peer support.

ICCP0004

DF/CHCC PEDIATRIC PATIENT AND FAMILY ADVISORY COUNCIL - WHERE WE STARTED, WHERE WE ARE AND HOW WE GOT HERE
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Purpose: To share the process of how Dana Farber/Children’s Hospital Cancer Care started their Pediatric and Patient Family Advisory Council, how it has evolved over the past 10 years, the projects we have worked on and where we would like to go from here. We believe and advocate for patient and family centered care in all we do.

Method: We will use PowerPoint, hand out literature, hold question/answer sessions. We will have founding members, members who joined a few years ago and members who are brand new to the council, all willing to share their insights, thoughts and experiences both on a personal level as a parent and also as a member of the council.

Results: We hope to empower those who may have reservations or question the need to have a child with cancer, unless they have been there themselves. There is an underlying amount of understanding and respect among the parents on our council.

Conclusion: Our council includes parents of children who have survived cancer, still fight the disease and those who have lost the battle. All parents’ stories and experiences are embraced and accepted by one another. No one knows what it is like to have a child with cancer, unless they have been there themselves. There is an underlying amount of understanding and respect among the parents on our council.

Our stories may not have all ended the same, but we were all parents of pediatric cancer patients at one time or another. It is important for institutions to utilize parents who can speak for those who can’t speak for themselves. The parents on our council want to help make the day to day lives of the patients we represent, as positive and meaningful as possible. We hope by sharing our stories, we accomplish just that.

ICCP0005

BUILDING SUPPORT SYSTEMS WHERE NO ONE KNEW THEY WERE NEEDED: PEDIATRIC CANCER PATIENT AND FAMILY SUPPORT IN JAPAN
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Purpose: Japan is the world’s second wealthiest nation in terms of GDP and has a national health care system that cases nearly the entire financial burden of pediatric cancer treatment. However, regarding the provision of psycho-social support for pediatric cancer patients, Japan lags behind its global counterparts. There are many complicated logistical and cultural factors that exacerbate this including: long hospitalization, social stigmas surrounding pediatric cancer and a traditionally non-conservative approach to open social communication.

Method: Since 2006, The Tyler Foundation for Childhood Cancer, a Japan-registered non-profit organization, implemented a novel approach in Japan to pediatric cancer patient and family support: placing clinical psychologists in the cancer ward to work on the frontline with patients and parents. In addition, the Tyler Foundation aims to fill the support gaps in the Japanese medical system by creating a variety of unique patient-driven activities and importing and adapting support systems from the US, Australia and other western countries.

Results: Data collected from patients, families and medical staff reveals that support systems have actually made a clear difference in the quality of life of pediatric cancer patients and families during treatment, in the case of death of a child and in the transition back to normal life after treatment is completed.

Conclusion: In order to provide optimal pediatric cancer patient and family care including psycho-social support, organizations and individuals may be best placed to fill these gaps in Japan’s medical care system since this has not historically been a top priority in the nation’s approach to health care.

ICCP0006

PARENTS EVALUATION OF PARENT SUPPORT GROUPS
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Purpose: Studies show that parents of seriously ill and chronic sick children experience a great deal of strain. Parent support groups can provide opportunity to share feelings, knowledge and coping strategies.

Method: We arranged 23 consecutive weekly group meetings. They were conducted by an experienced oncology nurse and a co-leader. By the end of each group meeting, the parents where asked to complete an evaluation form with both multiple-choice questions and open-ended questions.

Results: There were 96 parents from 11 different departments who participated. The Questionnaire was completed by 83 parents (87%). All (100%) parents evaluated the group meetings to be useful and supportive. 48 parents (58%) said they got new ideas about how to cope with their challenging life, and 43 parents (52%) wrote what new ideas they had got. 34 parents (41%) wrote other comments. All of them had positive attitude.

Conclusion: The parents evaluation confirms the need for parent support groups in hospitals focusing on coping strategies. There is a need for further studies to find out why parents who got invitation did not attend.

ICCP0007

AUSTRIAN MENTORING PROGRAM FOR SURVIVORS
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2Austrian Children’s Oncology Group (ACOG), Vienna, Austria

Purpose: The aim of the Austrian Pediatric Oncology Group (APOG) was to offer a partnership program for childhood cancer survivors.

Method: A mentor program was developed and provided in 80 web seminars attended by 1,500 mentors and survivors.

Results: There were 96 patients from 11 different departments who participated. The Questionnaire was completed by 83 patients (87%). All (100%) parents evaluated the group meetings to be useful and supportive. 48 parents (58%) said they got new ideas about how to cope with their challenging life, and 43 parents (52%) wrote what new ideas they had got. 34 parents (41%) wrote other comments. All of them had positive attitude.

Conclusion: The parents evaluation confirms the need for parent support groups in hospitals focusing on coping strategies. There is a need for further studies to find out why parents who got invitation did not attend.
**ICCCPO008**

**CREATION OF CHILDHOOD CANCER SURVIVORS GROUP IN INDIA: STEPS, PROCESS AND VISION FOR FUTURE**

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3Tata Memorial Hospital, ACT Clinic, Pediatric Oncology, Mumbai, India

**Purpose:** To initiate young adult survivors of childhood cancers attending After Completion of Therapy (ACT) Clinic at Tata Memorial Hospital to form a childhood Cancer Survivors Group (CCSG)

**Method:** Action Research and Rapid Appraisal method with a 22 point questionnaire was administered to 28 survivors and their care- taker who attended the 39th Annual conference of SIOP, 2007 in Mumbai. The aim was to elicit responses regarding current life domain, leadership qualities, level of independence and their motivation to form a childhood cancer survivor’s group (CCSG). Data was analyzed to gauge parental attitude towards CCSG and find leaders and harness potential for formation of CCSG

**Results:** 11 committed survivors aged 17–22 were identified who were then groomed and mentored extensively towards formation of CCSG. They were given a conducive platform to interact socially on the occasion of National Cancer Survivors Day (NCSD) on 8th June 2008. Their inspiration was a courageous and creative survivor who eventually succumbed to the disease in 2009. The highly motivated group interacted during 2008-2009 and crystallized the formation of first CCSG in the western zone of India on NCSD on 7th June 2009 which was christened UGAM which means – TO RISE. Their scope of work includes recreational activities, structured peer counseling, fund raising, networking and blood donation drives. 48 members have been enrolled in less than 1 year. They attribute their success to inspirational interactions at the 39th SIOP conference in Mumbai (54%) and to effective nurturing provided by the team leader of ACT clinic (78%). The group is going from strength to strength and now operates under the umbrella of Indian Cancer Society’s Survivorship Programme.

**Conclusion:** All of the above has empowered the hitherto faceless survivor. UGAM envisages to incorporate longitudinal auditing process at significant junctures to record group dynamics, collate/disseminate data with other survivor groups for advocacy issues in the larger socio-political processes.

**ICCCPO009**

**CONTINUUM OF CARE THROUGH THEAEPUTIC RECREATION CAMPS**

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**Purpose:** To inform ICCPO members of the importance of therapeutic recreation in the continuum of care for cancer survivors.

**Method:** Present Barretstown Camp as an example of how a camp can do this and what is required to provide such a service.

**Results:** This presentation will demonstrate how therapeutic recreation is an important step to recovery and providing children with a better coping mechanism in returning to normal, daily life.

**Conclusion:** To demonstrate how therapeutic recreation has worked for children that have attended Barretstown and how we are endorsed by the medical staff in our Lady’s Hospital, Dublin Ireland and many other hospitals throughout Europe. They have endorsed this presentation under SIOP member number 1805 and are hopeful that our application will be accepted as they feel it is essential that more parent organisation avail of Barretstown or adapt our facility to work in their own country.

**ICCCPO010**

**PREDICTORS OF ENGAGEMENT IN FOLLOW-UP CARE OF YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER**

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**Purpose:** The need for long-term follow-up care for childhood cancer survivors is essential given potential treatment-related morbidities (i.e., late effects) and new cancer diagnoses. However, less than 20% receive cancer-related follow-up care as adults and there is little know about predictors of attendance at follow-up care. Further, up to 50% of survivors experience post-traumatic stress (PTS), which has been found to impact health care utilization and behaviors, and to relate to psychological impairment. The current study examines the association of posttraumatic stress, in addition to disease and demographic variables, to attendance at follow-up oncology appointments.

**Method:** The study used an existing dataset of young adult survivors (N = 101, ages 18 to 30) that includes data on PTS, treatment intensity, perceived life threat, and severity of late effects. Additional chart reviews were conducted to assess whether or not survivors attended an oncology follow-up appointment in the previous three years.

**Results:** Survivors who attended a follow-up oncology appointment (n = 44, 44%) were more likely to have clinical PTS symptoms of re-experiencing and arousal symptoms, have higher perceived life threat, have less time elapsed since treatment ended (10.0 vs 12.6 yrs), and to be older at diagnosis (10.2 vs 7.3 yrs). Avoidance PTS was not related to care.

**Conclusion:** Results confirm a relationship between PTS and engagement in follow-up care. With the exception of avoidance PTS, more PTS related to higher engagement in care. More research is needed to confirm whether or not symptoms of arousal and re-experiencing may provide motivation to continue seeking care, or if coming back to clinic may facilitate/maintain such symptoms. Moreover, those who are further out from treatment, younger at time of treatment, and have less perceived life threat are less likely to return to clinic and may require anticipatory counseling to maintain their engagement in care.

**ICCCPO011**

**MEDICAL SUPPORTING SYSTEM FOR CHILDHOOD CANCER SURVIVORS**

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4St. Luke’s Hospital, Pediatrics, Tokyo, Japan

**Purpose:** We report on a mutual aid project that supports childhood cancer survivors who face the difficulty with getting life insurance.

**Method:** First, we researched on the present status of life insurance needs of childhood cancer survivors by questionnaires sent to 213 families (survivors and their parents). 164 families answered (the response rate was 78.8%) and 84% of them reported that they needed a life insurance and felt uneasy for their future without it. Second, we worked on insurance companies. An insurance company got interested in development a new medical insurance product for survivors, but it wasn’t realized because of the too small number of survivors to sustain it on commercial basis. Finally, we decided to establish a mutual aid project cooperated with an affinity consulting company. Again, we conducted questionnaire survey of survivors and their families.
who answered the first questionnaires for understanding of their health status to set the premiums, terms and conditions.

Results: Oncologists who are leading the pediatric oncology in Japan joined as directors and it was named as “HEART LINK”. It provides two products, one is intended for survivors and the other one is intended for anybody healthy. It is a mutual aid project, namely, healthy policyholders support survivors. We have 293 policyholders and have experienced to cover 5 people since we started the activity.

Conclusion: The population of childhood cancer survivors now is large and growing. It is very important to support childhood cancer survivors for their long life. They are supposed to be the next generation to shoulder the future of our earth.

ICCCPO012

CLINICAL LONG TERM FOLLOW-UP WITH SURVIVORS
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Children Cancer Association of Japan, Survivor group, Tokyo, Japan

Purpose: Now in Japan, happily, we have many survivors who are over 20 years old. But at the same time, survivors can experience many problems of late effects including psychological issues. They face difficulties to get the correct information about their treatment they got in their childhood. Also survivors need to know the effects of treatment, information of life-style related disease, the correct timing to change the doctor from pediatrics and how to think or handle our disease when we face our life events like study problems, getting jobs and marriage.

Method: It is important to build the clinical long term follow-up system including other supports like social and psychological.

Results: North America started CCSS/Childhood Cancer Survivor Study and already build up the system, but in Asia including Japan it has not been build up yet. Though now in Japan, doctors’ group have started to make up clinical long term follow-up system, and we survivors are also making our own efforts. In Japan, there are already 13 survivors’ group and each group does their original activities. They exchange the information as well as support each other. We have guidelines for survivors and have published some books to send information to the general public. The survivor’s networks are not only very helpful to ourselves but also we hope we can convey our thoughts and wishes to those in the medical field in the hope that we can contribute to the developing follow-up system.

Conclusion: To build up an effective follow-up system, the clinical work is essential. But we survivors have our part to play in making a good follow-up system and I believe our survivors’ network may contribute to that. For that reason we try to keep our network operating effectively, deal with it actively and hope to produce good and fruitful results.

ICCCPO013

POSSIBILITIES FOR JOB INTEGRATION AFTER CANCER
Maren Boesel
German Child Cancer Foundation (ICCCPO), Survivor, Heidelberg, Germany

Purpose: Based on the results of exchange of experiences, the participants should discuss the gained knowledge in following meetings with physicians and psychologists.

Method: This workshop, designed for survivors, deals with job integration. This topic is getting more and more important for long-term survivor. Based on the German social system, different structures in other countries will be compared. Following aspects will be discussed in further detail: Which kind of indications cause survivors to need support in job integration? Which types of expert advice are there in the respective countries? Are there any social laws in the field of occupational rehabilitation? In which ways are survivors supported to complete a professional education and to enter in the job market?

Results: no applicable

Conclusion: no applicable

ICCCPO014

ART HEALING AND SURVIVING 2
Sean Nurcombe
BCCSSBC, Long Term Survivor Group, Abbotsford, BC, Canada

Purpose: To continue my SIOP presentation from SIOP 2008 where I presented Art Healing and Surviving in a poster presentation.

I would like to continue to share and create another glass art piece from artwork survivors that attend Boston SIOP.

Method: I would get survivors to draw a simple sketch and I would reproduce in on glass and share our piece via mail and or facebook. I would bring a version of the Berlin SIOP piece, that many survivors participated in, to be viewed in Boston.

Results: The results would be creativity and sharing by survivors of childhood cancer and ongoing communication to maintain support for each other.

Conclusion: I would like to continue to have survivors find healing through art and carry on with the comradeship that was created in Vancouver. Berlin and hopefully Boston. I would like to meet international survivors and share with each other our experiences through art.

ICCCPO015

TREATMENT REFUSAL AND ABANDONMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN INDONESIA: AN ANALYSIS OF CAUSES AND CONSEQUENCES
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Purpose: Treatment refusal and abandonment are common causes of treatment failure in childhood acute lymphoblastic leukemia (ALL) in many developing countries. In most studies reasons for abandonment were based on the opinion of health-care providers, very few studies have focused on the parental point-of-view. Aims of the study were to analyze the parents’ reasons of abandonment and to ascertain the fate of children who abandoned treatment in a pediatric oncology centre in Yogyakarta, Indonesia.

Method: We conducted home-visits to interview families of ALL patients, diagnosed between January 2004 and August 2007, who refused or abandoned treatment.

Results: From January 2004 to August 2007, 159 patients were diagnosed with ALL of which 40 children (25%) refused or abandoned therapy. Thirty-seven (93%) of these children were home-visited. Reasons for abandonment were complex. Most parents mentioned several reasons. Financial and transportation difficulties were not the only, or even the main reasons, for abandonment. Belief of ALL incurability, experience of severe side-effects and dissatisfaction with health-care providers were also important considerations. Most patients (64%) abandoned treatment during the diagnostic-evaluation or remission-induction phase. Of the 57 patients who refused or abandoned treatment, 26 (70%) children died, and 11 (30%) children were still alive, 2 of them more than 2 years after abandonment.

Conclusion: Reducing treatment abandonment of childhood ALL in developing countries requires not only financial and transportation support, but also parental education, counseling and psychosocial support during therapy, improvement of quality-of-care and adequate management of side-effects.

ICCCPO016

PERCEPTIONS ABOUT COMPLEMENTARY AND ALTERNATIVE MEDICINE USE AMONG CHINESE IMMIGRANT PARENTS OF CHILDREN WITH CANCER
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4University of British Columbia, Pediatrics, Vancouver, Canada

Purpose: Research indicates an increase in the use of complementary and alternative medicine (CAM) among paediatric oncology patients. The use of CAM is prevalent in many Asian countries, yet little is known about its use in Chinese immigrant families living in Canada. This presentation describes 25 Chinese immigrant parents’ perception about the use of CAM with their child with cancer in Canada.

Method: A constructivist grounded theory approach was used (Charmaz, 2006). The findings are part of a larger study of the caregiving experiences of both first generation Chinese and South Asian parents of children with cancer. Parents of children at least
SIOP ABSTRACTS

PA001

METHYLENETETRAHYDROFOLATE REDUCTASE C677T & A1298C POLYMORPHISM AS A RISK FACTOR FOR CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA AND HOMOCYSTEINE LEVEL DURING INDUCTION CHEMOTHERAPY

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Purpose: To assess methylenetetrahydrofolate reductase (MTHFR) polymorphism as a risk factor for developing acute lymphoblastic leukemia (ALL). To delineate association between MTHFR polymorphism and homocysteine levels during induction therapy.

Method: All newly diagnosed ALL patients treated as per UK ALL XI protocol were included in this case control study. Controls consisted of adult patients with no history of hematological or other malignancies. Both patients and controls were Indians by birth. MTHFR polymorphism A1298C and C677T test was done after DNA extraction by PCR amplification on cases and controls. Homocysteine level were done on day-1, day-8 and day-29 of induction therapy.

Results: MTHFR polymorphism was done for 30 patients (male-22, female-8) with average age 5.1 years (1–8 yr). Controls were 29 (male-22, female-7) with average age 29.44 years (24–44 yr). MTHFR 677 polymorphism allele frequency was 33.3% vs. 34.5% for controls. Frequencies of MTHFR 677CC, 677CT and 677TT genotype were 66.7%, 20% and 13.3% vs. 65.5%, 27.6% and 6.9% in controls. For MTHFR 1298, we observed a polymorphic allele frequency of 56.7% vs. 34.5% in controls. Frequencies of MTHFR 1298AA, 1298AC and 1298CC genotypes were 43.3%, 46.7% and 10% vs. 34.5%, 37.9%, and 27.6% for controls, respectively. We did not observe difference in the prevalence of either the MTHFR 677 or 1298 genotypes between the cases and controls. No significant protective nature observed except 1298CC which was found to be about 2 fold protective. Average homocysteine level on day-1, day-8 and day-29 were 11.54, 9.25 and 8.7 micromoles/L respectively. Only on day 8 of chemotherapy 677CC showed lower homocysteine values than 1298CC but these were statistically insignificant (p value-0.097, OR = 2, 95% CI-1.1–3.7).

Conclusion: MTHFR polymorphism has no relation with susceptibility to develop ALL in Indian children. MTHFR polymorphism has no correlation with homocysteine levels during induction chemotherapy of ALL.

PA002

METHYLENETETRAHYDROFOLATE REDUCTASE/MTHFR AND THIOPURINE METHYLTRANSFERASE/TPMT GENE POLYMORPHISMS AND THERAPY RESPONSE IN INDIAN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA

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Purpose: Functional polymorphisms in MTHFR and TPMT genes have been shown to modulate the response to methotrexate (MTX) and 6-mercaptopurine (6MP), during maintenance therapy of pediatric acute lymphoblastic leukemia (ALL). The aim of this study was to evaluate the impact of mutations in MTHFR and TPMT genes on therapy response in Indian children with ALL. The primary objective of this study was to evaluate the impact of mutations on MTHFR and TPMT genes on therapy response in Indian children with ALL.

Method: Samples of 82 children, 0–18 yrs of age, with ALL, treated on the modified BFM-90 protocol, were analyzed for MTHFR C677T and A1298G and TPMT*2, *3A and *3C polymorphism by PCR-RFLP or allele-specific PCR techniques. Medical records were retrospectively reviewed for therapy response and toxicity.

Results: The MTHFR genotypes were observed in 677CC (65%), 677CT (30%) and 677TT (5%), while the 1298AA, 1298AG, 1298GG genotypes in 35%, 56% and 9% cases respectively. The frequency of the TPMT alleles were *1/*3C (4%), *1/*2 (4%) and *1/*3A (9%). Occurrence of hematologic, hepatic and gastrointestinal toxicities were similar among all MTHFR genotypes, although mucositis was more frequent (35% vs 13%, p = 0.08) and median SGPT values were higher (131 IU vs 91 IU) among C677T mutants (p > 0.05). All patients achieved complete remission with RFS of 88% at a median follow-up of 30 months. The RFS for wild vs C677T mutants was 9% vs 17% (p > 0.05). Frequency of relapse by MTHFR genotypes were 11%, 677CC, 20%, 677CT, 0%, 677TT, 0%, 1298AA, 8%, 1298AG, 0%, 1298GG. None of the TPMT mutants relapsed (100% RFS) and the toxicities were comparable among the various genotypes, however the tolerated median 6-mercaptopurine doses were 14 mg/m2 lower among the mutants (p = 0.005).

Conclusion: This study reports the observed prevalence of MTHFR and TPMT polymorphisms, in Indian children with ALL. The relapse rate and mucositis was higher among patients with C677T polymorphism while those with TPMT polymorphism had lower relapse rates; highlighting the importance of pharmacogenetics in modern day ALL therapy.

PA003

RFCl AND MTHFR GENE POLYMORPHISMS AND RISK OF PEDIATRIC ACUTE LYMPHOCYTIC LEUKEMIA WITH COMMON ACQUIRED ALTERATIONS

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Purpose: To assess methyltetrahydrofolate reductase (MTHFR) polymorphism as a risk factor for developing acute lymphoblastic leukemia (ALL). To delineate association between MTHFR polymorphism and homocysteine levels during induction therapy.

Method: All newly diagnosed ALL patients treated as per UK ALL XI protocol were included in this case control study. Controls consisted of adult patients with no history of hematological or other malignancies. Both patients and controls were Indians by...
PA005
THE GLUTATHIONE-S-TRANSFERASE P1 105 ILE > VAL POLYMORPHISM (GSTP1 105 I > V) MIGHT BE ASSOCIATED WITH POORER RECURRENCE-FREE SURVIVAL IN PEDIATRIC PATIENTS DIAGNOSED WITH ACUTE LEUKEMIA

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Purpose: One of the most challenging issues in oncology is the prediction of disease progression and response to therapy. The inter-individual differences in response to drugs are due, at least in part, to genetic polymorphisms. Therefore, the aim of this project is to identify genetic markers that might help to predict acute leukemia (AL) progression, resistance to chemotherapy and/or development of therapy-related side effects.

Method: We have recruited pediatric patients diagnosed with AL from one Hospital Center in Buenos Aires. The protocol was approved by the Ethic Committee and follows the ethical principles for medical research involving human subjects enunciated by the Declaration of Helsinki. Patients’ relatives or guardians signed an informed consent before sample donation. We draw peripheral blood and extracted lymphocyte DNA. We genotyped 6 polymorphisms (4 SNPs and 2 gene deletions) within genes related to xenobiotic metabolism: glutathione-s-transferases (GSTP1 105 I > V, rs11371, GSTT1 null; GSTM1 null), ATP-binding cassette B1/multidrug resistance gene 1 (ABCB1/MDR1 3435 C > T, rs1045642), cytidine deaminase (CDA -451 C > T, rs52545), and 5,10-methylenetetrahydrofolate reductase (MTHFR 677 C > T, rs1801133). GSTT1 and GSTM1 polymorphisms were assessed by PCR multiplex reactions, and the rest by PCR-RFLP.

Results: Preliminary results from 100 specimens showed a non-significant trend to a higher frequency of GSTM1 null genotype in pediatric AL (60%) compared to adult AL (25%) (Fisher p = 0.07). We also found that homozygote patients for the GSTP1 105 V allele had poorer recurrence-free survival compared to homozygote GSTP1 105 I patients (log-rank p = 0.03).

Conclusion: Our findings showed that GSTP1 and GSTM1 polymorphisms might be involved in AL development and progression. The study of GST polymorphisms might become an important tool to choose the best follow-up schema for each patient; increasing the survival and quality of life. Therefore, these results warrant the study of more AL patients and performing multivariate analyzes.

PA006
GILBERT’S SYNDROME AS A POTENTIAL RISK FACTOR FOR ETV6/RUNX1 POSITIVE CHILDHOOD ACUTE LYMPHBLASTIC LEUKAemia (ALL)

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Purpose: Acute lymphoblastic leukaemia (ALL) is the most common malignant disease in childhood. Although the introduction of treatment protocols has improved survival, inter-individual differences in drug responses are an important cause of resistance to treatment and adverse drug reactions. Pharmacogenetic studies are providing a rational basis for further treatment efficacy and reduction of complications. Methotrexate (MTX) is a key component in the treatment of childhood ALL. Two polymorphisms have been described in the methylene tetrahydrofolate reductase (MTHFR), that catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate in the folic acid cycle, interrupted by methotrexate. The polymorphisms C677T and A1298C are nonsynonymous aminocid changes that have been associated with the decreased activity of MTHFR and increased levels of homocysteine. Previous works have associated MTHFR 1298C and 677T alleles with toxicity.

The aim of the present study was to determine if there was a correlation between MTHFR C677T and A1298C polymorphisms and toxicity and/or outcome during therapy in paediatric Spanish ALL patients treated with the LAL/SHOP protocol.

Method: DNA was extracted from blood samples of 120 paediatric ALL patients treated with the LAL/SHOP 99 and 2005 protocols by standard phenol-chloroform method. We analyzed MTHFR C677T and A1298C polymorphisms by PCR-RFLP.

Results: The individuals with a less functional variant in homozygosis or heterozygous for both showed a significantly slower methotrexate clearance, than the rest of individuals analyzed, only when they were treated with 3g/m2 MTX. No differences were found when 5g/m2 were administered.

Conclusion: Differences in the clearance of methotrexate are dependents of the genotype and the methotrexate dose. Other genes of this pathway, such as SLCO1B1, might be subject of study to clarify the results obtained.
Purpose: To determine the frequency of Gilbert’s syndrome (GS), a mild glucuronidation defect caused by polymorphisms in the UGT1A1 gene, in Childhood B-precursor acute lymphoblastic leukemia (BpALL) and to determine if the frequency varies in the different cytogenetic subgroups.

Method: 95 children with ALL diagnosed between January 2000 to January 31, 2010 and following at least 9 months were tested for polymorphisms in the promoter for the UGT1A1 gene using the FDA approved Invader assay and by a TaqMan PCR assay. ETV6/RUNX1 was tested by fluorescence in situ hybridization in 82 and by PCR in 6; seven were excluded from statistical analysis either because the samples for UGT1A1 testing were obtained after a bone marrow transplantation, diagnostic blasts cell samples were not available for retrospective testing for ETV6/RUNX1 and two were not part of our institutional cohort of cases.

Results: The frequency of GS was higher in children with ETV6/RUNX1 ALL compared to other BpALL cases - 9/31 children with ETV6/RUNX1 ALL vs 4/57 with ALL with other cytogenetic findings. Odds ratio 5.42 with confidence intervals of 1.33, 23.76; p = 0.0095 by 2 tailed Fisher exact Test. Of 13 children with GS, 11 were homozygous for UGT1A1 [A (TA)7TA] allele and two African American children had (TA)5(TA)8 genotype.

Conclusion: This study was triggered by the observation that the first two children with BpALL molecularly confirmed to have GS in our clinic, also had ETV6/RUNX1 associated BpALL. Certain environmental carcinogens, such as heterocyclic polynamines, topoisomerase II inhibitors and flavonoids are eliminated by glucuronidation and are substrates for UGT1A1; thus exposure to these agents may be increased in those with GS. Our studies showed an association of GS and ETV6/RUNX1 ALL, suggesting that carcinogens eliminated by glucuronidation may be involved in the pathogenesis of a common variant of BpALL.

### PA008

**MRNA GENE EXPRESSION OF SERP1, XPO7 AND XPC ARE ASSOCIATED WITH PROGNOSIS IN CHILDHOOD CD10 B-LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA**

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Purpose: The aim of this study was to validate the 13 genes more differentially expressed in B-lineage ALL samples with good and poor response to induction therapy identified in a previous microarray study and to analyze their association with clinical/biological features and prognosis in consecutive B-lineage ALL samples.

Method: Relative mRNA expression of 13 genes (CCNDBP1, CREG1, SERP1, SNFT, TAXBP1, FUT1, XPO7, BAG4, CSK1B, IGSF4, CYP4A11 and CYP11A1) was validated in 88 consecutive B-lineage CD10 positive ALL children, classified and treated according to GBTLI-ALL 99 protocol, by quantitative real time PCR. The association of the expression values of the selected genes with the clinical and biological features was made by Mann-Whitney test. Five-years event free survival was analyzed by Kaplan-Meier and log-rank test.

Results: Significant association was observed between initial WBC count > 50,000/ mm³ and higher expression levels of XPC (P = 0.02); response at day 7 and higher levels of the genes SNFT (P = 0.005), FUT1 (P = 0.02), XPO7 (P = 0.05) and BAG4 (P = 0.04); bone marrow M2/3 at day 28 and higher levels of XPO7 (P = 0.04); minimal residual disease at day 28 and genes CREG1 (P = 0.01) and CYP4A11 (P = 0.04), complete continuous remission and higher levels of SERP1 (P = 0.02) and unfavorable event (relapse or death) with higher levels of XPO7 (P = 0.01) and XPC (P = 0.02). Five-years EFS according to expression values lower or higher than percentile 75 (P75) were 78.8 versus 95.5 (P = 0.06) to SERP1; 88.7 versus 68.0 (P = 0.04) to XPO7 and 86.1 versus 72.5 (P = 0.05) to XPC genes.

Conclusion: The present results indicate genes that may play a key role in the induction therapy response in B-lineage ALL, and that could represent potential therapeutic target for the management of poor responders ALL children.
miR24, miR155, miR16, miR128b, miR142–3p, miR29b, miR223. Values were normalized to normal B- and T-cells.

Results: The overexpression of the studied miRs is well-known in several type of tumors and were described also in diffuse large B cell lymphomas (DLBCL). Our results showed, that this overexpression is not general characteristic in different types of lymphoma and leukemia cells. Overexpression of the all examined oncomiRs were found only in BHDL1 - DLBCL - and KM-H2 - Hodgkin-lymphoma - cells. The upregulation of miR21 and miR155 – well known oncomiRs – was found only in these cell lines. However, miR155 expression failed in all other cell lines except one Burkitt lymphoma cells. MiR21 was only slightly expressed or missed in the studied non DLBCL NHL, and Hodgkin lymphoma and leukemia cells. Interestingly, miR128b was overexpressed in all cell lines, but extremely high values were measured in ALL cell lines and isolated ALL cells.

Conclusion: Our results suggest that different hematological malignancies have distinct oncomiR expression profiles. Increasing knowledge of miR expression signatures may help to characterize and distinguish tumor subtypes, predict prognosis, and identify their regulatory role in cellular processes.

Support: OTKA-T68341-T81624

PA010

INCIDENCE AND FOLLOW-UP OF PEDIATRIC PATIENTS WITH BCR/ABL POSITIVE ACUTE LYMPHOBlastic LEUKEMIA

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Purpose: Determine frequency and follow up of pediatric BCR/ABL positive ALL patients at Children’s Hospital “JM de los Ríos”, from January 2005 to December 2008. Assess hematologic and molecular remission, disease free survival, mortality, adhesion and side effects of imatinib.

Method: Patients diagnosed with ALL underwent evaluation for BCR/ABL oncogene, those positive received our high risk protocol plus imatinib. Data were obtained from charts, statistically processed with Epi-Info, Med-Calc and expressed in Kaplan Meier graphs.

Results: 107 patients were diagnosed with ALL, 10 (9.34%) were BCR/ABL positive. Of these, the mean age of diagnosis was 5.9 years. 3 girls and 7 boys. Initial WBC less than 50,000/mm³. 60% had < 5% blasts in bone marrow at day 15, but all obtained remission at induction. 20% had infiltration to scalp and 66% had hepatosplenomegaly. 90% received imatinib 340 mg/m² from the moment BCR/ABL oncogene was obtained. One patient did not receive imatinib and died from relapse during consolidation.

Imatinib was started at different times. 1 patient at induction, 3 in consolidation, 5 during maintenance. One patient abandoned treatment after relapse and two discontinued temporally due to medullary toxicity. Eight patients achieved hematologic and molecular remission, 7 before and 1 after starting imatinib. One patient finished protocol and is on imatinib, hematologic and molecular remission. Two died in relapse: 1 from sepsis, another with refractory disease. Overall survival was 72% and free of event survival 54%. None had compatible donor for transplant. From all patients (107) 19 relapsed and 3 (15.7%) of them were BCR/ABL positive. Conclusion: Incidence of pediatric BCR/ABL positive ALL in this study is high. No patient had high WBC, 20% achieved remission at day 15. Imatinib did not modify free of event survival but could prolongate remission. BCR/ABL results were not available on time for most patients. Curative treatment is hematopoietic stem cell transplant.

PA011

EVALUATION OF RETICULIN FIBER DENSITY AND MICROVESSEL DENSITY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: The aim of this study was evaluation of BM stroma in pediatric acute lymphoblastic leukemia (ALL) patients in respect to microvessel density (MVD) and reticulin fiber density (RFD) and investigation of the relation between these stromal characteristics with other proposed prognostic factors.

Method: A hundred sixty seven bone marrow iliac biopsies obtained at diagnosis from children 1 to 15 years of age with ALL were retrospectively evaluated of which 119 biopsies were available with sufficient quality. RFD was defined as volume reticulin fibers per volume reference tissue.The micro vessels were stained immunohistochemically with anti-Factor VIII-related antigen (anti v-WF) (DAKO).

MVD was the mean value of counted microvessels in 3 fields at ×40 for each biopsy. Results: RFD was found higher in B-cell precursor ALL compared to T-ALL patients. In patients with leucocyte count less than 20,000/mm³ at admission, RFD was found higher compared to ones with more than 20,000/mm³. In B-cell precursor ALL group, RFD was inversely correlated with leucocyte count. Opposite to this, MVD was found higher in patients with higher leucocyte count at admission. However any significant correlation between WBC and MVD was not detected. Although RFD was found higher in nonresponders to treatment evaluated both at day 8 and day 15, any effect on relapse ratio, overall and event free survivals were not shown. Similar to this MVD was not shown to have any prognostic effect on relaps ratio and survivals.

Conclusion: The marked difference in RFD between B-cell and T cell ALL, in line with a previous publications further emphasize the biological differences between these two entities and the need for analysing and may be also treating them separately. The reason why RFD was negatively correlate with WBC is a question. Similar studies will provide comparison and better interpretation of the results and help to clarify our findings.
SIOP ABSTRACTS 853

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Purpose: Chemotherapy protocols currently used in children for the treatment of acute lymphoblastic leukemia (ALL) have increased the complete remission rate. However, a subset of patients can develop drug resistance or drug side effects, which may hamper the efficacy of treatment and its outcome. An isomorph of Manganese-superoxide-dismutase (MsSOD) was recently isolated and sequenced for the first time from a human Liposarcoma cells and obtained in recombinant form. The protein, which is active as an antioxidant enzyme, showed a specific and selective cytotoxicity on many cancer cell lines. The aim of this study was to test the ability of this molecule to inhibit or to interfere with the growth of leukemic cultured pediatric cells.

Method: Lymphoblastic cells of children with ALL B or T cell, cultured in RPMI medium, supplemented with 1% PEN STREP and 10% BSA, at 370 °C, were treated for 3 hours with MsSOD. After cell fixation, immunocytochemical reaction at light and electron microscopy was performed by using a specific polyclonal antibody directed against the uncleaved leader peptide of MsSOD. Western blot assay was used to evaluate the expression of apoptotic proteins (Bel-2, BAX, Bcl-XI).

Results: Following MsSOD treatment, ALL cells displayed an intense cytoplasmic positivity to anti-MsSOD antibody, a reduction in size, nuclear apoptotic fragmentation in some of them and an increased expression of Bel-2 and BAX genes.

Conclusion: MsSOD is able to enter into cancer ALL cells and induce stimulation of apoptotic pathway These preliminary data are consistent with those previously obtained in breast cancer cells (Mancini et al; Int J Cancer.119: 932-943; 2006) and suggest that this molecule may play a role as anti cancer agent in LLA too.

PA016

DIFFERENTIAL GENE EXPRESSION PROFILES IN STEROID TREATMENT EARLY RESPONSE FROM CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: The steroid initial treatment response of Acute Lymphoblastic Leukemia (ALL) patients is an important component of the classification criteria, designating high risk for those cases that do not present a suitable response. Nevertheless, these classification criteria do not have enough precision to assign the treatment according to the neoplastic behavior in the all cases. With the aim of identifying the associated patterns of genomic expression related to steroid initial treatment response, we propose a prospective, comparative and cross-sectional study using Affymetrix microarray platform with the HG-U133 2.0 Plus array.

Method: We included 50 pediatric patients with confirmed diagnosis of Acute Lymphoblastic Leukemia treated at the National Institute of Pediatrics, Mexico. Once we obtained the consent, we performed bone marrow aspirate by usual methodologies for diagnosis confirmation and lymphoblast sampling for microarray hybridization. The diagnosis, treatment and response evaluation were realized according to the conventional procedures of the National Institute of Pediatrics. The statistic analysis was performed with Affymetrix Expression Console v1.1 and Partek’s Genomics Suite for quality assessment and gene expression profiles detection. The quality control assay with Robust Multi-Chip Results: Average algorithm showed a correlation between all the included microarrays from .83 to 1.0, considering all the microarray data adequate for the statistic analysis. We found a list of genes differentially expressed according to the steroid treatment response and to the B/T immunophenotype and integrated the metabolic pathways apparently related to differentially expressed genes.

Conclusion: These results show that gene expression profiles may clearly differentiate ALL patients according to their steroid treatment response including differences in the immunophenotype B or T. Differential gene expression profiles in ALL are being analyzed as a diagnostic tool to provide a more accurate allocation criteria for antineoplastic treatments in patients with this disease and allow us to understand the neoplastic behavior on different treatment response scenarios.
PA017

INCIDENCE OF Ig/TCR GENE REARRANGEMENTS IN A SINGLE INSTITUTION IN ARGENTINA: SETTING UP MINIMAL RESIDUAL DISEASE IN CHILDHOOD ALL

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Purpose: The functional regions of rearranged immunoglobulin (Ig) and T-cell receptor (TCR) genes are considered as DNA fingerprints of the leukemic cells and are currently considered as excellent targets for minimal residual disease (MRD) detection. We present the first results of Ig/TCR gene rearrangements characterization in ALL, as part of the setting-up of MRD detection and describe the rearrangements’ frequencies and the first patient-specific allele-specific oligonucleotide (ASO) primers designing results.

Method: DNA samples from 146 non-T-ALL children (121 older than 1 year-old and 25 infants) were retrospectively analysed. Amplification of rearranged IGH, IGK, TCRD, TCRG and TCRB genes was performed in multiplex PCR-heteroduplex (BIOMED-2). The homoduplex bands were purified and sequenced. The ASO-primers were positioned within and around the specific junctional region and designed according to standard guidelines.

Results: At least one rearrangement was found in 139 (95%) patients and > 2 in 119 (82%) patients. In total, 444 rearrangements (mean patient: 3) were detected: 151 IGH, 87 IGK, 32 TCRB, 72 TCRD, 102 TCRD. The incidences of rearrangements were: in children > 1 year-old: 74% IGH, 58% IGK, 36% TCRB, 45% TCRD, 63% TCRD and in infants: 76% IGH, 16% IGK, 12% TCRB, 8% TCRG, 24% TCRD. The VDJ region showed an average of 2.7 (0–33) deleted germinal nucleotides and 2.1 (0–41) randomly inserted nucleotides. At present, we have designed 103 ASO-primers for 53 patients from which 81 ASO-primers (45 patients) have been applied for RQ-PCR-MRD.

Conclusion: The frequencies of Ig/TCR gene rearrangements found in our patients > 1 year-old did not show major differences with the published data, except for IGH (p < 0.02). The incidence of rearrangements in infants was significantly lower than in the older children (p < 0.0001). The sensitivity and quantitative range were adequate for MRD quantification in 79% of the designed ASO-primers. The presented data support the opportunity of conducting RQ-PCR-MRD-based protocols.

PA018

CLINICAL SIGNIFICANCE OF IMMUNOPHENOTYPIC MARKERS IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: Cell-marker profiling has led to conflicting conclusions about its prognostic significance in T-ALL. The aim of this study was to investigate the prevalence of the expression of CD34, CD10 and myeloid associated antigens (CD13/CD33) in childhood T-ALL and to relate their presence to initial clinical and biologic features and early response to therapy.

Method: This study included 67 consecutive patients with newly diagnosed T-ALL recruited from the Children’s Cancer Hospital in Egypt during the time period from July 2007 to June 2008. Immunophenotypic markers and minimal residual disease (MRD) were studied by five-color flow cytometry.

Results: The frequency of CD34 was 34.9%, CD10 33.3%, while CD13/CD33 was 8.8%. No significant association was encountered between CD34, CD10 or myeloid antigen positivity and the presenting clinical features as age, sex, TLC and CNS leukemia. Only CD10+ expression had significant association with initial CNS involvement (p = 0.039). CD34 and CD13/CD33 expression was significantly associated with T-cell maturation stages (p < 0.05). No relationship was observed for age, TLC, gender, NCI risk or CNS involvement with early response to therapy illustrated by BM as well as MRD day 15 and day 42. CD34+, CD13/CD33+ and early T-cell stage had high MRD levels on day 15 that was statistically highly significant (p < 0.01), but CD10+ had statistically significant lower MRD level on day 15 (p < 0.049). However, only CD34 retained its significance at an MRD cut-off level of 0.01%.

Conclusion: CD34, CD10, CD13/CD33 expression, as well as T-cell maturation stages, may have prognostic significance in pediatric T-ALL as they have a significant impact on early clearance of leukemic cells detected by MRD day 15.

PA019

NOTCH1 AND PTEN MUTATIONS IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA – IMMUNOMOLECULAR ASPECTS

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Purpose: Recent studies have shown an important connection between these genes, since NOTCH1 activation blocks PTEN function in the PI3K-AKT pathway, resulting in constant activation. Moreover, PTEN mutations inactivate this gene, leading to constant activation. Since NOTCH1 activation blocks PTEN function in the PI3K-AKT pathway, resulting in constant activation.

Method: The series of T-ALL consecutive Brazilian cases was evaluated regarding the following variables: age range (< 1 - < 9; 9 - 21 years-old), T-ALL subtypes, and gene mutations. T-ALL diagnosis was made according to morphology and early response to therapy.

Results: Our results showed that mutations frequency was 52.3% for NOTCH1 and 8.1% for PTEN, and 2.7% of cases presented both alterations. Concerning the domains involved in NOTCH1 mutations, the HD and PEST domains, which were screened by PCR and sequencing. PTEN mutations were evaluated in exons 1 and 7 by PCR, heteroduplex assays and sequencing.

Results: Our results showed that mutations frequency was 52.3% for NOTCH1 and 8.1% for PTEN, and 2.7% of cases presented both alterations. Concerning the domains involved in NOTCH1 mutations, the HD and PEST domains, which were screened by PCR and sequencing. PTEN mutations were evaluated in exons 1 and 7 by PCR, heteroduplex assays and sequencing.
predominantly found in T-III (NOTCH1) and T-II (PTEN) stages, but this correlation was not significant.

**Conclusion:** This is the first study in a representative T-ALL Brazilian series of cases establishing the frequencies of NOTCH1 and PTEN mutations. We also showed no prognostic relevant relation between these alterations and T-cell maturation stage. Determined the frequency of mutations, we will perform a prognostic analysis considering mutation status and age-related T-ALL.

**PA020**

**A NEW ENTITY OF T LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA (T-ALL) RESPONDING TO TYROSINE KINASE INHIBITOR (IMATINIB-MESYLATE): COMPLETE CHARACTERIZATION OF A PEDIATRIC CASE WITH RESISTANT DISEASE**

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**Purpose:** Prognosis in pediatric T-ALL has improved in recent years but some cases suffer from relapse/resistant diseases, which are mostly fatal. New methodologies have shown that several genes with tyrosine kinase activity are involved in the leukemogenic process. Our aim was to characterize a case of pediatric T-ALL who showed a clinical response to Imatinib Mesylate (IM).

**Method:** We performed immunophenotypic, conventional karyotype, FISH, RT-PCR, sequencing, western-blots analyses, detection of minimal residual disease (MRD), SNP's arrays.

**Results:** A 4-year-old black boy from Mauritius with T-ALL during maintenance of AIEOP-BFM 2000 protocol showed a bone marrow isolated CD10+CD13+CD117+/c-kit- relapse. Karyotype showed a 47,XY.+8.del(11)(q13q23). The MLN gene involvement was excluded. After two courses of IDA-ARAC, the patient recovered with circulating blasts. Based on these data, we designed a therapy with IM (300 mg/mq daily). We shortly observed a dramatic reduction of peripheral blasts count and splenomegaly. He achieved a partial remission, but after 6 months he suffered from a relapse and died for progressive disease. Sequencing analyses of cKit gene did not show any alteration. Detection of MRD confirmed that the clone of relapse was the same as diagnosis. By SNPs, we found deletions in band 9p21.3 (CDKN2 genes) and band 16q22.1 (NFATC3 gene). FGFR, cKit, PDGFRB, ABL1 genes, encoding putative IM targets, did not show copy number abnormalities or loss of heterozygosity. Conversely we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity. Conversely, we observed a loss of 0.6 Mb at 4q12 including PDGFRB gene which encodes a tyrosine kinase receptor. A del(4q)q12(12) of about 800 kb generating a putative IM target, did not show copy number abnormalities or loss of heterozygosity.

**Conclusion:** We pointed out on a potential new entity of T-ALL subtype which could benefit from treatment with tyrosine kinase inhibitors. Further studies with a larger population are needed.

**PA021**

**GENE EXPRESSION PROFILING INDICATES A DOMINANT NEGATIVE ROLE OF PAX5/TEL ON ENDogenous PAX5 IN PRE-BI CELLS**

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**Purpose:** PAX5 is a transcription factor essential for B-cell development, frequent target of abnormalities in B-cell precursor ALL cases, including monosomalic loss, point mutations or chromosomal translocations. The role of these lesions is poorly understood. We previously showed that PAX5/TEL protein in mouse pre-BI cells acts as an aberrant transcription factor with repressor function, causing a block on B-cell differentiation, short-term IL-7 independence resistance to the anti-proliferative and pro-apoptotic effects of TGFβ1. Moreover, PAX5/TEL enhances cell migration towards CXCL12, with the overexpression of CXCR4.

**Method:** We analyzed gene expression profile in pre-BI cells transduced either by MGR-PAX5/TEL-GFP or by MGR-PAX5 (Affymetrix GeneChip technology) in order to comprehensively understand how PAX5/TEL interferes with PAX5 and TEL pathways and to identify cellular processes affected by its expression.

**Results:** Gene functional classification analyses suggested that PAX5/TEL induces gene clusters functionally related to fundamental cellular processes, such as phosphorylation and kinase activity, transcription, B cell receptor signalling, as well as regulation of transmembrane molecules involved in adhesion.

**Conclusion:** These analyses further sustain the role of PAX5/TEL as a repressor of transcription, with dominant negative effect on endogenous PAX5, interfering with the expression of its target genes, mainly responsible for the process of B-cell differentiation.

**PA022**

**LOW DIETARY INTAKE OF CALCIUM ASSOCIATED WITH INCREASED RISK OF FRACTURE IN MALES UNDERGOING TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA**

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**Purpose:** Bone fractures occur frequently in children undergoing treatment for acute lymphoblastic leukemia (ALL). Prospective studies suggest that high dietary calcium intake is associated with improved bone mineralization and reduced fracture risk in healthy children and adolescents. Preliminary results of a prospective multi-institution study investigating dietary micronutrient intake and treatment related toxicity in children receiving treatment for ALL are reported.

**Method:** Assessment of dietary intake is incorporated within the ongoing DFCI ALL Consortium Protocol 05-001. Institutional review board approval was obtained by each participating center. Dietary intake is assessed in children ages 2–18 yrs using the pediatric Harvard Food Frequency Questionnaire. Associations between dietary intake and risk of fractures were analyzed for those participants for whom bone toxicity data were available using SPSS®v17.

**Results:** Dietary intake at diagnosis and its association with bone toxicity was analyzed for 176 participants. Mean age was 6.6 yrs (SD 4.4) and 77 were female, 98 were male. Leukemia risk classification included 112 Standard Risk and 63 High Risk. Daily calcium intakes less than the Daily Recommended Intake (DRI) were observed in 42 (54%) females and 69 (70%) males at time of diagnosis of ALL. Fractures were subsequently observed in 11 females and 11 males. Among males only, calcium intake below the DRI at diagnosis was associated with an increased risk of fracture (OR 5.5; 95% CI 1.5, 20.7), even after adjusting for age or leukemia risk category. Risk of fracture further increased in males with intake < DRI for both vitamin D and calcium (OR 8.0; 95% CI 1.1, 55.1).

**Conclusion:** Males undergoing treatment for ALL with low intakes of calcium are at increased risk for developing fractures, independent of age and leukemia risk group. Dietary interventions aimed at improving intake of calcium and vitamin D during treatment for ALL requires further study.

**PA023**

**MANAGEMENT OF THROMBOEMBOLISM IN CHILDREN AND ADOLESCENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA**

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**Purpose:** To describe the management of thromboembolism (TE) in children and adolescents with acute lymphoblastic leukemia (ALL).
**POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN CHILDREN WITH ACUTE LYMPHOBластIC LEUKEMIA**

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**Purpose:** Children affected by acute lymphoblastic leukemia (ALL) are well known to be a high risk population for central nervous system (CNS) complications. Posterior reversible encephalopathy syndrome (PRES) is a neurological disorder characterized by clinical and radiologic signs. The characteristic radiologic findings are bilateral gray and white matter edema in the posterior regions of the cerebral hemispheres.

**Method:** We retrospectively analyzed clinical and radiologic findings in ten children with the diagnosis of ALL and PRES.

**Results:** Ten patients were diagnosis of acute lymphoblastic leukemia and PRES syndrome. All patients were received cytostatic therapy and intrathecal methotrexate. The most common presenting symptoms were seizure and altered mental status; others included headache, hypertension, convulsions, amaurosis, evidence of nerve palsy and cortical blindness. In addition to physical examination, all patients underwent electroencephalography (EEG), magnetic resonance imaging (MRI) and lumbar puncture to exclude CNS leukemia and infection. EEG was pathological in nine patients. MRI revealed multifocal abnormalities in parietal and occipital regions in all ten patients. All patients received anticonvulsive and antithyptertensive drugs and cytostatic therapy was continued with favorable outcome. In nine patients no steady lesions were confirmed and one had had discrete facial nerve palsy. Control MRI showed nearly complete or complete resolution in all patients.

**Conclusion:** PRES syndrome was clinically reversible event in all patients.

**PA027**

**CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA WITH HYPERLEUKOCYTOSIS AT PRESENTATION: MANAGEMENT EXPERIENCE AND LESSONS FROM A TERTIARY CARE INSTITUTION IN INDIA**

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**Purpose:** Survival for childhood acute lymphoblastic leukemia (ALL) has reached 80% over the last decades. In order to further increase survival, new technologies and medication are being developed, adding to budgetary constraints in healthcare. This study determined the quality of life (QoL), direct costs of care, and costs per quality adjusted life year (QALY) for the two most recent Dutch ALL protocols, based on a representative single-center cohort. The aim was to assess the effect of incorporating more expensive medication (pegasparaginase) and a new diagnostic technique (minimal residual disease levels) in the latest protocol.

**Method:** Patients between the ages of 1–18 years, diagnosed between 2002–2006, and treated with chemotherapy only were included. QoL was assessed at least six months after the end of treatment using the Health Utilities Index Mark 3. All direct medical costs, including costs made in satellite hospitals, were determined for the duration of treatment.

**Results:** Most children (53–67%) were in optimal health state. There was a clinically important difference in overall QoL in favor of the newest protocol (scores 0.80 ± 0.28 vs. 0.85 ± 0.26). Compared to norms, children with ALL scored lower on emotion and overall QoL. Mean direct medical costs were between 85,821–127,255, depending on risk group. In-hospital days and daycare accounted for 50%, 33% was spent during the induction phase. Costs per QALY were 3,871–8,708. Costs per QALY gained for treatment according to the latest protocol were 19,730.

**Conclusion:** Costs per QALY for the treatment of childhood ALL are in the range of costs of other intensive treatments of pediatric diseases. Costs per QALY gained for treatment including more expensive medication and new high-tech diagnostic tools has an acceptable cost-effectiveness. In future (ALL) treatment protocols, costs in relation to effects should be taken into account in order to enhance cost-effective disease management without jeopardizing survival and QoL.
Purpose: Data from developing-countries addressing childhood acute lymphoblastic leukemia (ALL) presenting with hyperleukocytosis (white-cell-count > 100x109/L) is scant. This study was designed to assess incidence, survival outcome and adverse features associated with hyperleucytocytic childhood ALL.

Method: Case-records of 760 patients with ALL aged 1-14 years managed over 18 years were analyzed. Information regarding the clinical-demographic profile, therapy and course of illness were recorded. Status and duration at last follow-up were utilized to generate Kaplan-Meier survival curves.

Results: Hyperleukocytosis was documented in 111 (14.6%) out of 762 patients: 88 (15.2%) males and 23 (12.6%) females (p = 0.25). Their mean-age at presentation was 6.1 ± 0.65 years. Significant-lymphadenopathy, massive-hepatomegaly, massive-splenomegaly, mediastinal-adenopathy, bulk-disease and superior vena-cava-obstruction (SVCO) were observed in 50 (45.04%), 55 (49.54%), 56 (50.45%), 29 (26.12%), 23 (20.72%) and 10 (9.09%) patients respectively. Overt-testicular disease was observed in 4. Patients with hyperleukocytic-ALL had significantly higher incidence of shorter symptom-diagnosis-interval (p = 0.01), massive hepatosplenomegaly (p = 0.04), significant-lymphadenopathy (p = 0.02), SVCO (p = 0.01) and lower platelet count (p = 0.001) at presentation compared to other ALL patients.

72 out of 111 opted for therapy; others predominantly cited financial/socioeconomic reasons for treatment refusal. Of these 21 relapsed, 25 died (predominantly early, infection-related/toxic/bleeds/tumor lysis syndrome) while only 10 are in continuous complete remission and active follow-up. There were 9,3 and 4 instances of isolated bone-marrow, testicular and CNS relapses respectively. Combined relapse was seen in 5 patients. The estimated mean survival was 10.5 ± 3.6 months which was significantly inferior to other ALL patients (p < 0.001,log-rank-test).

Conclusion: Incidence of hyperleukocytosis was similar to data emanating from developed nations. However, it is associated with high-risk features. Outcome was dismal, in sharp contrast to high cure rates in developed nations. Aprovement in supportive management, hydration therapy, intensive laboratory monitoring, appropriate management of tumor lysis syndrome alongside use of aggressive upfront and risk-adapted therapy with discernible improvement in holistic management of ALL should improve outcome of hyperleukocytic ALL.

PA028

OPTIMIZING OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) CARE IN CHILDREN IN PARAGUAY

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Purpose: Better outcomes for children with ALL have been achieved in several low-income countries in recent years. The pediatric service of the Centro Materno Infantil is a 150 bed public hospital, the hemat-oncology unit cares for 60 new patients with ALL per year corresponding to over 50% of expected pediatric ALL cases in Paraguay. Three local foundations buy cancer care drugs; provide supplemental salaries and infrastructure support at this center. To improve outcomes of ALL care, we optimized access to oncology and support personnel; clinical data management; and consistent access to resources of patient care and services. Here, we report contributors to successful outcomes of ALL in our center.

Method: Since 2008, our intervention consisted of (1) improving access to and capacity of oncology and support care personnel; and (2) implementing needed patient care projects (improving patient and hospital hygiene, addressing lost-to-follow-up events). We used POND database (www.cure4kids.org) to store our results and the statistical analysis to evaluate rates of event free survival, toxic deaths, and abandonment.

Results: We believe that through this multi-prong approach the event free survival has increased from 19 ± 3% in 2000/07 to 53 ± 4% in 2008/09 periods, possible contributors were lower abandonment (26 ± 2% in 2000/07 to 10 ± 3% in the 2008/09 period), lower toxic mortality (from 24 ± 2% in 2000/07 to 9 ± 3% in 2008/09 period) and relapse (from 59 ± 9% in 2000/07 to 16 ± 6% in 2008/09 period).

Conclusion: Our preliminary results highlight the importance of multi-institutional collaborations and the local promotion of pediatric cancer for best outcome of children with cancer in a low income country providing a model to replicate in other similar situation.

PA029

SOCIOECONOMIC AND INSURANCE STATUS IN MINORITY PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN ALABAMA

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Purpose: Approximately 2500 children per year in the United States are diagnosed with Acute Lymphoblastic Leukemia (ALL). Overall survival is over 80% with current treatment strategies. Although the incidence of leukemia in African-American children in lower than in other ethnic groups they are more likely to present high-risk disease and historically have lower overall survival. Even when controlling for high-risk disease, African-Americans still have a lower survival rate than whites. This study evaluated differences between African-American and Caucasian patients with ALL in Alabama.

Method: All children diagnosed and treated for ALL at The Children’s Hospital of Alabama for the time period 1999–2009 were included in the study (n = 237). Demographic variables were collected on all patients including age, race and insurance status, and compared to patient outcomes.

Results: 75.4% of the sample were Caucasian, 18.6% African American and 5.9% Hispanic. African-American children were less likely to have private insurance than the other groups (22% versus 69%, p value = 0.001). African-American children were less likely to identify a primary pediatrician at diagnosis (32.8% versus 14.3% of Hispanics and 12% of Caucasians, p = 0.015). African-American patients lived in zip codes with less of the population working (59.35% vs. 62.4%, one-way ANOVA p value = 0.036) and lower median household income ($33131 versus $39951, p = 0.0089). Overall survival in this small sample was not significantly different between groups (80% for African-Americans, 83% for Hispanics and 88.5% for Caucasians).

Conclusion: The reasons for the disparities in outcomes for childhood ALL are not well understood. In this small, single-institution sample, preliminary analysis identifies some intriguing differences between African-American and Caucasian patients in terms of insurance status, baseline demographics and socioeconomic variables. Further research is needed to identify specific potential causes for the worse outcomes observed in minority patients with pediatric ALL.

PA030

QUALITY OF LIFE EVOLVEMENT DURING THE FIRST YEAR OF TREATMENT FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: With the improvement of childhood ALL survival, Quality of Life (QoL) has become increasingly relevant. QoL during treatment is impaired, but longitudinal studies evaluating evolvement of QoL, its determinants and affected domains are sparse. Therefore, a national multi-centre study was initiated to assess QoL during treatment. Results of the first two assessments are presented here.

Method: The Child Health Questionnaire (CHQ) and Pediatric Quality of Life Cancer version (PedsQL) were used to obtain parent proxy-reports 4–6 weeks after diagnosis (T0) and after one year (T1).

Results: 131 children were included, mean age was 8.39 ± 5.10 months, 52% were male.

CHQ: QoL at T0 was significantly lower than Dutch norms. At T1 QoL improved but remained lower than Dutch norms, with exception of family cohesion, which was
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better than the norm at T0 and similar at T1. Behaviour and general health deteriorated at T1. In the first weeks of treatment pain, mental health and parental emotional impact improved. Risk factors for an impaired QoL were higher risk group, higher age (pain and physical role limitations), and female gender (mental health and parental emotional impact).

PedQoL: overall QoL, procedural and treatment anxiety improved at T1. Lowest scores (indicating low QoL) were found for pain and procedural anxiety. Risk factors for an impaired QoL were age (older: worries, cognitive problems and physical appearance; younger: procedural and treatment anxiety) and female gender (overall QoL). Treatment risk group did not influence QoL.

Conclusion: QoL improved during the first year of ALL treatment but was still substantially impaired compared to the norm. Affect QoL domains were age-specific and girls seemed to experience a more diminished QoL than boys. Some domains are particularly impaired in the period immediately after diagnosis. Follow-up of this cohort will help to better understand the effect of childhood cancer treatment on QoL over time.

PA031


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Purpose: In this study we describe variability in survival from leukaemia and Non-Hodgkin lymphoma (NHL) by age group and time period.

Method: The study is based on data from the national cancer registration system in England and covers all registered cases of acute lymphoid leukaemia (ALL), acute myeloid leukaemia (AML) and NHL in individuals aged from 0 to 29 from 1990 to 2006. Survival was estimated using the Kaplan-Meier method.

Results: The five year survival was 77% for those with ALL (7077 Cases), 53% for those with AML (2628 cases) and 73% for those with NHL (4596 cases). Five year survival varied by age at diagnosis, with the highest rates in ALL being among 1 to 5 year olds (88.5%), and the lowest rates in Uncr 1 year olds, (52%) and 24 and 25 year olds, among whom it is steady at around 43%.

Conclusion: Our results support a hypothesis which links DNA repair phenomena with leukaemic CNS infiltration. Patients with NBS are at risk for CNS involvement at diagnosis of ALL.

PA034

TREATMENT OF PEDIATRIC T-CELL ACUTE LYMPHOBlastic LEUKEMIA WITH NEW YORK 1 REGIMEN

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Purpose: Children with acute lymphoblastic leukaemia with T- immunophenotype, are at increased risk of short term remission and extramedullary recurrence, and are in need of better therapies.

Method: In this retrospective analytic study, 39 children with T-Cell ALL admitted to Ali Asghar children's hospital between years 1993 and 2004 were entered. 29 patients were treated by NY1 regimen (group A) and LSA2-L2 was used for others (group B).

Conclusion: The patients in group A (NY1) had better outcome than group B (LSA2-L2).
PA035

HOW IMPROVEMENT IN THE OUTCOME OF T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA COULD BE ACHIEVED?: EXPERIENCE OF NATIONAL GUARD HOSPITAL, JEDDAH, SAUDI ARABIA

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Purpose:
Background: T-cell (T-ALL) is representing 10% of pediatric ALL. Use of intensive treatments and risk adapted therapy have improved the outcome of patients with T-ALL and EFS rate of 60–70% are now reported. Our published data showed that T-ALL phenotype fared poorly with 5 year survival of 27% versus 83% for precursor-B-ALL (Recent advances Research Update, Fryer C, et al.: 2006; 7, 1, P 51–56).

We reviewed patients diagnosed with T-ALL to assess risk classification according to NCI criteria, therapy received, overall survival (OS) and causes of mortality.

Method: Retrospective review of all patients files diagnosed with T-ALL from 1989–2009 with data including: sex, age, (WBCs), CNS disease, type of protocol used, outcome. Risk and response stratification with intensification for therapy of T-cell ALL in our center may prove to be beneficial. Therapy remain an important prognostic factor.

RESULTS: Mean age was 7.32 ± 3.53 yrs (range 1.5–14). Cranial prophylactic radiotherapy (18 Gy) was done for 61% of enrolled patients (60% of group A and 70% of group B). Median time of follow-up was 54 month. Estimated 5yrs overall survival for all enrolled patients were 81.5% ± 6%. However, this rate for group A and B was 82.4% and 80%, respectively. But estimated 5yrs event free survival was better in group A than group B (75.2% vs. 51.9%) while the patients of group A had significantly poorer outcome for risk group (p = 0.001). In addition, relapse rate for group A was less than another group (24% vs. 40%) while duration of relapse free was the same in both groups. Also, treatment related mortality of group A was less than group B (17% vs. 36.5%).

Conclusion: It appears that New York 1 regimen has improved outcome with less toxicity in children with T-Cell ALL in developing countries, especially in the situations that reliable methotrexate level measurement is not easily available.

PA036


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Purpose: To identify an optimal strategy of chemotherapy for childhood acute lymphoblastic leukaemia (ALL) in Russia.

Method: A comparative analysis of three chemotherapy regimens (modified version of BFM-protocol [ALL-BFM 90m]), two versions of ALL-Moscow-Berlin protocol [ALL-MB 91, ALL-MB 2002] and two modified versions of the German study COALL-92 [PECO-92, COALL-Saint-Petersburg 92] was performed in pediatric oncology/hematology centres of Moscow and Saint-Petersburg. Outcomes were examined in two time periods. Between 1993 and 1999, 477 newly diagnosed patients with ALL aged 0–18 years were treated on three protocols: ALL-BFM 90m (n = 139), ALL-MB 91 (n = 124) and PECO-92 (n = 214). From April 2002 to January 2007, patients were treated according the protocols ALL-MB 2002 (n = 292) and COALL-Saint-Petersburg 92 (n = 126). Two treatment strategies have been implemented: intensive polychemotherapy (ALL-BFM 90m, COALL-92m) and non-intensive prolonged chemotherapy on ALL-MB protocols (detailed information concerning the protocols design has been published).

RESULTS: Over the first time interval the 13-year event-free and overall survival probabilities (pEFS/pOS) were 75% ± 4%/80% ± 4% on ALL-BFM 90m, 72% ± 4%/78% ± 4% on ALL-MB 91 and 60% ± 3%/70% ± 3% on PECO-92. Induction death (ID) rate was 2.9%, 3.2% and 3.3%; remission death rate was 2.9%, 8.0% and 4.2%, respectively (n.s.). Relapses occurred in 16.5%, 17.7% and 26.6%, respectively (p = 0.028 BFM-PECO). Analysis over the second time interval did not reveal significant survival differences: the 7-year pEFS/pOS by protocols ALL-MB 2002 and COALL-Saint-Petersburg 92 were 78% ± 3%/80% ± 5% and 78% ± 4%/83% ± 4%. ID rate was 1.4%, and 0.8% (n.s.); remission death rate was 2.1% and 6.3% (p = 0.036). Relapses occurred in 16.1% and 19.7%, respectively (n.s.).

Conclusion: Almost identical results were achieved over the second time period with both treatment strategies. However, lower toxicity and easier implementation of ALL-MB 90m protocol appear to be crucial aspects for the choice of optimal treatment strategy for childhood ALL in Russia.
PA038

DOWN SYNDROME PATIENTS WITH ACUTE LYMPHOBlastic LEUKemia HAVE AN INTERmEDIATE PROGNOSIS WITH HIGH INFECTIOUS MORBIDITY

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Purpose: Even with modern therapy the outcome of ALL in children with Down’s syndrome (DS) remains inferior to non-DS patients. The higher incidence of infections in this group of patients may result not only in toxic-mortality, but may also impact on leukemia-related outcomes due to therapy omissions and delays.

Method: This retrospective analysis looks at the outcome of DS patients with ALL treated during 1997 and 2009 at our institution.

Results: Of 24 patients, 14 were males with a median age of 4.8 years (mean 5.0–0.53 years; range 1.4–12.8) at diagnosis. Two patients had corrected congenital cardiac defects. The median WBC count was 35.8 x 10^9/L (SEM = 24.66; range 0.89–500). All patients had precursor B-cell phenotype, two had CNS disease and none had any risk-associated cytogenetic features. Two patients received 3-drug induction and 21 were started on a 4-drug induction. There were three early deaths during induction; one patient died of parainfluenza-related ARDS, one with multi-organism sepsis and H1N1 influenza infection and the third with disseminated aspergillosis. Of 22 patients who were evaluated for BM response at day 14 only one had residual leukemia, with 50% blasts. All 21 patients who completed induction achieved CR. OS at a median follow-up of 3 years is 69% compared to 81% for non-DS pre-B ALL patients treated during the same time period with similar protocols.

Conclusion: All patients with DS need to be treated with fairly intensive therapy in order to improve disease related outcomes; however one has to balance this with the increased risk of infections, particularly during induction and intensification phases.

PA039

REDUCED TREATMENT FOR GOOD RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: LESS IMMUNE DAMAGE AND A MAJOR DECREASE IN INFECTIOUS MORBIDITY

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Purpose: Current chemotherapy for childhood acute lymphoblastic leukemia (ALL) is intensive and accompanied by considerable infectious morbidity and morbidity. Thus reducing infectious complications has become an important goal to improve childhood ALL survival. We compared cellular and humoral immunity as well as infectious morbidity during and following reduced and intensive chemotherapy for ALL.

Method: Between 2004 and 2007, 171 patients treated in the Dutch Childhood Oncology Group ALL 10 trial were included in this study. We prospectively analyzed the reduced (standard risk; SR group; 54 patients) and intensive chemotherapy (medium risk; MR group; 117 patients) groups. Both reinduction and maintenance treatment was reduced in the SR compared to the MR group. Admittances for fever were recorded during ALL treatment. In a subgroup of patients, various B and T cell subsets, immunoglobulins and antibody levels against vaccine-preventable diseases were analyzed during and 1 year after chemotherapy.

Results: During reinduction and maintenance treatment, SR patients were admitted for fewer median 0 times (range 0–3) compared with MR patients 2 times (range 0–14) (P < 0.001). Infections were less severe in SR patients leading to less days hospitalization, less chemotherapy interruptions and no ICU admittances. Flowcytometric analyses showed that transitional and naive B cells, IgM+ and IgM+ memory B cells were severely affected during chemotherapy, particularly in the MR group. Importantly, the various memory B cells and NK cells had not completely recovered 1 year after cessation of chemotherapy though levels were comparable in both groups. In addition, immunoglobulins and antibody levels against vaccine-preventable diseases were less affected in the SR as compared with MR group.

Conclusion: Reduced treatment is associated with a lower infectious morbidity and less damage of especially the memory B cell compartment. Future treatment protocols should aim to stratify patients to a reduced treatment arm if warranted.

PA040

BOTTLENECK OF CHILDhood LEUKEmia: IS IT STILL A MYSTERY?

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Purpose: To elucidate why only 1/100 children born with TEL-AML1 develops TEL-AML1+ acute lymphoblastic leukemia (ALL). All patients had precursor B-cell phenotype, two had CNS disease and none had any risk-associated cytogenetic features. Two patients received 3-drug induction and 21 were started on a 4-drug induction. There were three early deaths during induction; one patient died of parainfluenza-related ARDS, one with multi-organism sepsis and H1N1 influenza infection and the third with disseminated aspergillosis. Of 22 patients who were evaluated for BM response at day 14 only one had residual leukemia, with 50% blasts. All 21 patients who completed induction achieved CR. OS at a median follow-up of 3 years is 69% compared to 81% for non-DS pre-B ALL patients treated during the same time period with similar protocols.

Conclusion: All patients with DS need to be treated with fairly intensive therapy in order to improve disease related outcomes; however one has to balance this with the increased risk of infections, particularly during induction and intensification phases.

PA041

BIOLoGIC FEATURES AND TREATMENT OUTcome of ACUTE LYMPHOBLASTIC LEUKEMIA in LEBANESE CHILDREN

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Purpose: To study the clinical and biological features, treatment outcome and complications in children with acute lymphoblastic leukemia at the Childrens Cancer Center of Lebanon.

Method: A risk stratified protocol, based on St. Jude Total XV, consisting of two treatment arms was developed.

Results: One hundred eleven patients < 20 years of age with ALL were diagnosed between April 2002 and August 2009. The mean age was 6.96 years; 8 months; the M:F ratio was 1.52. Sixty five patients received the low risk arm and 46 received the standard/high risk arm. Eighty six (77%) were between 1 and 10 years of age. Eighty-five had an initial WBC < 50,000. Ninety five patients had B lineage and 16 patients (14.5%) had T lineage ALL. Fifteen patients (13.5%) had t (12; 21), 3 (2.7%) had t (9; 22) and 3 (2.7%) had t (1; 19). Fifty-five patients (49.5%) had normal karyotype, eight (7.2%) had ploidy between 47 and 50 chromosomes, nine patients (8%) had hyperploidy, > 50 chromosomes, and one patient had tetraploidy. DNA index > 1.16 was present in 8/52 (15.4%) patients tested. With a mean follow up of 39.5 months; the 3 year event free survival and overall survival were 91.8% and 94.7% respectively. The 5 year EFS and OS were 80% and 88.4% respectively. Bacteremia occurred in 30.6%; 6% had seizures, 3.6% developed pancreatitis, 3.6% developed deep vein thrombosis and (4.5%) developed sagittal sinus thrombosis. Thirty patients developed CMV infection and 9 patients had low immunoglobulin levels with recurrent infections requiring IV Ig therapy. One defined risk group of low risk groups not requiring intensive therapy and pharmacogenetic studies may improve the toxicity profiles of future protocols.

Conclusion: An aggressive risk stratified protocol for ALL was implemented in a developing country with an OS of 88.4%. The toxicity was substantial. Better definition of low risk groups not requiring intensive therapy and pharmacogenetic studies may improve the toxicity profiles of future protocols.

PA042
SURVIVAL OF CHILDREN WITH ACUTE LYMPHOBlastic LEUKEMIA (ALL) USING A UNIFORM PROTOCOL OVER A 10 YEAR PERIOD: RESULTS FROM A MEDICAL COLLEGE HOSPITAL IN SOUTHERN INDIA

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Purpose: The results of childhood acute lymphoblastic leukemia (ALL) have improved over the last four decades primarily due to systematic treatment. We report here the results of newly diagnosed ALL patients treated on a uniform protocol over a 10 year period.

Method: From January 2000 to December 2009, 104 children with newly diagnosed ALL received treatment in the Pediatric Hematology Oncology unit. Of the 85 children who were diagnosed before December 2007, 81 who were treated on the MOP 841 protocol were analyzed.

Results: The median age was 5 years (range 1 to 15 years). Male to female ratio was 1.16. Sixty five patients had low risk arm and 46 received the standard/high risk arm. Eighty six (77%) were between 1 and 10 years of age. Eighty-five had an initial WBC < 50,000. Ninety five patients had B lineage and 16 patients (14.5%) had T lineage ALL. Fifteen patients (13.5%) had t (12; 21), 3 (2.7%) had t (9; 22) and 3 (2.7%) had t (1; 19). Fifty-five patients (49.5%) had normal karyotype, eight (7.2%) had ploidy between 47 and 50 chromosomes, nine patients (8%) had hyperploidy, > 50 chromosomes, and one patient had tetraploidy. DNA index > 1.16 was present in 8/52 (15.4%) patients tested. With a mean follow up of 39.5 months; the 3 year event free survival and overall survival were 91.8% and 94.7% respectively. The 5 year EFS and OS were 80% and 88.4% respectively. Bacteremia occurred in 30.6%; 6% had seizures, 3.6% developed pancreatitis, 3.6% developed deep vein thrombosis and (4.5%) developed sagittal sinus thrombosis. Thirty patients developed CMV infection and 9 patients had low immunoglobulin levels with recurrent infections requiring IV Ig therapy. One defined risk group of low risk groups not requiring intensive therapy and pharmacogenetic studies may improve the toxicity profiles of future protocols.

Conclusion: An aggressive risk stratified protocol for ALL was implemented in a developing country with an OS of 88.4%. The toxicity was substantial. Better definition of low risk groups not requiring intensive therapy and pharmacogenetic studies may improve the toxicity profiles of future protocols.

PA044
LOW COST RATIONALLY DESIGNED PROTOCOL FOR TREATMENT OF PEDIATRIC ACUTE LYMPHOBlastic LEUKEMIA IN DEVELOPING COUNTRIES: WHO WILL IT BENEFIT?

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Purpose: To test feasibility, toxicity & cost effectiveness of rationally designed low cost protocol for treatment of ALL in children from financially challenged families in India.

Method: Previously untreated ALL patients age > 1 < 20 were screened for socioeconomic status using Kuppuswami and wealth index scores. Affordable group was offered MCP841 protocol. Published data: European Journal of Cancer 41; 2005;1570–1583;Motivated families below poverty line were given option of IRB approved low cost protocol against no therapy. All who consented (except mature B ALL) were included. Protocol consists of 3 drugs induction (VCR, L-Asp, Dexamethasone), consolidation, cranial prophylaxis (IT&CRT), Reintensification & maintenance(24±8 months for girls & boys respectively). Protocol cost(treatment supportive care)of approx $2000, stay & family support in Mumbai were met with 3 strong approach.

Results: 120 patients are enrolled from June 2005 till January 2010. Mean age 7.4 years (1.5–17) M: F 2.2:1. Four(3%) patients were excluded as lost to follow up/treatment induction. 85(98) were B ALL (60% STD risk, 40% high risk according to NCRI criteria, 53 (65%) were standard risk and 28 (35%) were high risk. Immunophenotyping was done in 63 children of which 73% were B ALL, 17.4% were T ALL and 9.5% were biphenotypic. The remission induction rate was 98.8% with one induction death secondary to tumor lysis syndrome. There were 17 relapses (10 early while on therapy and 7 late). Site of relapse was bone marrow in 10, central nervous system (CNS) in 1, combined marrow and CNS in 2, testes in 3, and extramedullary in 1. There was only one remission death and 5 patients were lost to follow up. 55 patients are alive in first remission and 3 patients in second remission with a 5 year EFS of 60% and OS of 70%.

Conclusion: The MOP 841 is an effective protocol that is easy to administer in a medical college hospital setup with reproducible results.

PA043
TREATMENT OF ACUTE LYMPHOBlastic LEUKEMIA (ALL) IN A LIMITED INCOME COUNTRY (LIC): THE EXPERIENCE OF THE UNIDAD NACIONAL DE ONCOLOGIA PEDIATRICA (UNOP) OF GUATEMALA.

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Purpose: About 300 children with a new diagnosis of cancer are treated each year at UNOP; around 40% of them have ALL. The purpose is to determine outcome of these patients in the setting of a LIC.

Method: Patients with ALL aged 1–18 years, diagnosed between July 1, 2007 and December 31, 2009 were analyzed using the Pediatric Oncology Network Database (POND) system. Data were collected prospectively by trained data managers. Patients were treated with BFM-like treatment protocol for 104 weeks. Chemotherapy included induction, consolidation, late intensification, maintenance, and CNS prophylaxis according to risk category and CNS status. Patients were classified into three risk categories according to clinical and biological characteristics (age, white blood cell count, prednisone response, bone marrow aspirate at days 15 and 33, translocations, CNS status). The MCP 841 protocol were analyzed for ALL received treatment in the Pediatric Hematology Oncology unit. Of the 85 patients, 76 high risk. Twenty-six patients had CNS 3 disease, and 17 patients had T lineage. Twelve patients died in induction (4.8%), 16 patients have relapsed, and 8 patients have abandoned treatment (3%) (more than 1 month without chemotherapy). EFS survival (abandonment as an event) is 75% for the 245 patients at 36 months of follow-up.

Conclusion: BFMT like therapy is feasible in a LIC. There is a higher proportion of the high risk patients and a high proportion of CNS 3 disease. Perhaps this is due to late diagnosis. There seem to be a lower proportion of T lineage ALL in Guatemala.
OPTIMIZATION OF E.COLI ASPARAGINASE TREATMENT FOR STANDARD RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA: MOSCOW-BERLIN 2002 STUDY EXPERIENCE

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Purpose: To define an optimal schedule of E.Coli asparaginase for standard risk childhood acute lymphoblastic leukemia (SR-ALL).

Method: A randomized multicenter study ALL-MB 2002 was performed in 37 pediatric oncology/hematology centres in Russia and Belarus. Between 01.05.2002 and 10.10.2006 815 newly diagnosed SR-ALL pediatric patients (pts) (WBC < 50,000/mm3, non-T cell phenotype, no CNS involvement, > 1 year, CR day 36, without t(4;11) and t(9;22)) were treated with 6-week induction (dexamethasone or methylprednisolone, vincristine, daunorubicin, intra-threal chemotherapy (IT[T])], followed by three 6-week consolidations (mercaptopurine, methotrexate, asparaginase, daunorubicin, vincristine, dexamethasone, IT) and maintenance (mercaptopurine, methotrexate, dexamethasone and vincristine pulses). TIT) until 2 years after diagnosis. 780 pts were randomised to 10000 (n = 390) or 500 pts (n = 390) U/m2 E.Coli asparaginase i.m.weekly during consolidation. Asparaginase activities were monitored on day 3 and 7 after application.

Results: The 8-year event-free survival (pEFS) was 76% ± 2% for the asparaginase (10000 U/m2) group and 79% ± 2% for asparaginase 5000 U/m2 group. Remission death rate was 6.9% and 3.3%, respectively (p = 0.03). Relapses occurred in 15.6% and 15.9%, respectively (n.s.). The main reason of relaps was infections (sepsis, pneumonia) and majority of these pts had methylprednisolone induction. There was the only case of severe pancreatitis. Non-lethal complications were identical in both groups and were not influence by steroid regimes during induction.

On day 3 mean asparaginase activities (+/-SD) of 542 U/L (+/-389 U/L; n = 221) were determined after application of 10000 U/m2 and 333 U/mL (+/-180 U/L; n = 165) after application of 5000 U/m2. On day 7 the asparaginase activities declined in mean to 67 U/L (+/-79 U/L; n = 162) and to 46 U/L (+/- 79 U/L; n = 153) after application of 10000 and 5000 U/m2, respectively (p < 0.05, Mann-Whitney Rank Sum Test).

Conclusion: 5000 U/m2 asparaginase weekly i.m. during consolidation is the optimal schedule of E.Coli asparaginase for SR-ALL patients in a setting of ALL-MB 2002 protocol.

TOXICITY DURING CONSOLIDATION PHASE WITH HDMTX 5 GR/M2 IN CHILDREN WITH ALL

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Purpose: The administration of high-dose Methotrexate (HDMTX, 5gr/m2), during consolidation phase, is an essential part of ALL treatment for prophylaxis from CNS and bone marrow relapse. The purpose of our study was to describe the complications during this phase and their correlation with folinic acid administration.

Method: We retrospectively studied 220 children with standard or intermediate risk ALL treated in our department from 11/1992 to 12/2005 with BFm protocols (90 or 95). Until 12/1999, folinic acid had been administered according to UKALL X protocol (group A), while after 01/2000, according to BFM 95 protocol (group B).

Results: We studied 106 children, who received folinic acid with the previous method (417 cycles) and 114 with the new (450 cycles). At least 1 complication was described in 70/417 cycles of group (42 children) and in 74/450 of group B (51 children). In detail, complications were gastrointestinal in 15 cycles (3.6%) of group A and in 22 (4.9%) of group B, conjunctivits in 6 (1.4%) and 6 (1.3%), severe infections or sepsis in 10 (2.4%) and 11 (2.4%), creatinine rise > 20% of normal in 5 (1.2%) and none, respectively. Finally, seziures have been described in 4 (HD7) cycles (0.9%) in the same child with preexisting epilepsy in group A, and in 1 (0.2%) in group B. None of these differences was statistically significant. The development of complications was correlated with the number of folinic acid doses in children of group A (p = 0.032) but not in B. All complications were successfully treated without discontinuing HDMTX.

Conclusion: The administration of HDMTX has been proved safe without major complications, which would necessitate its discontinuation. The correlation of folinic acid doses’ number with complications’ rate in children, who received more doses with the previous method is probably due to prolonged HDMTX excretion.

CORRELATION OF FOLINIC ACID ADMINISTRATION AFTER HDMTX WITH PROGNOSIS IN CHILDHOOD ALL

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Purpose: High-dose Methotrexate (HDMTX) administration during consolidation phase is a basic component of childhood ALL treatment not only for CNS but also for bone marrow prophylaxis from relapse. Our purpose was to study if the HDMTX excretion and the boinic acid doses received were correlated with ALL prognosis.

Method: We retrospectively studied 220 children with standard or intermediate risk ALL treated in our Department from 11/1992 to 12/2005 with BFm protocols (90 or 95). Prolonged methotrexate excretion was considered the need for folinic acid administration for > 72 hours (≥9 doses, previous method, group A) or > 54 hours (≥4 doses, new method, group B).

Results: We studied 106 children in group A (417 cycles) and 114 in group B (450 cycles). Prolonged excretion has been noticed in 23/450 in group B, while only 1/223 in group A (p = 0.001). Thirty children (28%) in group A relapsed (bone marrow 21; bone marrow and CNS 3; CNS 1; testicles 5) and 19 (17%) in group B (bone marrow 10; bone marrow and testicles 2; CNS 6; testicles 1) (p = 0.036). No correlation was detected between the site of relapse and folinic acid administration
method. Overall survival was 81% (86/106) in group A and 94% (107/114) in group B (p = 0.008).

Conclusion: The new method of folic acid administration after HD-MTX, according to BFM protocol, seems to result in reduced relapse rate and increased overall survival in childhood ALL. The site of relapse was not found to correlate with folic acid administration method.

PA048

CENTRAL NERVOUS SYSTEM RELAPSES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED ON TWO CONSECUTIVE BRAZILIAN COOPERATIVE TRIALS: GBTLI ALL-1993 AND -1999

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Purpose: To analyze the incidence and pattern of CNS relapse among 2051 children up to 18 years of age, enrolled in two Brazilian ALL trials (GBTLI ALL-93, n = 867 and ALL-99, n = 1184).

Method: GBTLI ALL-93 consisted in intensive systemic and triple intrathecal therapy (21 doses) in addition with prophylactic CNS radiation (18 Gy) only for high risk patients (NCI criteria). GBTLI ALL-99 protocol consisted in equivalent intensive systemic and intrathecal therapy with no CNS radiation for all patients. Isolated and combined CNS relapses were examined and the relationship with patient characteristics were assessed.

Results: 7 years Event-free survival for all patients according to treatment were 69.0 ± 2.4% (ALL-93) vs 68.0 ± 1.8% (ALL-99), p = 0.50. Isolated CNS relapses occurred in 3.9% of patients treated according to GBTLI ALL-99 (12 low risk and 30 high risk, among 1135 pts analyzed); combined CNS relapses were diagnosed in 15 pts. When all patients were considered for analysis, both isolated (n = 12) and combined (n = 4) CNS relapses were significantly lower in GBTLI ALL-93 in comparison to the ALL-99 study (p < 0.001 and p < 0.001, respectively). For low risk patients no difference in CNS relapses was seen according to treatment regimen (p = 0.17). High risk pts treated on GBTLI ALL-99 without prophylactic CNS radiation had highly significant CNS relapse rates in comparison to high risk ALL-93 study (p = 0.0002), with no significant difference concerning leukocyte counts higher than 100.000/mm3 at diagnosis (p = 0.33) and no association with poor or good response to initial treatment (p = 0.64). Calla antigen negativity (CD10) was strongly predictive of CNS relapse, both for F (p = 0.025) or T-precursor ALL (p = 0.037).

Conclusion: Prophylactic CNS radiation is still necessary for high risk CD10 negative ALL patients.

PA051

MUSCULOSKELETAL MANIFESTATIONS IN PEDIATRIC ACUTE LEUKEMIA: A REPORT FROM ITALY

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Purpose: Children with acute leukemia (AL) at presentation can mimic several orthopaedic pathologies. This problem may result in fractures, loss of mobility and deformity, with resultant adverse consequences on quality of life.

For this reason we studied the clinical and radiological musculoskeletal manifestations in children with AL.

Method: We reviewed 328 children, 208 males (62%), median age 7.2 years, with acute lymphoblastic (279: 85%) or myeloid (49:15%) leukaemia, treated between 1990 and 2009. We reviewed the outcome of the protocol over a 7 year period.

Results: 5-year EFS of S2 patients with or without HSCT were 67% and 55% respectively (p = 0.078), while 5-year EFS for S3 and S4 group received HSCT were 57% and 14% respectively. There were no survivors in S3 and S4 patients treated with chemotherapy only.

Conclusion: HK ALL-Relapse 2000 protocol achieved second remission of 88%. HSCT improved survival in S3 group but not S2 group. Prognosis of S4 group remained poor despite intensive treatment.
Purpose: The aim of the study was to evaluate the frequency of metabolic syndrome and its components and the effect of radiotherapy on the development of metabolic syndrome and its components in patients with acute lymphoblastic leukemia (ALL) who completed therapy.

Method: Age of diagnosis, time elapsed since discontinuation of treatment and gender were recorded for 40 ALL patients with completed therapy who were enrolled in the study. Metabolic syndrome parameters were determined. The patients’ height SDS, body mass index (BMI) and BMI percentiles were calculated. WHO (modified) criteria were used for diagnosing the metabolic syndrome. HOMA-IR > 4 was accepted as insulin resistance for evaluating insulin resistance.

Results: A total of 40 patients, 24 females and 16 males, were enrolled in the study. Median age was 49 months (16–165), and the median time elapsed since discontinuation of treatment was 12 (1–96) months. Half of the patient received radiotherapy. Five (12.5%) patients were metabolic syndrome. While no difference was observed between those who did not receive radiotherapy in terms of each of metabolic syndrome parameter. Three patients had height measurements below –2SDS. A difference could not be observed between the radiotherapy and non-radiotherapy groups in terms of metabolic syndrome parameter. However, the importance of monitoring weight, height, and metabolic parameters during routine controls of children with ALL who completed therapy is once more underlined as metabolic syndrome parameter.

Results: A difference could not be observed between the radiotherapy and non-RT groups in terms of shortness in height. Three patients had height measurements below -2SDS. A difference could not be observed between did not receive radiotherapy in terms of each of metabolic syndrome parameter. However, the importance of monitoring weight, height, and metabolic parameters during routine controls of children with ALL who completed therapy is once more underlined as metabolic syndrome was seen in 12.5% percent of the study subjects.

Purpose: To evaluate the efficacy and toxicity profiles of the combination of fludarabine, cytarabine, idarubicin and G-CSF (FLAG-IDA) in the induction of refractory or relapsed acute leukemias in children.

Method: Between January 2001 and December 2008, we retrospectively evaluated 48 children (21 AML, 25 ALL, and 2 biphenotypic leukemia) with refractory, relapsed or secondary acute leukemia receiving FLAG-IDA regimen as rescue chemotherapy.

Results: Sixty and 64% of the patients with AML and ALL achieved complete remission respectively. Overall survival was 53.4 ± 9% with a median follow up of 270 days. None of the patients which did not respond to FLAG-IDA respond to other regimens. Event free survival of patients which respond to FLAG-IDA was 19 ± 10%.

Conclusion: The FLAG-IDA regimen shows a reasonable efficacy with acceptable toxicity to induce complete remission in pediatric patients with relapsed or refractory acute leukemia, and will allow the patients to perform an allogeneic stem cell transplantation with a curative intention.

Purpose: Rasburicase, a recombinant form of urate oxidase, is approved for prevention and treatment of hyperuricemia and tumor lysis syndrome in pediatric patients. Although usually well tolerated, several adverse reactions are of particular concern.

Method: Case summary. We report a case of a 6-year-old boy diagnosed with acute lymphoblastic leukemia and hyperuricemia (200x10^9/L). Rasburicase was administered (0.2 mg/kg/day, intravenously) to avoid tumor lysis syndrome. Few hours after administration of the second dose, the patient developed moderate methemoglobinemia (max. 17.3%) and hemolytic anemia (hemoglobin 3.3 g/ dl). The product was discontinued prior to the third dose as methemoglobinemia and hemolytic anemia have been described as infrequent complications of rasburicase administration, and the patient was given supportive medical management (strict monitoring and oxygen administration). As patients with G-6-PD deficiency are more prone for severe hemolytic reactions, analysis for this deficiency was performed but remained negative. The patient revealed an unclarified pancreatitis on day 2 (abdominal pain and values of amylase 380 U/L and lipase 1024 U/L). All complications resolved after 3 days. To determine the level of causality of adverse reaction, a Naranjo probability scale was applied. A score of 8 was obtained, suggesting that rasburicase was the “probable” cause of hemolytic anemia and methemoglobinemia. Other drugs administered at that moment (prednisone, colchicine) were not suspected for these adverse reactions. So far, there are no previous reports on the association between rasburicase and pancreatitis.

Purpose: Biphenoletic leukemias represent a heterogeneous, rare category of acute leukemia for which the treatment options are unclear till date. We present the outcome of acute biphenoletic leukemia treated uniformly with a hybrid acute leukemia protocol (Modified MCP 841) at our institute.

Method: This retrospective review includes 19 patients, diagnosed with acute biphenoletic leukemia as per St. Jude’s criteria from 2003 – 2009. All the patients received ALL type four drug induction (prednisone, vincristine, L-asparaginase, daunorubicin and intrathecal methotrexate) followed by AML like consolidation with high dose cytarabine (16 gm/m^2). After consolidation patients received cranial radiotherapy (12 Gy), followed by re induction and maintenance (mercaptopurine, methotrexate) for two years.

Results: The median age at diagnosis was 11.4 years (range: 2–24 years). The male to female ratio was 2.8:1. One patient had CNS 3 disease. Eight patients each, had B-lymphoid/myeloid (B/M) [42.1%] or T-lymphoid/myeloid (T/M) [42.1%] phenotype and three (15.8%) had T/B-lymphoid phenotype (T/B). Overall 17 of the 19 patients (89.5%) achieved complete remission (CR) after initial induction therapy. One (T/M) had no response to therapy and the other (T/M) died during induction due to septic shock. Three of the 17 patients relapsed at 6.5 (B/M), 17 (T/M) and 31 (B/M) months.
From 1994 to 1996, we adopted a modified method: the prognosis of Chinese childhood acute myeloid leukemia (AML) has improved for T and the Infantile types. The relapse rate in AML was 56% (10 patients); 9 died from other causes and 1 is alive. 16.7% died from other causes, mainly treatment related. Out of the 17.4% relapsed ALL, 13.9% died and 3.5% survived. 7% died from other causes and 0.9% from resistant disease. Most of the relapses were early with a median of 8.8 months, (range 2.6–10.4 months) in the AML and 16.5 months (range 1.9–60.9 months) in the ALL. Survival curves were derived by Kaplan-Meier method. The 3-year OS and EFS was 33.3% and 27.8% in AML and 78.3% in ALL. 15.5% of ALL had CNS disease and 21.7% had WBC count above 50,000 at presentation. Karyotyping was done on 97 patients: 62.8% were diploid, 26.8% hyperdiploid and 0.6% hypodiploid. PCR testing of 82 patients revealed 2.4% t(9;22), 3.6% t(11;19), 12% t(12;21) and 69.5% with no translocations.

Conclusion: The early relapse seems to be a significant predictor of poor outcome in these patients. Other clinical prognostic factors may be contributing. The introduction of MRD during therapy might improve EFS.

PB004

INCIDENCE AND PREDICTORS OF TREATMENT RELATED MORTALITY IN CHILDREN WITH ACUTE MYELOID LEUKEMIA IN CENTRAL AMERICA

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Purpose: Cure rates for children with AML in low-income countries (LICs) are lower than in high-income countries (HICs). Higher rates of treatment related mortality (TRM) account for a significant portion of this survival gap. We describe the incidence, timing and predictors of TRM among children with AML in El Salvador, Guatemala and Honduras, to facilitate future interventions to improve outcomes.

Method: We included patients < 20 years old, diagnosed with AML between January 2000 and March 2008, treated in any of the three countries. Biologic, socioeconomic and nutritional variables were collected prospectively by trained data managers and examined as potential predictors of TRM.

Results: Among 279 patients, TRM occurred as a first event in 65 (23%); 21 (6%) occurring before induction, 30 (11%) during induction and 16 (6%) after induction. Median time to TRM was 22 days from diagnosis (inter-quartile range [IQR] = 10–44). Major causes of TRM included infection (n = 29; 45%) and hemorrhage (n = 13; 20%). Infection-related mortality (IRM) accounted for a greater proportion of TRM following induction compared with during or before induction (77% vs. 40% vs. 33%; P = 0.03). Rates of total TRM, induction TRM and IRM did not significantly change over the 9-year study interval. Only a lower initial platelet count predicted the risk of induction TRM (odds ratio [OR] per 10x10^9/L decrease: 1.2, 95% CI 1.0–1.4; P < 0.01).

Conclusion: In this large study of pediatric AML in 3 LICs of Central America, TRM remains a significant cause of treatment failure. Median time to TRM was 3 weeks, suggesting a role for early supportive care interventions. Children who presented with low initial platelet counts were at highest risk of induction TRM and should be monitored particularly closely.

PB005

TREATMENT OF DS-AML WITHOUT HDARAC DOES NOT IMPACT ON DISEASE OUTCOME

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Purpose: Disease related outcome for DS children with AML is higher than non-DS patients, but with more toxicity. Optimally intense therapy for DS-AML needs to be determined.

Method: We retrospectively reviewed the outcome of DS-AML at our institution between 2000 and 2009 treated on two different protocols; Group A utilized HDARAC post-induction and Group B was treated without HDARAC.
PB006

CYTOGENETIC EVALUATION OF RESPONSE TO IMatinib Mesylate in the Treatment of Chronic Granulocytic Leukemia in Pediatrics.

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Purpose: Evaluate the clinical, hematologic and cytogenetic remission in pediatric populations with LGC treated with imatinib mesylate (IM) and evaluate the secondary toxicity.

Method: Descriptive, prospective, longitudinal study. Upon entering the service confirmed the diagnosis of LGC in patients with or without conventional treatment before the onset of MI, using peripheral blood smears and bone marrow in making qualitative search by FISH of t (9:22) and by RT PCR. Clinical data were recorded including age, gender, type of previous treatment, clinical, hematological admission and follow-up after the start of IM. The results of cytogenetic and molecular tests (FISH and/or RT-PCR) in diagnosis and treatment response assessed by FISH/RT-PCR at 6, 12 and 18 months of starting treatment with IM, is performed monthly blood count to document myelotoxicity attributable to the drug.

Results: We included a total of 16 patients with confirmed diagnosis of LGC by cytomorphology and FISH study and RT-PCR, of which exclude a patient for treatment dropout before completing the three time series, therefore only 15 patients were evaluated, of which 60% (9 patients) were females and 40% were male, age of patients was in the range of 6 to 14 years with a median of 13 years after 6 months of treatment 53% (8 patients) had a cytogenic response as measured by FISH, for 12 months cytogenetic response was 60% (9 patients) and for 18 months of treatment the response was present in 86-6% of patients.

Conclusion: Imatinib Mesylate achieved complete cytogenetic and molecular remission in more than 80% of children treated for chronic granulocytic leukemia, toxicity is not severe and all praise is tolerated by pediatric patients evaluated in this study. Patients were maintained with treatment with IM, so far there is no study indicating that it is time to stop therapy in pediatric populations.

PB007

ACUTE PROMYELOCYTIC LEUKEMIA IN CHILDREN: A SINGLE CENTER EXPERIENCE IN A LOW INCOME COUNTRY

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Purpose: Acute promyelocytic Leukemia (APL), can achieve high cure rates with modern risk adapted chemotherapy protocols, except in many Low Income Countries (LIC). The objective of this review is to present the results of the adaptation of the LPA/99 PETHEMA protocol in a LIC.

Method: We performed a retrospective review of patients less than 18 years of age treated for APL in our center. Demographic data and outcomes are described.

Results: A total of 22 patients were diagnosed with APL between January 2005 and February 2010. Diagnosed in all patients was based on morphology and flow cytometry. In 11 patients FISH test for PML-RAR was positive. Median age at diagnosis was 10.3 years (range: 2–16). Thirteen patients were male (59.1%) and 11 female (40.9%). Risk classification was assigned as follows: 11 cases as High Risk (>10,000 leukocytes), 8 as Intermediate Risk (<10,000 leukocytes and <40,000 platelets) and 3 as Low Risk (<10,000 leukocytes and >40,000 platelets).

All patients received treatment based on the APL PETHEMA protocol, with the same doses and chemotherapy agents as in the original including all-trans retinoic acid (ATRA) and all-cytarabines. Seventeen patients completed the treatment plan and 5 were lost of follow-up (were transferred to another hospital). Six patients died: 5 in the low risk group and in the 1 intermediate risk group. Two deaths resulted from progressive disease, 3 from intracranial hemorrhage and 1 from DIC. The overall survival at 60 months was 66%.

Conclusion: This initial outcome provides a framework for additional clinical investigation in this highly curable form of leukemia. These results show that some patients can be cured in selected centers in LIC with current treatment strategies. Adverse events occurred mainly in the High Risk Group. Aggressive supportive therapy and exploring adaptation of protocols to LIC infrastructure and local circumstances is warranted.

PB008

CHILDHOOD ACUTE PROMYELOCYTIC LEUKEMIA (APL): RESULTS OF TREATMENT IN A SINGLE INSTITUTION IN ARGENTINA

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Purpose: APL accounts for 15% of AML in Argentina. Our aim was to evaluate the results of APL cases admitted at our Hospital.

Method: From Jan-90 to May-99, 64 children (41 M/23 F) with APL were diagnosed and treated. Median age: 8.5 (0.9–17) years, median WBC: 18,600, range (0,080–180,000)/mm3, median platelet count: 29,000 (range: 4–168,000)/mm3 and ICD was present in 90% of the pts. FAB M3 variant was diagnosed in 6 pts. Cytogenetics and PCR studies confirmed the diagnosis in 94% pts. Four consecutive protocols were administered: AML90 (n = 14), AML95 (n = 22), AML99 (n = 23) and AML08 (n = 5). ATRA was included from AML95 protocol.

Results: Response to induction: CR: 50 (78%), death (DOI): 13 (20.5%) and null response: 1 (1.5%). The causes of DOI were: ICD-related bleeding (8 pts) (CNS 5 pts before treatment), cerebral infarction (1 pt), purpura fulminans (1 pt), acute renal failure/MOF (1 pt) and sepsis (2 pts). Five of the pts who died during induction were M3v. From the 50 pts who achieved CR, 10 relapsed (bone marrow), 1 died in CR and 1 developed a therapy-related acute leukemia. Five pts (4 relapses and 1 null response) remain in second CR after chemotherapy (1 pt), allo-SCT (3 pts) and auto-SCT (1 pt). Median follow-up of 115 mo (range: 8–236), pDFS (SE) was 57 (6%), pOS (SE) was 67 (6%) and pDFS (SE) was 72 (7%). The pDFS (SE) for the 2 pre-AIDA protocols (n = 27/36) was 62 (9%) and for 2 AIDA-based protocols (n = 23/28) was 87 (8%) (p-value = 0.0904).

Conclusion: 1- DOI were mainly related to bleeding, especially in M3v pts. 2- pDFS was acceptable, but DOI should be decreased. 3- Half of relapses were salvaged by SCT and chemotherapy. 4- Although AIDA-based studies disclosed non significant differences due to low number of pts, these 2 protocols show a trend to achieving better results.

PB009

LONG TERM OUTCOME AND CYTOGENETIC RESPONSE WITH IMATINIB IN CHILDHOOD CHRONIC MYELOID LEUKEMIA

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**Purpose:** Long-term results with Imatinib in children with CML are uncertain. Majority of children with CML in India receive Imatinib, courtesy the Glivec.

**Method:** Study was retrospective. Cytogenetic response was assessed by conventional karyotyping from venous blood. Set-up for evaluating molecular response was unavailable.

**Results:** Imatinib was available since May 2004. 25 children received Imatinib. Median age at diagnosis was 10 years (range: 2–13). The M:F ratio was 2:1.1. All patients, except one, were in chronic phase at the time of initiating imatinib. In 21 patients, hydroxyurea or busulfan had been previously administered for 1–48 months (median: 2.5). The dosage of Imatinib was 260 mg/m² and 340 mg/m² daily, in chronic phase and blast crisis, respectively. 3 patients abandoned treatment while being in hematological remission. One dropped out after a period of 4 years and another after being on Imatinib for 12 years. Of the evaluable 22 patients, 6 (27%) died. One child had blast crisis after 2 months of Imatinib and 2 children after 7 months of therapy. The patient in whom imatinib was started following the blast crisis died as well.

Remaining 2 achieved hematological remission lasting 1–3 years, to die of blast crisis subsequently. 16/22 (73%) children were in complete hematological remission at a laboratory and pathological peculiarities in our children and to identify subsets of

**Purpose:** The ultimate objective of the study is to analyze basic clinical, laboratory and pathological peculiarities in our children and to identify subsets of

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Remaining 2 achieved hematological remission lasting 1–3 years, to die of blast crisis subsequently. 16/22 (73%) children were in complete hematological remission at a laboratory and pathological peculiarities in our children and to identify subsets of

**Conclusion:** Overall survival was 73%, at a median duration of 55 months of Imatinib therapy. Majority of deaths were in the first year of treatment. Cytogenetic response was complete in 79% of children with prolonged hematological response. Late abandonment of treatment is a concern.

**Purpose:** The ultimate objective of the study is to analyze basic clinical, laboratory and pathological peculiarities in our children and to identify subsets of

**Method:** Study was retrospective. Cytogenetic response was assessed by conventional karyotyping from venous blood. Set-up for evaluating molecular response was unavailable.

**Results:** Imatinib was available since May 2004. 25 children received Imatinib. Median age at diagnosis was 10 years (range: 2–13). The M:F ratio was 2:1.1. All patients, except one, were in chronic phase at the time of initiating imatinib. In 21 patients, hydroxyurea or busulfan had been previously administered for 1–48 months (median: 2.5). The dosage of Imatinib was 260 mg/m² and 340 mg/m² daily, in chronic phase and blast crisis, respectively. 3 patients abandoned treatment while being in hematological remission. One dropped out after a period of 4 years and another after being on Imatinib for 12 years. Of the evaluable 22 patients, 6 (27%) died. One child had blast crisis after 2 months of Imatinib and 2 children after 7 months of therapy. The patient in whom imatinib was started following the blast crisis died as well.

Remaining 2 achieved hematological remission lasting 1–3 years, to die of blast crisis subsequently. 16/22 (73%) children were in complete hematological remission at a laboratory and pathological peculiarities in our children and to identify subsets of

**Conclusion:** Overall survival was 73%, at a median duration of 55 months of Imatinib therapy. Majority of deaths were in the first year of treatment. Cytogenetic response was complete in 79% of children with prolonged hematological response. Late abandonment of treatment is a concern.

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new treatment approaches. In a country with a territorial extent of 8,511,996.3 km² there are remarkable challenges due to the wide ethnical and cultural differences. It has been difficult to join physicians for multicentric studies, due to the large distance between centers, facing different technological resources and discrete difficulties as well. **Method:** The board BCG-MDS-PED reviewed, at no cost, the laboratory results and the slides from BM aspirates and biopsies. If MDS is confirmed, we offer complementary studies and an interview the parents to better understand the epidemiology of the disease in our country. Patients can be evaluated by a clinical geneticist whenever it is necessary. The referring physicians can discuss treatment approach. **Results:** 339 patients from 66 centers from 18 states were reviewed: 27 retrospectively (before 1997-6 centers/22 states), and all others prospectively: 135 from 1997–2002 (37 centers/11 states) and 177 from 2003–2009 (51 centers/6 states). Of 331 evaluable, 43% (n = 141) had MDS: 16 RA/RCMD, 83 RAEB/RAEB-t, 22 JMML, 7 secondary MDS, 8 Down and 4 unclassifiable. In 61 cases diag was not possible (inconclusive smears or poor samples) and 127 had other diagnoses, including acute leukemia (50 cases - 39 AML). **Conclusion:** BCG-MDS-PED is now a reference for Brazilian physicians. Our studies have been presented in national and international meetings or journals to offer better attention for general hematologists and pediatricians. The number of patients has progressively grown. The most frequent are RAEB or RAEB-t. We will continue our effort to teach pediatric MDS morphology and to start a prospective treatment protocol.

**PB013**

**FLT3 MUTATION AND RELATION WITH PROGNOSIS IN CHILDHOOD ACUTE LEUKEMIAS**

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**Purpose:** The fms-like tyrosine kinase 3 (FLT3) is now recognized to be a critical mediator in the pathogenesis of myeloid and some lymphoid leukemias. We want to investigate FLT3 mutation and relation with prognosis in patients with acute leukemia. **Method:** 40 acute myeloid leukemia (AML) and 80 acute lymphoid leukemia (ALL) patients were evaluated from December 2000 to December 2009. Peripheral blood samples were studied with Real-Time(RT)-PCR and high-resolution melting analysis technique (HRMA). ITD and D835 mutations were investigated. **Results:** FLT3-TKD (D835) point mutation was not observed in 120 patients (wild tip). FLT3-ITD mutation was found in 9 of 40 AML (22.5%) ve 60 of 80 ALL patients (7.5%). Unidentified mutation detected in 3 AML patients with HRMA method was considered as a suspicious mutation. 4 boy and 5 girl AML patients had FLT3-ITD mutation. Relapse was seen in 2 of 9 patients. Of 5 were died including relapsed patients. 3 of 9 patients are on maintenance therapy yet and 1 of them are followed up without chemotherapy. FLT3-ITD mutation was positive in 4 boys and 2 girls ALL cases. Relapse was seen in 2 of 6 cases. 3 cases were died including relapsed patients. One is on maintenance therapy and 2 cases are still receiving chemotherapy. While three-year overall survival (OS) was 33% in AML patients with FLT3-ITD mutation, AML patients with normal FLT3-ITD had 90% three-year OS. The difference of OS in between normal ITD and ITD mutation was statistically significant. (p < 0.05). Three-year event free survival (EFS) was 60% and 89% in AML patients with FLT3-ITD mutation and normal FLT3-ITD, respectively. There is no statistical difference in ALL patients in terms of OS and EFS (p > 0.05). **Conclusion:** FLT3-ITD mutation was an important indicator for the determining of prognosis in AML patients.

**PC001**

**NON-ANAPLASTIC PERIPHERAL T-CELL LYMPHOMA IN CHILDHOOD AND ADOLESCENCE: A REPORT FROM THE TAIWAN PEDIATRIC ONCOLOGY GROUP (TPOG)**

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**Purpose:** To know the subtypes and their outcomes of peripheral T-cell lymphoma (PTCL) other than anaplastic large cell lymphoma (ALCL) occurring in children and adolescents in Taiwan. **Method:** We collected patients younger than 18 years of age diagnosed with non-anaplastic PTCL and registered to the TPOG during the period 1998–2009. The histologic subtypes, stages, primarysites, and the treatment outcomes as of February 28, 2010 were analyzed. **Results:** From January 1998 to December 2009, totally 498 patients aged < 18yr were registered to the TPOG with the diagnosis of non-Hodgkins lymphoma (NHL), 46 of them (9.2%) were diagnosed with non-anaplastic PTCL with a median age of 12.9yr. The histologic subtypes were: (1)PTCL, NOS in (median age: 11.5yr), primary site was head/neck in 7/4 died of disease), mediastinum in 3 (all died), others in 5 (all died); (2)Cutaneous T-cell lymphoma(CTCL) in 13(median age:10.8yr) including 3 lymphomatoid papulosis, only one with EBV-associated cutaneous NK/T-cell lymphoma case died; (3)Subcutaneous panniculitis-like T-cell lymphoma(SPTCL) in 9(2M/7F; median:14.3yr), 3 known dead; (4)Nasal NK/T-cell lymphoma(NKTCL) in 5(median:17yr), 2 known dead; 2 remain in CCR for 7.9 and 11.2yr; (5)Hepatosplenic T-cell lymphoma(HSTCL) in 2 boys(10&16yr), both presented as leukemia and died of refractory disease; (6)Angioimmunoblastic T-cell lymphoma(ATL) in 2, 1 died; (7)Enteropathy-type T-cell lymphoma(EATL) in one 6.9yo boy; (8)Aggressive NK-cell leukemia in a 13yo girl, died soon. The survival time for the 20 patients known dead ranged from 1.7-22.8mo with a median of 5.6mo only. All 5 EBV-associated/3 PTCL-NOS, 1 CTCL, 1 NK-cell leukemia) cases ever presented with HLH died. The overall survival rate should be lower than 60% for these 46 PTCL patients. **Conclusion:** Non-anaplastic PTCLs are rare in young people, most of them present with advanced and aggressive diseases except CTCL, and bare worse prognoses than other usual subtypes of NHL occurring in this age group.
INTENSIVE CHEMOTHERAPY IMPROVES OUTCOME OF ADOLESCENTS AND YOUNG ADULTS (AYA) WITH GERMINAL CENTER B-CELL-LIKE SUBTYPE OF DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

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Purpose: DLBCL is a generic term for a clinically and biologically heterogeneous group of tumors. Depending on a gene expression profiling of DLBCL has revealed molecular subtypes that include germinal center B-cell-like (GCB) and activated B-cell-like (non-GCB). The prognosis of pediatric DLBCL mostly GCB has improved since short intensive multi-agent chemotherapy regimens like NHL-BFM 90 was introduced. The purpose of this study was to determine the efficacy of NHL-BFM 90 protocol for AYA with DLBCL.

Method: From 10.1998 to 04.2008, 28 (m-14, f-14) patients (pts) with de novo DLBCL were treated with 6 chemotherapy cycles similar to those in NHL-BFM 90. Before 2006, 18 pts received a modified treatment cycles with the reduction of methotrexate (1 g/m²/36h instead 5 g/m²/24h). Since 2006, 10 pts received therapy on a national pediatric protocol B-NHL-2004M. This protocol differed from BFM by adding rituximab 375 mg/m² on the first day of each cycle and reduction of methotrexate doses only in the first 2 cycles (1 g/m²/24h instead 5 g/m²/24h). The cases were classified as GCB or non-GC by immunohistochemistry (Hans, 2004).

Results: Median age was 7.45 (range: 0.23) years. 59% (56/95) of patients achieved complete remission after 6 cycles of chemotherapy. 74% (71/95) had complete response post chemotherapy.

Conclusion: AYA with immunohistochemically determined GCB-type DLBCL have an improved prognosis as a result of intensive BFM-like therapy in contrast to non-GCB.

THE USE OF ULTRASOUND AT DIAGNOSIS IN ENDEMIC BURKITT LYMPHOMA IN CAMEROON

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Purpose: Endemic Burkitt’s lymphoma (eBL) is the most prevalent childhood cancer in sub-Saharan Africa, described in the literature as primarily a cancer of the jaw. Ultrasoundography (US) has recently become more available in sub-Saharan Africa, described in the literature as primarily a cancer of the jaw.

Method: From 1/2002 to 12/2008 to determine the clinical, pathological features, treatment and outcome of patients with relapsed mature B-cell Non Hodgkin’s Lymphoma who relapsed or were refractory after intensive first line treatment.

Results: Four of 32 (12%) patients relapsed. Their age ranged from 5.2–15.3 years. There were 3 males and one female. Clinico-pathological features at initial diagnosis included: 3 Burkitt’s lymphoma and one diffuse large B cell lymphoma. Stage III in 3 and stage IV in one (CNS positive with CSF blasts). Stage III patients had both mediastinal and abdominal involvement. None of the patients had bone marrow (BM) involvement. Three patients had elevated LDH above twice upper limit of normal for age. All patients were treated per FAB/LMB96 protocol: 3 group B and 1 group C. All patients were good reduction phase responders and achieved complete remission before relapse.

Conclusion: Time to relapse was very short, 37–215 days (median 82 days). Sites of relapse were at least one primary site, combined with BM in 2. The patient with initial CNS involvement relapsed in the CNS and BM. His CNS remission was very short with only 37 days to relapse in the CNS.

OUTCOME OF RELAPSED MATURE B-CELL NON HODGKIN’S LYMPHOMA

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Purpose: To study the clinico-pathological features, treatment and outcome of patients with relapsed mature B-cell Non Hodgkin’s Lymphoma (B-NHL) who relapsed or were refractory after intensive first line treatment.

Method: Retrospective review of patients who were diagnosed with relapsed B-NHL from 1/2002 to 12/2008 to determine the clinical, pathological features, treatment and outcome.

Results: Four of 32 (12%) patients relapsed. Their age ranged from 5.2–15.3 years. There were 3 males and one female. Clinico-pathological features at initial diagnosis included: 3 Burkitt’s lymphoma and one diffuse large B cell lymphoma. Stage III in 3 and stage IV in one (CNS positive with CSF blasts). Stage III patients had both mediastinal and abdominal involvement. None of the patients had bone marrow (BM) involvement. Three patients had elevated LDH above twice upper limit of normal for age. All patients were treated per FAB/LMB96 protocol: 3 group B and 1 group C. All patients were good reduction phase responders and achieved complete remission before relapse.

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Death or treatment failure were documented in 31% (29/95), and 29% (28/95) were lost to follow-up, leaving a known overall survival (one year) of 40% (29/95).

Conclusion: We demonstrate that US contributes to more accurate staging of eBL than clinical exam. Abdominal disease at presentation appears to be as frequent as disease of the jaw. Further study should determine if more accurate staging is useful in risk-stratifying treatment and following response.
performed in any due to the very brief duration of responses achieved. All patients died of disease progression.

Conclusion: With current intensive front line therapy, the outcome of relapsed B-NHL remains very poor with fatal outcome in the majority of patients. Effective therapy incorporating novel therapeutic approaches in patients at high risk of relapse, as patients with CNS positive disease or high LDH, remains under investigation.

PC007

EPSTEIN BARR VIRUS EXPRESSION AND LATENCY PROFILE IN PEDIATRIC BURKITT LYMPHOMA, ITS CORRELATION WITH APOPTOSIS MARKERS

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Purpose: There are three epidemiological forms of Burkitt Lymphoma (BL) according to Epstein Barr virus (EBV) association. The “endemic”, in children in areas with holoendemic malaria, is 100% EBV+. The “sporadic”, mainly in children, is 15%-20% EBV+ in Western countries and with a higher EBV association in locations like equatorial Brazil. The “AIDS-BL”, in HIV-infected individuals, is 30%-40% EBV+. Objective: To characterize EBV association and latency pattern in pediatric BL population from Argentina, and to correlate this with apoptosis markers.

Method: We analyzed 28 BL pediatric patients (3 HIV+), age range 1 to 16 ys (median: 5ys), male:female ratio 17:11. EBV expression was evaluated by EBERs in in situ hybridization, and aCas3, bax and bcl2 expression was assessed by immunohistochemistry in formalin fixed-paraffin embedded lymph node biopsies. RNA extraction was performed with Qiagen RNAeasy FPPE kit, and in RNA+ samples, EBV RNA expression was characterized by RT-PCR for EBERs, LMP1, LMP2A, BZLF1 and BHRF1.

Results: Ten out 28 cases (35.7%) were EBERs positive, 7 immunocompetent samples, EBV RNA expression was characterized by RT-PCR for EBERs, LMP1, LMP2A, BZLF1 and BHRF1. Even though, in Kaplan Meier survival analysis, 5 ys event-free survival (EFS) in EBV+ cases was 42%, lower than 79% observed in EBV- cases, this different was not statistically significant (p = 0.1431, log rank test).

Conclusion: EBV expression in immunocompetent patients showed the “sporadic” pattern described in Western population, and in the immunocompromised ones, a 100% of EBV expression, higher than the observed in AIDS-BL. We described a type I latency pattern. EBV presence did not alter the apoptotic pathway analyzed. Further analysis with a larger series of pediatric patients will be needed to confirm the trend to a worse 5ys EFS observed in EBV+ patients.

PC008

HUNGARIAN EXPERIENCE WITH THE NHL-BFM95 PROTOCOL

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Purpose: In the time period 1998–2008 all of the Hungarian pediatric oncology centres treated the NHL patients according to the NHL BFM95 protocol. During this time period 205 patients (until 18 years of age) were diagnosed with non-Hodgkin’s lymphomas.

Method: The distribution of treatment groups according to histological subtypes included approximately 34% TGI (lymphoblastic lymphomas), 48% TGI1 (B-cell lymphomas) and 18% TGII (anaplastic large cell lymphoma) patients. From the TGII patients 55% had Burkitt lymphoma, 31% diffuse large B-cell lymphoma, 5% primar mediastinal large B-cell lymphoma and 9% other histological subtypes.

Results: 18% stage I, 25% stage II, 37% stage III, 19% stage IV. The 3 year disease free survival was 72% in TGI, 84% in TGII and 67% in TGIII. In TGII event free survival rates according to stages: were 100% in stage I, 96% in stage II, 79% in stage III, 82% in stage IV, 68% in stage V. Disease free survival rates (at 3 years) of NHL patients improved in the last decades from 73% in the time period 1998–2002, to 84% in the time period of 2003–2008. 12% of patients relapsed during examination period. Death caused by therapy related toxicity was 4% in the last decade, while it was 10% earlier.

Conclusion: The prognosis (OS and EFS rates) for children and adolescents with non-Hodgkin’s lymphoma has improved in the last decade in all three treatment groups, while toxic death cases and infectious complications decreased. This study was supported by the Hungarian Pediatric Oncology Group.

PC009

THE ROLE OF FDG-PET/CT IN FOLLOW-UP OF CHILDREN WITH LYMPHOMA

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Purpose: Positron emission tomography using 18F-fluorodeoxy-glucose (FDG-PET) is considered as an excellent tool for monitoring disease status in patients suffering from lymphoma.

Method: We retrospectively reviewed results of PET/CT scans performed 4–6 weeks after completing of chemotherapy in 60 children with lymphoma (29 Hodgkin lymphomas and 31 non-Hodgkin lymphoma). 23 females and 37 males were examined. The median age of the patients at PET/CT was 13.5 years (2–20 years). The median follow up time after scan was 33.5 months (1–108 months). 129 examinations were carried out and analysed.

Results: 74 scans showed a complete metabolic remission and all clinical investigations proved a complete remission of the malignant disease. From the 55 positive PET/CT scans 20 were false positive (histological examination negative or during closed follow up no progression). The other 35 positive scans detected residual tumor mass after therapy or relapse/progressive disease. Most of the false positive metabolic activities were detected in peripheral lymph node regions (neck, axilla, inguinal lymph nodes). The negative predictive value (NPV) of PET/CT was 100%. However, the positive predictive value (PPV) was 63.6%.

Conclusion: According to our data a negative PET/CT scan during routine follow up for children with lymphoma strongly suggests absence of the malignant disease but a positive PET/CT scan has a lower PPV and should be interpreted with caution.

PC010

CTLA4 POLYMORPHISMS INFLUENCE HISTOLOGICAL, AND CLINICAL CHARACTERISTICS AND OUTCOME IN PEDIATRIC HODGKIN LYMPHOMA

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Purpose: Introduction: Classical Hodgkin lymphoma (cHL) is characterized for a low percentage (1–10%) of Hodgkin and Reed-Sternberg cells (HRS) amidst a high number of inflammatory cells, mostly with a suppressor profile. The cytotoxic T-lymphotcyte antigen-4 (CTLA4) encodes an immune receptor molecule that inhibits T cell proliferation. Its polymorphisms appear to differentially influence its inhibitory activity though the efficiency of processing and expression level of the molecule. Objective: To investigate if CTLA4 polymorphisms influence the tumor microenvironment condition, clinical characteristics and outcome in pediatric cHL.

Method: Methodology: 104 children (until 18y, median 16) were included. DNA was extracted from peripheral blood or tumor diagnostic samples. Three CTLA4 polymorphisms (-1722A/G, 49AA, 49AA) were more frequent in the low-risk group (p < 0.016) were detected in samples from children with CTLA4-49AA. Patients bearing the CTLA4-49AA genotype were more frequent in the low-risk group (p = 0.037). CTLA4-49AA (high inhibitory potential) was associated with a better event-free survival (EFS) (87% CTLA4 +49AA vs 66% in other genotypes;
p = 0.045). The CTLA4 haplotype 49/GC60G was associated with a low EFS (p = 0.015).

Conclusion: Conclusion: This is the first study to investigate CTLA4 polymorphisms in HL, and shows a potential effect of CTLA4 variants on CHL microenvironment, clinical presentation and outcome. CTLA4 may be useful as a prognostic marker and therapeutic target in pediatric HL.

PC011 CIRCULATING EPSTEIN-BARR VIRUS DEOXYRIBONUCLEIC ACID AS A BIOMARKER OF TREATMENT RESPONSE IN CHILDREN WITH HODGKIN LYMPHOMA

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Purpose: Hodgkin lymphoma (HL) is one of Epstein-Barr virus (EBV)-induced malignancies. EBV genome and EBV-encoded latent membrane proteins (LMP) are frequently detected in tumor cells of HL patients, particularly in children. Circulating EBV-DNA has been detected in 40–60% of untreated HL cases. We assessed the value of EBV-DNA as a biomarker of treatment response in EBV-associated pediatric HL.

Method: In this prospective study, all newly diagnosed cases of HL younger than 18 years of age were enrolled between August 2007 and May 2009. Age and sex-matched controls were selected. Pre-treatment plasma samples of HL cases were tested by EBV real-time quantitative-PCR (RQ-PCR) with LightCycler2.0, Roche, and by EBV serology (VCA-IgG and EA-IgG). EBV-LMP1 immunohistochemistry was done on HL lymph-node biopsies. ABVD chemotherapy was administered. Post-chemotherapy EBV RQ-PCR was reassessed after the first, second and last cycles.

Results: Eleven children with HL and 31 controls included. HL cases had stage I, II, III (2 cases each) and IV (5 cases). EBV immunohistochemistry was positive in 8 out of 9 (89%) analysed. Nine out of 11 cases had detectable EBV-DNA, while all the controls were negative (p < 0.001). There was no significant difference in markers of tumor burden (stage, bulky disease, number of nodal areas involved, LDH) between RQ-PCR positive and negative HL cases. 58% of HL cases showed late EBV infection vs. 48% of controls (not significant) while none had EBV reactivation. All cases initially positive for EBV-DNA showed clearance 4 weeks after the first cycle while clinical and imaging response after 2 cycles was partial response, very good partial response or complete response in 3 cases each. All were in complete remission and EBV RQ-PCR negative at the end of therapy.

Conclusion: EBV-DNA becomes undetectable early after initiating HL chemotherapy. Circulating EBV-DNA can be used as a biomarker of treatment response in EBV-associated HL.

PC012 ESCALATED BEACOPP IN CHILDREN WITH ADVANCED HODGKIN’S LYMPHOMA

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Purpose: Fifty-five patients with advanced-stage Hodgkin’s lymphoma (HL) were enrolled in this study from May 2003 to March 2010. Patient’s age: 3–16 yrs (median 11.8 ± 3). Fourteen pts (25.5%) with large mediastinal mass had III a, 16 pts (29.1%) = III b, 25 pts (45.5%) = IV a, 52 pts (96.4%) had mediastinal mass, 22 pts with lung and 7 pts with bone lesions, 45 pts (81.8%) had B-symptoms.

Method: Induction therapy consisted of four cycles of escalated BEACOPP (BLEO 10 mg/m² 8 d, IFOP 200 mg/m² 1–3 d, DOXO 35 mg/m² 1 d, CPM 1200 mg/m² 1 d, VCR 8 mg/m² 8 d, PROC 100 mg/m² 1–7 d, PRED 20 mg/m² 1–14 d). Response rate was assessed after four courses of chemotherapy. Forty-seven pts, with PR > 70% continued therapy: females - 4 cycles of COPP/ABV without RT and males - 2 cycles of ABVD with RT (20 Gy). Slow responders (6 pts), discontinued therapy: females - 4 cycles of COPP/ABV without RT and males - 2 cycles

Results: Fifty-two patients are in CR, 1 pts relapsed (alive in CR2 after auto PSC transplantation), 2 pts did not responded (1 died from PD, 1 alive in CR after auto PSC transplantation), 1 pt died from sepsis in CR. Twenty-three females haven’t got RT. Median follow-up is 73.2 ± 2.6 mo. 5-EFS = 92.5% ± 3.6%; 5-RFS = 94.4% ± 3.2%; 5-OS = 96.2% ± 2.7%.

Conclusion: We suggest that escBEACOPP regimen is tolerable and shows good treatment results in patients with advanced stages HL.

PC014 OUTCOME OF HODGKIN’S LYMPHOMA IN PAKISTANI CHILDREN TREATED ACCORDING TO MODIFIED UKCCSG HD 2000 PROTOCOL - SINGLE INSTITUTIONAL EXPERIENCE

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Purpose: To review the outcome of children with newly diagnosed Hodgkin’s Lymphoma(HL) treated according to modified UKCCSG HD 2000 protocol and to review treatment related toxicity.

Method: All newly diagnosed children with HL under 18 years, treated at our centre between January 2002 and April 2008 were included in the study. Treatment included alternating chemotherapy courses of Chlorambucil, Vinblastine, Prednisolone and Procarbazine (ChlVPP); and Doxorubicin, Bleomycin, Vinristine and Dacarbazine (ABVD). Children with large mediastinal masses and those with residual disease at the end of chemotherapy received involved field radiotherapy (IFRT; median dose 27 Greys).

Results: There were 292 patients (236 males) eligible for the study. Median age was 10 years. Mixed cellularity subtype was found in 157 (53%) patients. Five (2%) patients had stage I, 118(40%) had stage II, 126(43%) had stage III and 42(14%) had stage IV disease. B symptoms were present in 98(33%) patients. IFRT was required in 93 (32%) patients. Grade 3 or 4 haematological, gastrointestinal and infectious toxicities were observed in 6%, 5% and 4% of children after ChlVPP cycles and 7.5%, 7.5% and 7% after ABVD cycles. Median follow up was 41(maximum 109) months. Overall survival(OS) and event free survival(EFS) were both 100% for stage I; 97% and 91% for stage II; 98% and 89% for stage III; and 85% and 82% for stage IV respectively. Children with B symptoms had OS of 94% and EFS of 87%. Advanced disease(stages IInd and IV) was associated with poorer OS and EFS (91% and 83% versus 98% and 95% for low stage disease: p = 0.005).

Conclusion: Excellent outcome is achieved with the current hybrid treatment for HL. This chemotherapy regimen was tolerated well by Pakistani children without significant toxicities. Long term toxicities of infertility and second malignancies need to be evaluated in future studies.

PC015 HODGKIN’S DISEASE IN PAKISTANI CHILDREN: EXCELLENT OUTCOME WITH COPDAC/ABVD CHEMOTHERAPY AND RADIONUROUWAY ONLY TO BULKY RESIDUAL DISEASE

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Purpose: To assess efficacy of chemotherapy with alternating courses of COPDAC/ABVD and radiotherapy only for residual bulky disease in children with Hodgkin disease.

Method: Between June 1997 to June 2009, 111 previously untreated patients were investigated, treated and analyzed for remission and survival. Depending on response assessed with CT scan 4 to 8 courses of COPDAC/ABVD chemotherapy were administered. Radiotherapy was given only to cases with residual bulky disease.
Results: There were 89 boys and 22 girls with a median age of 8 years. 26% were less than 5 and 70% were less than 10 years old. Neck was the most common (86%) primary site followed by abdomen (39%), and chest (32%). Spleen was involved in 8 and bone marrow in 7 cases. Mixed cellularity was most common subtypes (68%). B symptoms were present in 52%. 68% had advanced stage disease (III-IV) 74% received 6 courses (3 COPDAC, 3 ABVD) 10% received 4 and 16% received 8 courses. Responses were assessed with CT scan only after every two courses. 15 (14%) patients received radiotherapy because of bulky residual disease at the end of chemotherapy. Four died during treatment and one child died due to pneumonitis after completing chemotherapy. Five patients relapsed (4 to 23 months after completion of chemotherapy). None had received prior radiotherapy. All relapses were salvaged with relapse protocol (EPIC and IF radiotherapy). With a median follow up of 4.9 years (range 9 months to 12.9 years) event free survival and overall survival is 91% and 95% respectively.

Conclusion: COPDAC/ABVD is an effective chemotherapy for Hodgkin’s disease demonstrating excellent event free and overall survival. Radiotherapy can be omitted in children without residual bulky disease assessed with CT scan at end of chemotherapy. Excellent survival can be achieved in developing countries without PET and Gallium scan.

PC0016
RADIOTHERAPY IN COMBINED TREATMENT IN I-III STAGE OF HODGKIN’S LYMPHOMA IN CHILDREN

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Purpose: Combined modality treatment using multidrug chemotherapy (CT) and radiotherapy (RT) is currently considered the standard of care in Hodgkin’s lymphoma (HL). To evaluate the efficacy of different approaches and level total doses of radiation therapy after modern chemotherapy on early and long-term results in combined treatment of HL in children.

Method: Five hundred and fifty-two patients with I-III stage biopsy-confirmed HL attending the hematology clinic from 1975 to 2003 were reviewed for personal data, tumor characteristics, laterality, treatment given etc. Prevalence of the process was evaluated according to WHO classification for diseases of hematopoietic and lymphoid tissues (1997).

Results: All children were evaluated according by stage HL (I – 69.2% and III – 27.5%), age (more than 10 years – 46.1%), sex (boys – 65.4%), histology (mixed cell – 57.1% and nodular sclerosis – 26.4%) etc. Complete (CR) and partial (PR) remission were achieved in stage I – 94.5% and 100%, II – 88.7% and 96.3% and stage III – 86.2% and 97.4% of pts, respectively. Local recurrences (LR) were detected in 16.5% pts from 3 to 133 (median – 16.6 months), and frequency of LR increases depending on the speed of onset of CR (after two courses CT – 7.2%, four courses – 14.3%, six courses – 21.3% and after CR – RT – 36%, p < 0.001).

Conclusion: The irradiation only involved fields in low level doses (20-26 GY) is the most effective and adequate method of preventive maintenance of local relapse in patients with complete remission after chemotherapy. At same time, the higher level doses (30-36 GY) in children with partial remission are necessary.

PC0017
HODGKIN’S LYMPHOMA IN LEBANESE CHILDREN

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Method: The charts of fifty patients <20 yrs with HD treated at the Children’s Cancer Center Of Lebanon were reviewed.

Results: The median age was 13 yrs; range (3–20 yrs). The M: F ratio was 2.6:1. Thirty eight (76%) had NS and seven (14%) had MC subtype. Fifteen (30%) had Group 1 disease: stages IA, IB, IIA and (no bulky disease, less than 4 nodal regions, and no hilar adenopathy). They were treated with four courses of COPP/ABV. Twenty (40%) had Group 2 disease (stage I or II with adverse disease features and all stage III patients) and received 6 cycles of COPP/ABV. Fifteen (30%) had stage IV disease and were treated with intensive chemotherapy (AraC/VP16, COPP/ABV, and CHOP). Patients with B symptoms or bulky disease as well as patients who did not achieve complete remission received a total dose of 21 Gy in 12 fractions to all involved fields. Twenty nine (58%) received IF radiotherapy. With a median follow up of 27 months, the 3 as well as the 5 year EFS and OS were 95.2% and 100% respectively. The relapses were a 9 years old male with stage IV B HD and MC histology, and a 16 years old female with stage IIIB, NS subtype and bulky disease. Both had received IF radiotherapy and both recurred after 30 months of therapy. Both were salvaged. No serious early toxicities occurred. FISH and LH measurements after finishing treatment were normal.

Conclusion: Lebanese children frequently present with advanced disease. NS is the most common histology. A CCG protocol was implemented in a developing country and was well tolerated. The EFS and OS were excellent. Relapse occurred in two patients despite radiotherapy.

PC0018
HODGKIN’S LYMPHOMA IN CHILDREN: LONG-TERM RESULTS OF TREATMENT WITH ABVD OR ABVD/MOP/COP PLUS RADIOThERAPY

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Purpose: The treatment of Hodkgkin’s lymphoma (HL) has been increasingly successful lately and the challenge is to decrease its aggressiveness and consequent acute and late toxicity, without impairing results. We describe our experience in treating children and adolescents with HD with an institutional protocol.

Method: Between 1990 and 2005, 68 patients with newly diagnosed HL (20±48 median age 9 yrs) were treated with 3 cycles of ABVD (doxorubicin 25 mg/m², bleomycin 10 mg/m², vinblastine 6 mg/m², dacarbazine 250 mg/m² – D1 and D15) and involved-field radiotherapy for low risk patients, and incremented with three cycles of MOP (mechlorethamine 5 mg/m², vincristine 1.5 mg/m² – D1 and D8 and prednisone 40 mg/m²/day, 14 days) or COP (replacing mechlorethamine by cyclophosphamide 600 mg/m²) and extended field radiotherapy for high risk patients. Stage distribution was: 9(13.2%) I A, 29(42.6%) II A, 5(7.4%) II B, 21.3% and after CR + PET and Gallium scan.

Results: Ten-year OS was 96.1% ± 3.8 for low risk group and 93.3% ± 4.5 for high risk (p = 0.027). The 5-year and 10-year EFS were 92.1% ± 4.4 and 88.9% ± 5.2 for low risk, and 86.5% ± 6.3 and 86.5% ± 6.3 for high risk patients (p = 0.969). No difference in OS and EFS between the use of MOP or COP was detected (p = 0.25). Six events occurred (4.5% VS 7.2%, four courses – 14.3%, six courses – 21.3% and after CR – RT – 36%, p = 0.001).

Conclusion: This protocol resulted effective for the control of HL, but the reduction of radiotherapy must be considered in future programs. The presence of mediastinal bulky disease has a negative impact on EFS and these patients require a special approach.
Purpose: Lymphoblastic lymphoma (LBL) is one of predominant childhood non-Hodgkin’s lymphoma (NHL) subtypes and consists 20–30%. The excellent outcome of children with LBL has been achieved with an acute lymphoblastic leukemia (ALL)-type treatments. The best results come from the BFM group. The purpose of this study was to investigate outcomes children and adolescents with LBL treated with protocol NHL-BFM 90 and 95 in the Moscow region.

Method: 58 (m = 40, f = 18) patients (pts) were enrolled from 05.1991 to 08.2008. Fifty-two (90%) patients were treated with ALL-like therapy protocol NHL-BFM 90 or 95 for non-B-NHL (ALL-type) and 6 (10%) – NHL-BFM 90 for B-NHL. These protocols differed from the original by reduction of methotrexate doses (1 g/m²/24h instead of 5 g/m²/24h).

Results: Median age at presentation was 11.0 years (range 1.5–21.6) years. 45 (90%) pts have a T-cell immunophenotype (T-LBL). 40 (69%) pts were male. 53 (91%) had advanced (III, IV) stage. The presenting sites of T-LBL included mediastinal mass and lesion of bone marrow in 35 (78%) and 13 (29%) cases respectively. The complete response (CR) rate was 94 and 83% for non-B-NHL and B-NHL respectively. 5-years event free survival (5y-EFS) was 0.80 (p < 0.05) (median of observation 4.1 years) and 0.67 ± 0.19 (5.1 years) respectively (p > 0.05). 5-years overall survival (5y-OS) was 0.85 ± 0.05 and 0.80 ± 0.06 respectively (p > 0.05). The situation without mediastinal involvement was a factor unfavorable prognosis for T-LBL: 5y-EFS – 0.56 ± 0.17 vs. 0.90 ± 0.05 (p = 0.036). Sex, age, LDH, slow or fast therapy response, involvement of the central nervous system or bone marrow did not affect on the prognosis (p > 0.05).

Conclusion: The NHL-BFM 90 and 95 for non-B-NHL protocols are effective therapeutic regimes for pediatric LBL and obtained long-term results are comparable with international data.
Leona was performed.

Purpose: Childhood Hodgkin lymphoma is highly curable. Unfortunately event free survival (EFS) in developing countries is still around 50%. AHOPCA is a collaborative group providing protocol driven therapy for children with malignant disorders in Central America and the Dominican Republic. We report here the comparison of results of patients on AHOPCA LH-2004 with hepatic involvement vs. no involvement.

Method: 143 Patients with Ann Arbor stages, IIIB and IV were treated with a modified Stanford V chemotherapy (doxorubicin 25 mg/m², vincristine 6 mg/m² weeks 1,3,5,7,9, 11; vincristine 1.4 mg/m², bleomycin 6 units/m² weeks 1,4,6,8,10,12; cyclophosphamide 600 mg/m² weeks 1,5,9,22 months but has not yet achieved significance. The EFS at 22 months (65%) is similar for both groups however, EFS of death (a), abandonment (b) of therapy (c) or lost to follow-up less than a year from end of therapy. The patients were divided into two groups: Group O no liver involvement and Group 1 liver involvement (hepatomegaly with or without lymphomatous infiltrates).

Results: The patients were divided into two groups: Group O no liver involvement and Group 1 liver involvement (hepatomegaly with or without lymphomatous infiltrates). 99 patients had no liver involvement, 24 had hepatomegaly, 12 lymphomatous infiltrates and 8 both. At last follow up 85 patients are alive and 58 have had an event: death (a), abandonment (b) of therapy (c) or lost to follow-up less than a year from end of therapy. The EFS at 22 months (65%) is similar for both groups however, EFS of the groups diverges beyond 29 months but has not yet achieved significance.

Conclusion: Our data suggest that in the setting of a low income country and modified Stanford V chemotherapy with IFRT, liver involvement with hepatomegaly or metastasis with HL may be predictive of poor outcome. Further follow-up of these patients is required to confirm this observation.

PC024

BURKITT’S LYMPHOMA TREATMENT IN SIERRA LEONE: FINAL RESULTS FROM A PROSPECTIVE PILOT TRIAL

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Purpose: Sierra Leone is a low-income-country in the endemic Burkitt’s lymphoma (BL) belt. In similar settings, promising results with Cyclophosphamide monotherapy have been reported. A prospective trial investigating the feasibility/efficacy of a reduced-intensity-chemotherapy protocol in a rural hospital in Sierra Leone was performed.

Method: Between 2005 and 2008 all children with a clinical diagnosis of BL were included. A biopsy, bone marrow aspiration, CSF-analysis, abdominal ultrasound, and involved sites plain X-ray were performed, when feasible. Treatment included a first intravenous dose of 40mg/Kg cyclophosphamide, followed by oral cyclophosphamide, weekly for two doses and bimonthly until a total of six doses. The protocol evolved with the inclusion of intrathecal methotrexate and pulses of prednisone. The treatment started once clinical diagnosis was achieved as pathology was available weeks later.

Results: Eighty-seven patients were included, 67.8% males, median age 7.4 years. Nearly half of patients presented with moderate/severe malnutrition. Biopsy was performed in 44 (41%) patients. 36 with a BL-verification. Most children presented with advanced disease (32% patients stage-II, 54% stage-III, 14% stage-IV). Although an initial response to treatment was appreciated in 82% of patients (initial complete response in 33(38%), partial in 38(44%) and progressive disease in 11(17%) patients, most of patients experienced relapse and refractory disease. Four children died before treatment, and 21 died during admission therapy, 10 of them with a sudden unexpected event probably related to treatment complications; 25 patients were eventually discharged with refractory disease after relapse. All but 2 patients in CR have been lost to follow up.

Conclusion: The constrictions to perform an adequate diagnosis/staging, along with a high incidence of advanced disease and high dropout-rate, might justify our poor results. To improve BL outcome in the rural environment of Sierra Leone with this reduced-intensity protocol, an earlier diagnosis and improved compliance are needed.

PD001

IMMUNOHISTOCHEMICAL ANALYSIS OF HEPARANASE IN NON-METASTATIC EWING SARCOMA

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Purpose: Heparanase is an endoglycosidase that specifically cleaves heparan sulfate side chains of heparan sulfate proteoglycans, activity strongly implicated in cell dissemination associated with tumor metastasis, and angiogenesis. Expression and significance of heparanase for sarcomas has not been reported.

Method: we examined heparanase expression and cellular localization in a cohort consisting of 69 patients diagnosed with non metastatic Ewing’s sarcoma, 39 pts under the age of 18 years old, 13 pts with a tumor less than 5cm, 36 pts with a tumor of 5–10cm diameter, 36 pts with a tumor larger than 10cm, 32 pts had less than 90% necrosis, 24 pts more than 90% necrosis, all the patients had a minimum follow up of 5 years, 42 pts (61%) are alive without disease, 21 pts (30%) died of disease, 5 pts are alive with disease. Specimens were scored according to intensity, extent and localization (cytoplasmic vs. nuclear) of the staining.

Results: All specimens stained positive for heparanase; in most cases (91%) high staining extent (i.e. > 50% of the cells) stained positively was observed. Weak staining intensity was scored in 62% of the specimens originated from small tumors (<5cm) while the rest 38% were scored as strong intensity, in contrast, 75% of the cases originated from large tumors (>10cm) were scored as strong intensity differences that are statistically significant (p = 0.04). Weak staining intensity was scored in the majority of patients (62%) diagnosed before the age of 18 while the rest 38% exhibited strong heparanase staining (p = 0.03). No correlation was found between the extent of staining or heparanase localization and age or size.

Conclusion: Heparanase staining intensity correlated with increased tumor size and with patients’ age, two prognostic factors associating with a worse outcome. Heparanase inhibitors may, therefore, benefit many types of cancers and incorporated into novel therapeutic modalities.

PD002

OCCASIONAL INVOLVEMENT OF THE OVARY IN EWING SARCOMA

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Purpose: Ewing sarcoma is a highly metastatic malignancy in young patients. Ovarian cryopreservation is often the only option for fertility preservation in cancer patients of reproductive age. Thus, the possibility of ovarian involvement in Ewing sarcoma needs to be elucidated.

Method: Eight patients aged 13–20 years with Ewing sarcoma participated in the study. Ovarian samples were fixed and prepared for light and transmission electron microscopy and frozen in liquid nitrogen for RNA extraction followed by reverse transcriptase polymerase chain reaction. Histological studies including immunostaining for CD99 were used to detect histopathological features. Sensitive molecular methods were used to detect translocations causing the formation of tumour-specific fusion genes.

Results: Seven patients had no evidence of Ewing sarcoma in the ovaries on pathological/molecular studies. However, in one patient molecular studies showed Ewing sarcoma translocation in spite of the lack of pathological evidence.

Conclusion: Ovarian involvement is possible in patients with Ewing sarcoma ovarian tissue should be examined for malignancy traces on both the pathological and molecular levels prior to grafting in order to eliminate the risk of reseeding the cancer.

PD003

AN INTEGRATED GENOMICS APPROACH UNRAVELS A ROLE FOR MICRO-RNAs IN EWS-FLI1 DRIVEN EWING’S SARCOMA PATHOGENESIS

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Purpose: MicroRNAs are non-coding small RNAs with wide-spread post-transcriptional gene-regulatory function. MicroRNAs have been demonstrated to regulate normal organism and tissue development, and aberrant expression is involved in oncogenesis and tumor progression. The EWS-FLI1 transcription factor drives Ewing’s sarcoma (ESFT) pathogenesis by direct and indirect mechanisms. Here, we explored the role of EWS-FLI1 modulated microRNAs for ESFT pathogenesis.

Method: RNA interference was used to silence EWS-FLI1 expression in 5 ESFT cell lines. Pan-genomic mRNA expression profiles were established by GeneChip analysis, and microRNA expression was quantified using a real-time PCR-based screening platform. To establish a EWS-FLI1 specific ESFT microRNA signature, the expression of microRNAs affected by EWS-FLI1 modulation in at least 4 of 5 ESFT cell lines was compared to their expression in primary tumors relative to mesenchymal stem cell samples. Chromatin immunoprecipitation coupled to next-generation sequencing was used to identify EWS-FLI1 binding sites next to microRNA loci. Two independent target prediction algorithms were applied to establish putative microRNA regulated ESFT target genes. This list was compared to the EWS-FLI1 mRNA signature, and genes with expression changes inversely correlated to EWS-FLI1 regulated microRNAs were functionally annotated using the DAVID algorithm.

Results: A ESFT-specific EWS-FLI1 microRNA signature was defined. Among activated microRNAs, members of the oncomir-1 cluster were prominent. Among repressed microRNAs, we identified hsa-mir-145, which we found involved in feedback regulation with EWS-FLI1, and a directly EWS-FLI1 bound microRNA cluster involved in normal endochondral bone formation. EWS-FLI1 modulated gene sets predicted to be targeted by repressed microRNAs showed a significant enrichment in mitosis-related functions, while activated microRNAs were associated with G-protein coupled signaling.

Conclusion: Our integrated genomics approach identified for the first time a role of EWS-FLI1 dependent microRNA expression in ESFT pathogenesis. As microRNA-based therapeutic approaches to cancer treatment are evolving, our data may open a new avenue to ESFT treatment.

PD004

MODULATING EWS/FLI WITH A CHEMICAL GENOMIC APPROACH

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Purpose: While progress has been made in treating patients with localized Ewing sarcoma, little advancement has been made for those with metastatic or recurrent disease. Current regimens employ cytotoxic chemotherapy, and targeted treatments are only beginning to emerge. The EWS/FLI-1 oncoprotein, detected in over 80% of Ewing sarcomas, presents an attractive tumor-specific target. However, because EWS/FLI-1 is a transcription factor, the identification of EWS/FLI-1-directed therapy using traditional pharmacologic approaches is a challenge.

Method: Here we describe an alternative approach to the simultaneous discovery of small molecules that inhibit EWS/FLI-1 and/or several of its downstream targets. We build upon our prior development of Gene Expression-based High-throughput Screening (GE-HTS), an approach to small molecule discovery using gene expression signatures. We capitalize on an improved ability to define a gene signature for EWS/FLI-1, dramatic improvements in signature gene detection and access to over 100,000 compounds.

Results: We have identified a 130 gene signature for EWS/FLI on versus off using the intersection of multiple Ewing data sets, including EWS-FLI1-directed RNAi, induced expression of EWS/FLI-1, and primary human tumors. We next adapted this signature to our GE-HTS assay using ligand-mediated amplification and a fluorescent bead-based detection. Performance was confirmed across five Ewing cell lines using two EWS-FLI1-directed RNAi constructs. In a pilot screen of 1,600 compounds, our assay identified among other novel hits, tapacymycin, a drug known to decrease EWS/FLI-1 protein levels. Next, we identified within the 130 gene EWS/FLI-1 signature multiple sub-signatures for known downstream targets of EWS/FLI-1 (NKX2.2, NROB1, and EZH2) and reanalyzed the pilot data for induction of these sub-signatures. In this way, multiple “screens-within-a-screen” can be performed in silico and the fusing of sub-signature hits in combination is expected to reveal molecules with additive or synergistic activity.

Conclusion: The validation of pilot screen hits and the screening of over 30,000 small molecules are ongoing.

PD005

IS CHROMOSOMAL AMPLIFICATION A MECHANISM OF RESPONSE TO CHEMOTHERAPY IN OSTEOSARCOMA PATIENTS?

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Purpose: Osteosarcoma (OS) is the most common primary malignant bone tumor in children and adolescents, being relatively chemoresistant. Patients with OS are currently treated with multiagent chemotherapy regimens. OS is characterized by high genomic instability, presence of aneuploidy, multiple unbalanced structural rearrangements, and gene amplification. Our objective was to compare the cytogenetic profiles of two sample groups: pre- versus post-chemotherapy samples.

Method: Comparative genome hybridization (CGH) analysis of 12 samples from 10 pediatric patients with high grade OS were performed, 5 at diagnosis and 7 after neoadjuvant chemotherapy. All the samples were microdissected and only tumor active regions were utilized. Two patients had paired samples (both pre- and post-chemotherapy). For identification of imbalances, thresholds were established through control experiments.

Results: CGH detected copy number changes in all 12 samples; gains were more common than losses. In the entire study group, the gains more common were at 2p13-14 and 4q21, while losses were in 3q22-24 and 11q13. When the samples were analyzed by sampling modality, more amplified regions in post-chemotherapy group (including 19 new minimal superposition regions with 70% of similarity) were noticed. Post-chemotherapy changes comprised +1p, +3p, +3q, +4q, +5p, +6q, +12q, +14q, +16p, +22q, +Xp, and all of them were not found in diagnostic samples. This was also found in patients with paired samples.

Conclusion: Mechanisms of gene amplification have been previously involved in acquired drug resistance in OS cell lines, however the genomic events underneath chemotherapy resistance of OS cells in vivo remains unclear. The biological significance of these results needs further investigation in a higher number of patients; nevertheless, the increased number of chromosomal amplifications in OS samples after chemotherapy when compared to OS biopsed samples before treatment suggests
that the amplification of specific genomic regions could be involved in cell selection and/or chemotherapy resistance in OS.

**PD006**

**RECONSTRUCTION AFTER WIDE RESECTION OF DISTAL TIBIA AND ANKLE JOINT WITH ENDOPROSTHESIS**

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**Purpose:** amputation is still now the most widespread operation at distal tibia. The purpose of our research is standardization of surgical treatment at such tumours.

**Method:** We report the clinical and functional outcome of limb preserving surgery and endoprosthetic reconstruction of the distal tibia and ankle joint in five treated between 2008 and 2010. There were all males, the most young patient was 12 years old. Two had osteosarcoma, one Ewing’s sarcoma, and two Giant cell tumour. We have used custom-made endoprosthesis of MUTARS® (Implantcast). All stems of endoprosthesis have been fixed by bone cement with Gentamicin.

**Results:** All patients carried ankle joint orthosis from 2 till 4 months. One patient developed a local recurrence and no patients – metastasis. We have not received any significant complications, such wound dehiscence or infection. The four patients who retained their endoprosthesis had a mean musculoskeletal tumour society score of 75%. All were pain free and able to perform most daily activities.

**Conclusion:** A custom-made endoprosthetic replacement of the distal tibia and ankle joint is good treatment for patients with a primary bone tumour in quality to alternative of amputation.

**PD007**

**FEW INFUSION RELATED SIDE EFFECTS AFTER MIFAMURTIDE**

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**Purpose:** Mifamurtide (L-MTP-PE) is approved in the European Union for treatment of osteosarcoma. Recommended dose and schedule is 2 mg/m² iv over 1 hour twice/week x 12 weeks, then weekly x 24 weeks. Mifamurtide has no known long-term toxicities; infusion related side effects are related to immune activation. We sought to obtain data about side effects encountered within 24 hours of mifamurtide infusions.

**Method:** MDACC Study 2007-0869 for high-risk metastatic and/or recurrent osteosarcoma was approved by IRB by all centers and informed consent obtained in all subjects. As of 15-March 2010, 67 subjects were registered. Initial dose was given at MD Anderson and then subsequent doses were given under the direction of a pediatric oncologist at 31 other centers in the US in 52/67 patients. Since July 2009 families have been requested to provide a 2-page checklist about side effects within 24 hours of each mifamurtide infusion as well as pre-med and post-med information (e.g. use of acetaminphen and/or ibuprofen and meperidine for chills).

**Results:** An initial sample of 200 infusion self-reports was analyzed. Over 100 reports are expected by August 2010. Infusion related toxicities have been modest and mostly grade 1 in severity; no grade 3 or 4 toxicities were seen. Fatigue (N = 46) and headache (N = 31) were the most common side effects. Chills (N = 11), nausea (N = 6), myalgia (N = 5) and fever (N = 4) occurred in 5% or fewer episodes. This may be because subjects, parents, or physicians chose to continue pre/post-meds (ibuprofen and/or acetaminophen) beyond our recommendation for initial few doses, then taper.

**Conclusion:** More physician, nurse, and patient education about pre-meds and post-meds before and after mifamurtide infusions is needed. Mifamurtide appears to be well tolerated with few reported post infusion related side effects. An algorithm to facilitate best immune activation and early pre/post-med tapering with adequate control side of effects will be presented.

**PD009**

**QUANTITATIVE CT STRUCTURAL ANALYSIS IS SPECIFIC FOR PREDICTING FRACTURE RISK IN CHILDREN WITH BENIGN SKELETAL LESIONS: A PROSPECTIVE CLINICAL STUDY**

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**Purpose:** The purpose of this prospective clinical study was to evaluate the specificity of structural rigidity analysis using sequential, trans-axial CT images to predict pathologic fractures in children with benign neoplasms of the appendicular skeleton followed for more than one year. The ability of the affected bone to support axial, bending and torsional loads was compared to the contra-lateral normal bone. Fracture was predicted if the load capacity of the affected bone was less than 67% of the normal bone.

**Method:** Fracture occurrence was evaluated prospectively in a cohort of 45 patients with benign neoplasms of the appendicular skeleton observed for more than one year after fracture risk was assessed using CT-based rigidity analysis (CTRA) and plain radiographs. Patients completed a survey reviewing fracture occurrence, pain and the UCLA physical activity score.

**Results:** Of the 45 patients, 38 completed the survey (84.4%). None of the 38 patients suffered a pathologic fracture one to six (mean 3.5) years after analysis. Fracture was predicted in two cases using CTRA while fracture was predicted in 37 cases using criteria based on lesion size measured on plain radiographs. No fracture was predicted in 6 cases using either method of analysis. The specificity of fracture predictions was 94.7% using CTRA compared to 15.8% using plain radiographs. Most patients reported high levels of physical activity that did not change after the neoplasm was diagnosed.

**Conclusion:** This prospective clinical study indicates that CTRA is more specific than current fracture criteria based on lesion size measured on plain radiographs since these criteria fail to account for the compensatory remodeling of the host bone in response to the neoplasm in a growing child. This study provides objective data to facilitate the decision as to whether to observe or treat a benign neoplasm affecting the appendicular skeleton.

**PD010**

**OSTEOSARCOMA IN CHILDREN AND YOUNG ADULTS: OUR EXPERIENCE IN SINGAPORE**

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**Purpose:** A significant proportion of patients with high grade osteosarcoma presented with pulmonary metastases at diagnosis. Most centers have used identical regimens for patients with or without initial pulmonary metastases. Therefore, we reviewed our institutional experience in osteosarcoma patients to identify the adverse factors on progressive or recurrent disease and survival.

**Method:** Between 1999 and 2007, 47 patients with osteosarcoma were retrospectively evaluated for overall survival (OS), progression free survival (PFS), local recurrence free survival (LRFS) and their determining factors. The treatment regimen composed of chemotherapy (6 cycles of cisplatin/doxorubicin and 4 cycles of carboplatin/ifosfamide) as well as primary tumor control and pulmonary metastasectomy.

**Results:** Thirty-one males and 16 females with a median age of 12 years (range 8–16 years) were analyzed. Twenty patients presented with evidence of pulmonary metastases (n = 16) and combined pulmonary and bony metastases (n = 4). A median follow-up time was 6.4 years (range 2.9–9.9 years). The 2- and 5-year OS was 45% and 30% and the 2- and 5-year PFS was 49% and 27%, respectively. The 2- and 5-year LRFS was 61%, and 52%. In univariate analysis, age at diagnosis (> 14 years) and bilateral lung metastases were significantly associated with lower OS and PFS (p = 0.02 and 0.04, respectively). Patients with initial bilateral lung metastases were at risk for local recurrent tumor (p < 0.004).

**Conclusion:** Bilateral pulmonary metastases at diagnosis was a significant prognostic factor in osteosarcoma patients. This presentation may be used for identifying the high risk patients for more intensive comprehensive therapy.

**PD008**

**INITIAL BILATERAL LUNG METASTASES INFLUENCED LOCAL RECURRENCE, PROGRESSION FREE SURVIVAL AND OVERALL SURVIVAL IN PATIENTS WITH OSTEOSARCOMA**

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**Conclusion:** Bilateral pulmonary metastases at diagnosis was a significant prognostic factor in osteosarcoma patients. This presentation may be used for identifying the high risk patients for more intensive comprehensive therapy.
Conclusion: Survival rates for osteosarcoma in SE Asia region are dismal. We report here our experience in Singapore in children and young adults with primary osteosarcoma.

Method: A detailed retrospective chart review was performed on 79 patients with primary osteosarcoma, seen and treated at Departments of Pediatric Hematology Oncology, KK Women’s and Children’s Hospital and National University Hospital, Singapore from October 1994 to December 2009. All study patients received chemotherapy and/or surgery with approximate length of therapy ranging six to 12 months.

Results: The median age at diagnosis was 11.9 (range, 4.6–24.9) years. Forty-one patients received 2 drug EOI regimen whilst from year 2003 onwards 35 patients received multi-drug T12 like regimen. 55 (70%) patients had localized osteosarcoma, 24 were metastatic (lungs, other bone). Surgery for primary tumor consisted mainly of limb-salvage or amputation. At the time of last follow-up, median 2.0 (range, 0–15.4) years, 41 were ANED, 19 DOD, 8 AWD, and 10 lost to follow-up. Forty-one patients relapsed in lungs and there were two local recurrences. The 5-year EPS and OS for cohort was 28.5% (95% CI, 16.3–40.7) and 65.6% (95% CI, 51.9–79.3) respectively. 5-year OS by metastatic status was 78.5% (95% CI, 61.4–92.4) for localized versus 27.6% (95% CI, 0.0–55.8) for metastatic patients, p < 0.05. Five-year OS by chemotherapy for cohort: T12 like was 73.0% (95% CI, 51.4–94.6) and for EOI like was 62.0% (95% CI, 43.2–80.8).

Conclusion: Survival for localized OS in children and young adult appears to be significantly better with institution of multi-drug regimen. Event-free and overall survivals for metastatic OS remains to be poor throughout. However, the generalizability of these findings is limited by the small number of patients and a variable number of patients who were lost to follow-up.

PD012

PHASE II STUDY OF CIS-PLATINUM AND ORAL VP16 IN PATIENTS WITH A REFRACTORY OR RELAPSED EWING SARCOMA OR A EWING SARCOMA FAMILY TUMOUR (ESFT).

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Purpose: Phase II trials demonstrate the activity of Cis-Platinum (CDDP) in patients with refractory Ewing sarcomas. Trials conducted in adults have demonstrated the feasibility and efficacy of short and intensive courses of CDDP with oral VP16.

Method: A three-staged Simon design was adopted for this phase II study to evaluate the activity and toxicity profile of CDDP administered with oral VP16 in patients with a ESFT.

CDDP was administered on a weekly basis on days 1, 8 and 15 and subsequently on days 29, 36 and 43. CDDP was administered at a dose of 70 mg/m2 for all patients less than 21 years of age and 50 mg/m2 for patients over 21 years of age or in patients who had a prior history of peripheral neuropathy. VP16 was administered at a dose of 50 mg/m2 on days 1–5 and days 29–43 inclusive.

Results: Between January 2003 and October 2006, 45 patients (67% male), aged between 5 and 46 (median 19) were enrolled, of whom 38 were evaluable. 27 had received prior HDCT, 80% primary tumour surgery and 66% radiotherapy. The median number of chemotherapy courses received was 2 (range 1 to 5).

Grade 3/4 neutropenia occurred in 71%, associated with fever in 20%. Grade 3/4 thrombocytopenia in 64%. Grade 3/4 alopecia in 18%. Grade 2/3 ototoxicity in 16%. Response after 2 cycles: 0 CR, 7 PR (19%), 13 SD (34%), 18 PD (47%).

Conclusion: CDDP combined with oral VP16 has clinical activity in refractory or relapsed ESFT. It is well tolerated and has acceptable side effects.
Purpose: To determine outcome and prognostic effects of pulmonary nodules and its characteristics were detected at presentation or during treatment patients with osteosarcoma.

Method: Methods: A series of 139 patients with osteosarcoma 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: Results: There were 84 male and 55 female with a median age of 12.9 ± 3.2 years. Primary tumor was located at lower extremity in 87.8% of patients and greater than 10 cm in diameter in 65%. Most of them (87%) were osteoblastic type. Pulmonary nodules observed at diagnosis and during treatment in 27(19.4%) and 15(10.4%) patients, respectively. Age, sex, duration of complaints, primary tumor location and histopathology were not significantly different in the patients with and without pulmonary nodules. Resolution and stabilization were more common in unilateral and subplevalar lung nodules than parenchymal and bilateral ones (p=0.021 and p=0.041, respectively). Progression were observed in nodules more than five and bigger than 5 mm (p=0.006 and p=0.032). Patients were followed 1 to 44 (37 ± 31) months. Three year overall survival were 65% and 33% in patients without and with nodules at presentation (p=0.005). Overall survival were S and 8% in patients unilateral and bilateral nodules (p=0.002). When number of nodules were more than five and bigger than 5 mm in diameter, the overall survival were significantly lower (p<0.0001, p<0.0001). The treatment modalities and its timing that were used for the primary tumor were not any effect on treatment.

Conclusion: Conclusion: Existence of pulmonary nodules at diagnosis has worse prognostic effect on osteosarcoma. Number, size and location of nodules have a significant effect on outcome of nodules and survival. Metastasectomy suggested for nodules bigger than 5 mm.

PD014

Ewing Sarcoma of the Head and Neck

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Purpose: Ewing sarcoma (ES) may arise from any bone or soft tissue. ES of the head and neck are rare and diagnosed in only 4% of the Ewing sarcoma patients. We analysed outcome and local treatment options in this group of patients.

Method: We analysed the event-free survival (EFS) and overall survival (OS) in 52 German patients diagnosed for Ewing sarcoma of the head and neck. Patients were diagnosed from 1998–2008. Thirty-nine patients were treated according to the EURO-EWING 99 protocol, 13 patients were not included into the trial, but gave informed consent for data analysis. Median age at diagnosis was 11.5 years. Statistical analyses were performed using the SPSS Statistical Package 14.02 and SAS 9.1.3. Survival was estimated by the Kaplan-Meier method.

Results: The majority of the patients were diagnosed for a primary of the skull (43%). Other primary sites were maxilla (13%), mandibula (12%), neck (10%), scalp (4%), face (2%) and other (13%). Large tumor volume was diagnosed in 11%. Local therapy consisted of surgery in 35%, surgery plus radiotherapy in 42% and radiotherapy in 17% of the patients. Three patients received no local treatment. In two patients this was due to progression under systemic treatment. The 3-Y-EFS and respective OS were 0.74 (SE = 0.07), 0.87 (SE= 0.06) in patients with localized disease and 0.25 (SE = 0.15), 0.38 (SE= 0.17) in patients with primary disseminated disease. In patients we analysed outcome according to local treatment approach. Patients, who underwent surgery had a 3-Y-EFS of 0.81 (SE = 0.13), after combined modality local treatment, the EFS was 0.72 (SE = 0.10) and after radiotherapy 0.80 (SE= 0.18).

Conclusion: In patients with Ewing sarcoma of the head and neck, stage and tumor volume at diagnosis are important prognostic factors. Symptoms at diagnosis and local treatment options will be discussed.

PD016

Lack of Cisplatin Induced Hearing Loss as a Predictor of a Poor Outcome in Children with Osteosarcoma

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Purpose: The objective of this study is to identify any correlation between cisplatin ototoxicity and the degree of tumor response to this agent. We hypothesized that subjects with no ototoxicity after 12 week neo-adjuvant therapy would be more likely to have a poor histological response (defined as under 90% necrosis) and worse survival when compared to those with hearing loss.

Method: Osteosarcoma patients at a single institution between 1990–2009 were retrospectively analyzed. All patients who received cisplatin and had complete data available (pathology at week 12, baseline and week 12 audiograms) were included. The cohort was separated into those with any degree of hearing loss (Grades 1 to 4) and those with no hearing loss (Grade 0).

Results: 44 of the 67 subjects have complete data collected and were included in this preliminary analysis. Hearing loss was seen in 22 subjects (50%). Of the 22 subjects with no hearing loss, favorable necrosis was seen in only 7 (31.8%). Of the 22 subjects with grade 1–4 hearing loss, favorable necrosis was seen in 15 (63.4%). Those with Grade 0 ototoxicity are more likely to have poor necrosis of tumor with an odds ratio of 3.75 with 95% confidence interval of 1.07–13.17 (p = 0.034). The 3 subjects with progressive disease had no ototoxicity. Overall survival rates are 77% in those with hearing loss, compared to 54% in those without hearing loss. Final results including Kaplan-Meier curves will be presented at the meeting.
Conclusion: These preliminary results suggest that a lack of cisplatin induced hearing loss may be associated with poor tumor response to chemotherapy and lower survival rates. This suggests that ototoxicity may be a predictor of outcome in Osteosarcoma. Further studies to explore these findings are needed.

PD017

EWING SARCOMA AS SECONDARY MALIGNANCY

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Purpose: Around 3–5% of patients with Ewing sarcoma will eventually following multimodal treatment with chemotherapy, radiotherapy and/or surgery present with a secondary malignancy. It is not however well documented how many patients are being diagnosed with Ewing sarcoma as secondary malignancy.

Method: The GOPOH (German Society of Pediatric Hematology and Oncology) database of two consecutive and nationwide Ewing sarcoma trials was reviewed for Ewing sarcoma as secondary malignancy. This included 2422 patients entered into and treated according to the EICESS92 and EURO-E.W.I.N.G.99 protocols from 1991–2009. The type of the primary malignancy, the interval from diagnosis of the first malignancy to the diagnosis of Ewing sarcoma and the event-free-survival (EFS) were analyzed.

Results: 26 cases of Ewing sarcomas as a secondary malignancy were identified. The most common primary malignancies were acute lymphoblastic leukemia (6) and lymphomas (4). The other diagnoses (16) included osteosarcoma (2), retinoblastoma (2) and other rare malignancies. Median time from diagnosis of the first malignancy to the diagnosis of Ewing sarcoma was 7.5 years (1–29). The median age at diagnosis was 16.5 years (6.7–59.8). 61% of patients presented with localized Ewing sarcoma, 39% with metastatic disease. 3yEFS was 0.77 (SE = 0.12) for patients with localized, and 0.11 (SE = 0.10) for patients with metastatic disease.

Conclusion: Approximately 1% of Ewing sarcoma cases are diagnosed as a secondary malignancy. The outcome appears comparable to the outcome of patients with primary Ewing sarcoma.

PD018

USE OF FDG-PET WITH NON-CONTRACTION BREATHHOLD CT-THORAX OBVIATES THE NEED FOR CONVENTIONAL IMAGING TOOLS FOR STAGING PATIENTS WITH Ewing’S SARCOMA: A LARGE PROSPECTIVE STUDY OF 190 PATIENTS

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Purpose: Ewing’s sarcoma (ES/PNET) is traditionally staged with bone scan, contrast-enhanced CT-scan of thorax (CEPT-thorax) and bone marrow examination. PET-scan is emerging as a promising modality for staging. In this prospective study, we sought to evaluate the role of PET-scan in staging.

Method: One hundred and ninety histologically proven cases of ES/PNET from 2004–2009 were prospectively staged with PET-CT scan with breath hold non-contrast CT-thorax (NCCT-thorax) apart from conventional staging tools including bone Scan, CECT-scan of thorax/abdomen and bone marrow examination. The diagnostic value of PET scan to pick up the primary and metastatic lesions was compared with conventional modalities.

Results: The site of primary disease was axial in 71 (37.3%) patients, appendicular in 100(52.6%) patients and extraskeletal in 19 (10%) patients. 50 patients (17.5%) were metastatic at presentation while 160 (84.2%) patients had localized disease. 11 patients with lung metastases, PET-CT with breathhold NCCT-thorax detected all metastases detected by conventional contrast CT-scan of thorax. Also, PET-scan detected all sites of bony metastases detected by bone scan in 5 patients with bony metastases. None of the patients had bone marrow metastases on bone marrow examination.

Conclusion: PET-CT scan with breathhold NCCT-thorax detects all the metastatic lesions picked up by bone Scan, CECT-scan of thorax and CECT-scan of abdomen at baseline in newly diagnosed patients of Ewing’s sarcoma and, hence, may obviate the need of these modalities in the staging of patients with Ewing’s sarcoma.
recurrent pneumothoraces. One had recurrence and was retreated successfully on salvage therapy (Cladribine and cytarabine based). Three patients with persistent disease needed same salvage therapy. One patient has progressive disease at last follow up. Mean follow-up duration is 4 years. Five of the six surviving patients have had symptomatic improvement but complete radiological resolution is not seen. Five year overall survival was 85.7 ± 13.1% and disease-free survival was 47.6 ± 22.5%.

Conclusion: All the children with PLCH had symptomatic lung involvement. Role of pleuritis for management of refractory cases need to be studied in bigger cohort. Defining response criteria and therapeutic end points in PLCH remain a challenge with radiological findings not always contributing to treatment decisions.

PE002
FRONT-LINE THERAPY OF HIGH-RISK LANGERHANS CELL HISTIOCYTOSIS WITH 2 CHLORODEOXYADENOSINE AND CYTOSINE ARABINOSIDE: AN UPDATE OF A SINGLE CENTER EXPERIENCE

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Purpose: Prognosis of Langerhans cell histiocytosis (LCH) varies from favorable to grim depending on risk organ (RO-þ) involvement and response to therapy. Overall survival in RO- patients is 69%. 2-Chlorodeoxyadenosine (2CdA) and cytosine arabinoside (AraC) are effective as salvage but were not used up-front. The aim was to evaluate response, long-term results and toxicity of 2-CdA + AraC therapy in RO+ LCH.

Method: Nine patients (4 boys/5 girls, median age 6 months) with RO+ LCH were enrolled. Seven patients received three courses of combined therapy (2-CdA 6–9 mg/m²/day, AraC 1000 mg/m²/day, Methylprednisone 5 mg/m²/day for 7 days). This was followed by 2-CdA monotherapy (6 mg/m²/day N5), total number 3 – 7 courses. One patient received four courses of combined therapy, followed by vinblastine (6 mg/m²/week N6) and 8 courses of 2-CdA monotherapy. All patients received maintenance therapy with 6-Mercaptopurine 50 mg/m²/day and Methotrexate 20 mg/m²/weekly until 18 months from therapy start. One patient died of severe respiratory failure caused by viral pneumonia and candidemia.

Results: All evaluable patients achieved partial response (active disease/better status) after first therapy course, at a median of 29 days (24–48). Median time to complete response (non-active disease) was 9 months (5.9–11.1 months). Median time to resolution of organ dysfunction was 5 months (2.9–8.5 months). No reactivations and permanent consequences were observed. Febrile neutropenia developed after all courses of combined chemotherapy (except a patient without initial haematopoetic dysfunction). Eight patients had severe multiple microbiologically documented infections. At last follow-up (median 20 months, 12–48) 8 patients are alive with complete resolution of disease. Five patients completed therapy and 3 are on maintenance therapy.

Conclusion: 2CdA + AraC combination therapy is very effective in RO+ LCH patients. The quality of remission is high with no reactivations and minimal permanent sequelae. This therapy has significant acute toxicity.

PE003
GENETIC STUDIES AND FAMILIAL PREDISPOSITION TO LYMPHOHISTIOCYTOSIS HEMOPHAGOCYTIC IN SPAIN

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Purpose: Genetic and molecular analysis plus familial history were included as diagnostic criteria for hemophagocytic lymphohistiocytosis (HLH) in HLH-2004 protocol. These patients need hematopoietic stem cell transplantation (HSCT) for cure. Genetic mutations have been described since 1999 and ethnic variations observed. The aims of the study were: genetic studies performed in Spanish children included in the protocol and review of epidemiological, clinical, laboratory and follow-up data.

Method: Twenty-eight children from 17 Spanish hospitals had genetic studies (perforin-PRF1 and/or HMUNC and/or STX) since 2004 to 2009. Only the PRF1 gene was sequenced in Spain. Information about consanguinity and familial background were collected. Descriptive and retrospective analyses of the variables were performed using SPSS program.

Results: Patients: 12 women/16 men. Median age: 2.9 years-old (Range: 0–14), 65% diagnosed before 2 age. Clinical data: 26/27 fever, 24/26 splenomegaly, 23/27 hypertriglyceridemia, 18/26 hypofibrinogenemia, 24/27 hyperferritinemia, 22/27 hemophagocytosis in bone marrow. Immunological results: sCD25 in 12 (9 high values) and NK cells activity in 18 (11low/absent).

In 4 patients with familial history, 2 sisters showed the same mutation in the PRF1 gene and in 3 PRF1expression was absent. In 5 patients with consanguinity, one HMUNC gene mutation was found. In the remaining 20 patients, positive results were HLH in 3 (1 PRF1 and 2 HMUNC) and 1 XLPE case, that means 25% of genetic confirmation. PRF1gene was analyzed in 25, HMUNC gene in 15 and other genes in 3.

Conclusion: Genetic studies in Spanish HLH patients showed mutations in 25% and in 2/8 with positive familial history or consanguinity (HMUNC and PRF1). In Spain these test are now incomplete, reference laboratories are not available and some results are still pending, so we do not know the real impact of genetic HLH. It is important its performance in clinical practice in order to differentiate between genetics and secondary forms.

PF001
MALIGNANT EXTRACRANIAL GERM CELL TUMOURS TREATED WITH SURGERY AND/OR CARBOPLATIN-BASED CHEMOTHERAPY AT A SOUTH AFRICAN CENTRE

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P002

EXTRACRANIAL GERM CELL TUMORS IN CHILDREN: RESULTS IN 20 YEARS IN A SINGLE CENTER

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Purpose: Germ cell tumors comprise 3% of all childhood malignancies. This study aims to evaluate demographic data and treatment results in children with extracranial germ cell tumors (GCTs) treated in the Istanbul University, Oncology Institute. Method: GCTs in children were excised without major morbidity or otherwise biopsied. Mature teratomas, stage I testicular and some ovarian GCTs were resected and monitored with AFP and B-HCG (“watch-and-wait” approach). Patients with recurrent stage I disease and all other patients received CEB (etoposide 100 mg/m²/ dx5 days, cisplatin 20 mg/m²/ x 5 days, and bleomycin 15 mg/m² on day 1). Courses were administered every 3 weeks until remission, and then two more courses were given. Results: Between 1989 and 2009, 92 patients with GCT were admitted. 15 were intracranial and 77 extracranial GCT. Among the extracranial GCTs, the median age was 4 years (0 months–16 years). 50 were gonadal (31 ovaries, 19 testes), 15 sacrococcygeal, 4 mediastinal, 3 nonmidline head and neck, 5 other location. Histologic subtypes were: yolk sac tumor (n = 46), dysgerminoma (n = 11), embryonal carcinoma (n = 1), or choriocarcinoma (n = 1), mix germ tumors (9), mature teratoma (5), immature teratoma (n = 4). Fifteen patients were treated with surgery alone, and the rest received CEB. The 5-year survival rate for all patients was 90%. The median follow-up after CEB treatment was 40 months (range, 0 to 228 months); the median number of courses was five (range, three to seven). Nonfatal hematologic toxicity was common. Two children with widespread metastasis, including brain metastasis died at diagnosis, an infant with malnutrition died due to infectious complications during treatment, four died due to disease progression. Conclusion: Conservative surgery, a watch-and-wait approach after complete excision, and CEB for those requiring chemotherapy produced high cure rates and no serious complications.

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P001

LOSS OF HETEROZYGOITY AT 11P13 AND 11P15 IN WILMS TUMOR IN INDIAN POPULATION

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Purpose: 11p13 and 11p15 deletions in Wilms tumor (WT) are the commonest reported molecular pathogenetic event in genesis of WT, in the white population. However, their reported prevalence is very variable in different populations. A Japanese report demonstrated a very low frequency of IGF2 LOH and perilobar nephrogenic rests. This study was conducted to determine the prevalence of 11p13 and 11p15 deletions in Wilms tumor (WT) occurring in the Indian population. Method: Twenty-two cases of WT were subjected to thorough pathological examination. Fresh frozen tissue was evaluated for Loss of heterozygosity (LOH) at sites close to WT1 (11p13) and IGF2 (11p15), using PCR for microsatellite markers (5 markers in 11p13 and 3 markers in 11p15 region). Results: Among twenty two consecutive cases of WT, 20 were unilateral and 2 were bilateral. Among these 22 cases, 6 showed LOH at 11p13 and only 1 showed LOH at 11p15. One of the cases with LOH at 11p13, had intrafetal nephrogenic rest in the adjacent kidney. Another specimen had perilobar nephrogenic rest in the adjacent kidney but did not show LOH for either 11p13 or 11p15 in the tumor. Conclusion: Prevalence of LOH at 11p13 is 27.27% in the Indian children with WT. This is similar to the reported prevalence in the white population. LOH 11p15 was seen in 4.54% of WT, which is much lower than that reported from white population, but it is similar to that reported for East Asian children by the Japanese. The low prevalence of LOH at 11p15 point to a different pathogenetic mechanism for the development of Wilms tumor in Indian children, which may be similar to other East Asian children with Wilms tumor.

PG002

STUDY OF ADRENOCORTICAL TUMORS IN CHILDREN AND ADOLESCENT BY TECHNIQUE COMPARATIVE GENOMIC HYBRIDIZATION (CGH)

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Purpose: Adrenocortical tumors (ACT) are rare neoplasms and frequently fatal, corresponding 0.2% of all pediatric cancers, high incidence of ACT in children in southern Brazil is 10–15 times higher than the world incidence, is divided into adenomas and carcinomas. Molecular aspects involved in tumorgenesis have been investigated but few molecular markers have proved useful for diagnosis of malignancy. Presence of genomic imbalances was found in large number of tumors and studies with CGH showed high degree of chromosomal instability in ACT. Method: 16 tumors were evaluated by CGH, 8 adenomas and 8 carcinomas of patients and two normal adrenal and placenta tissue. Validation of the findings was done by analysis of expression of gene measured by RQ-PCR. Results: All TAC presented CNAs. Adenomas showed a total of 158 changes with an average of 19.7 changes per case. The total number of gains was 113 (71.5%) and losses were 45 (28.5%). Carcinomas showed 284 changes with an average of 35.5 per case; where the total number of gains was 200 (70.4%) and the total number of losses was 84 (29.6%). In adenomas the most frequent changes were: gain of 4p15.1-p15.3 (87.5%) and loss of 20p11.2-p13.2 (100%). In carcinomas the most frequent changes were: gain of 2q14.1-q24.3 (100%) and losses of 3q21.1-q26.2, 20q12-qter, 22q11.2- q13.3 (100%). The most frequent changes in adenomas and carcinomas were gains of 1p21-p31.2, 2p21-p21 (75%) and loss of 20p11.2-p12 (93.7%). The expression of the IGFI gene, located in 11p15.5, was higher in samples than that reported for white population, (p = 0.022). Conclusion: It was shown that there is a large genomic instability in the ACT which is proportional to tumor size, regions of gain and loss may have genes candidates to oncogenes or tumor suppressor genes.

PG003

A NOVEL ONCOFETAL PROTEIN - GLYPICAN 3 - CAN BE A TUMOR MARKER FOR PEDIATRIC RENAL TUMORS, INCLUDING NEPHROBLASTOMAS AND CLEAR-CELL SARCOMAS OF THE KIDNEY

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Purpose: Glypican-3 (GPC3) is a membrane-bound heparan sulfate proteoglycan and is reportedly a tumor marker for hepatocellular carcinoma. GPC3 is expressed in several tumors, including hepatoblastomas and testicular and ovarian germ cell tumors. Here, we investigated the expression of GPC3 on pediatric renal tumor cells and measured the serum GPC3 level in patients to determine whether this protein can be used as a tumor marker for pediatric renal tumors.

Method: Between 1990 and 2010, we encountered 8 pediatric cases of renal tumors. Of these, 7 were classic nephroblastomas (NBs); 1, clear-cell carcinoma of the kidney (CCK). GPC3 expression in the tumor cells was investigated for 6 patients by immunohistochemical staining. Of these 6 patients, 5 were found to be cases of NB and 1 of CCK. Individual blood samples were collected before operation and stored at –80°C until analysis. Serum GPC3 level was measured using the GPC3 ELISA kit (Cusabio Biotech Co. Ltd.)

Results: Immunohistochemical analysis of NB tumors of the 6 patients revealed that all tumor cells expressed GPC3 in varying degrees. Further, GPC3 was immunoreactive for most of microglomerulotubular structures in tumors. The serum GPC3 level increased in 5 out of 6 patients; of these patients, 3 patients showed very high serum GPC3 levels (>.40 ng/ml). Moreover, the serum GPC3 level in 2 of the 3 patients decreased and was within the normal range shortly after tumor resection.

Conclusion: There are no reliable tumor markers for pediatric renal tumors, and this makes postoperative follow-up very difficult for pediatricians. Our data presented here suggests that serum GPC3 can serve as a good tumor marker for pediatric renal tumors, including NB and CCK.

PG004

LOSS OF HETEROZIGOSITY AT CHROMOSOME 1P IDENTIFIES A POORER PROGNOSIS WILMS TUMOR SUBGROUP: RESULTS FROM ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA (AIEOP) TW-2003 PROTOCOL

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Purpose: Specific aims of the AIEOP-TW-2003 protocol included to prospectively analyze/validate the association between tumour loss of heterozygosity (LOH) and clinical variables or outcome in children with Wilms tumour (WT).

Method: Between 9/2003 and 11/2008, 125 children with newly-diagnosed stage I to IV non-anaplastic WT, eligible for AIEOP-TW-2003 protocol, were investigated for 1p, 1q, 11q, 16q, 22q LOH, using appropriate microsatellite markers as designated by the protocol. The analyzed cohort of children was representative of the whole protocol population, as far as stage distribution and patient age (stage I, 42 patients; stage II, 44; stage III, 28; stage IV, 11).

Results: 19% of cases had chromosome 1p LOH, 12% 16q LOH, with 4% of cases displaying LOH at both chromosomal regions. Three-year DFS and OS probability were 0.87 (95%CI: 0.81-0.93) and 0.98 (95%CI: 0.96-1.0), respectively, for the patients as a whole. In the designed statistical model, LOH at 1p was significantly associated with worst DFS and OS, independently from tumour stage and patient age (DFS probability for patients with 1p LOH: 0.67, compared to 0.92 for patients without 1p LOH; log-rank p<.0009). No difference in DFS probability was reported for subgroups of children bearing LOH at other tested chromosomal regions. LOH at chromosomes 1p and 16q were less frequently seen in children <24 months of age (13% and 7%, respectively) compared to children >24 months (22% and 15%), despite not reaching statistical significance. The rate of LOH was not different among tumour stages.

Conclusion: LOH for chromosome 1p represents an adverse risk factor in non-anaplastic WT, however we could not confirm the negative prognostic impact of 16q LOH in our cohort of children. The worst outlook for children older than 24 months of age seemed to be independent from LOH pattern distribution in the chosen age groups.

PG005

AN EVALUATION OF THE UTILITY OF FINE NEEDLE ASPIRATION CYTOLGY IN PAEDIATRIC RENAL MASSES: A STUDY OF 124 CASES FROM INDIA

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Purpose: The utility of pre-operative fine needle aspiration cytology (FNAC) on paediatric renal masses was evaluated with limited use of immunocytochemistry(IICC) for diagnosis.

Method: 242 aspirates from pediatric intra-abdominal masses from January 2004 to February 2010 were reviewed of which 124 cases were clinically and radiologically from the kidney. Papanicolaou and May-Grunwald-Giemsa stained smeared and WT-1 (in 20 aspirates) were evaluated.

Results: The mean(SD) age of the 124 patients was 4.2(3.72) years, of which 75% cases were less than 5 years of age. 81/124 were Wilms tumour (WT), 21/124 were malignant small round cell tumor unspccified, 7/124 were clear cell sarcoma, 4/124 were renal cell carcinomas, and one each of mesoblastic nephroma, germ cell tumor and cystic partially differentiated nephroblastoma were seen. Of 102 suspected WT, 81 could be diagnosed on the basis of identifying tubulipbs or positivity for cytokeratin or WT-1. WT-1 was uniformly positive in all 20 aspirates in which it was done, with strong nuclear positivity in scantly cellular aspirates also. In 21 aspirates a conclusive diagnosis on aspiration could not be made. 3/124 (2.41%) aspirates yielded blood and 5/124 (4.03%) were scant, thus 6.44% of aspirates were unsatisfactory. Early accurate identification of clear cell sarcoma was possible on FNAC. A total of 11.2% of paediatric renal masses had a diagnosis other than WT on FNAC. The four patients of renal cell carcinoma were aged 18, 15, 10 and 9 years. Two patients, who had ultrasound guided aspirations for smaller renal masses had bleeding post procedure, requiring emergency nephrectomy.

Conclusion: FNAC helped in pre-operative assessment of paediatric renal tumors and is ideal for large renal masses seen in developing countries. FNAC has limited utility in small renal masses requiring ultrasound guidance and in older children with higher frequency of renal cell carcinoma.

PG006

ANGIOGENIN EXPRESSION IN WILMS TUMORS CORRELATES WITH PECAM1 EXPRESSION AND CHEMOTHERAPY STATUS

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Purpose: Wilms tumour (WT), is the most common tumor of the pediatric kidney, and it has a mortality rate of 10-15%. Increased microvascular density and angiogenic growth factors, such as vascular endothelial growth factor, correlate with poor survival in WT. Anti-angiogenic therapy remains an alternative to conventional modalities for treating children with relapsed, chemoresistant or metastatic disease. In this study, we compared the expression of angioatin (ANG) in WT's and nephrogenic rest (NR) precursor lesions to ANG expression in fetal kidneys and non-tumoral kidney (NK) samples.

Method: The expression of ANG and PECAM1 mRNA in fetal kidneys, NK and WT samples was compared by using quantitative PCR. ANG and PECAM1 mRNA expression levels were increased in NK compared to fetal kidneys, but they were significantly down-regulated in post-chemotherapy WT's compared to paired NK
samples. This effect was confirmed by measuring ANG protein using enzyme-linked immunosorbent assay.

**Results:** ANG protein levels were higher in pre-chemotherapy and relapse/metastatic WT samples than in post-chemotherapy WT samples. Strong, diffuse ANG immunoreactivity was seen in the glomeruli of fetal kidneys and NK. ANG immunostaining was moderately intense in the metanephric blastema and tubules of fetal kidneys. In NRs and post-chemotherapy WTs, ANG immunostaining was of variable intensity in all the three components of WTs and the endothelia of the vessels. However, ANG immunoreactivity was strong in the glomerular component. Nuclear staining was observed in 10% of WTs. All three components of metastatic and relapsed WTs showed ANG immunoreactivity. The intensity and extent of immunostaining was significantly higher than in post-chemotherapy samples but comparable to that seen in the pre-chemotherapy samples. There was a significant correlation in ANG and PECAM1 mRNA expression in post-chemotherapy WTs.

**Conclusion:** These results suggest that angiogenin is a potential therapeutic target in WTs and that anti-angiogenic treatment may benefit patients with relapsed or metastatic WT.

**PG007**

**AUTOANTIBODY RESPONSE PATTERN IN WILMS TUMOUR PATIENTS: NEW WAYS TOWARDS MINIMAL INVASIVE DIAGNOSTIC OF MALIGNANT CHILDHOOD TUMOURS**

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**Purpose:** Many studies demonstrate the ability of specific auto-antibody patterns to differentiate between malignant and non-malignant diseases as well as between different stages of tumour disease. To our knowledge this is the first study addressing a childhood tumour in this matter. Wilms tumour (WT) is the most frequent childhood renal tumour. Up to date diagnosis is based on radiological findings alone prior to preoperative chemotherapy (CT) in SIOP trials. The risk of treating a benign tumour with preoperative CT is in the range of 1%. Therefore markers predicting a correct diagnosis before treatment are of utmost importance.

**Method:** A pool of human fetal kidney mRNA (21 – 37 gestational weeks, n = 32) was used to construct a cDNA expression library. A total of 54,000 cDNA expression clones were screened with the SEREX method with 5 different pools, with each of them containing up to 5 sera from different histological WT subtypes and stages. After screening of the cDNA library, positive clones were picked and verified twice before DNA isolation was performed. DNA sequence was then analysed using publicly available databases.

**Results:** We were able to identify more than 90 different potential antigens. The most frequently identified antigens are heat shock protein, kinase1/kinase 1 receptor protein, high density lipoprotein binding protein, makoring finger protein, Meningeoma expressed antigen 5, STE20 like kinase and serologically defined colon cancer antigen 1.

**Conclusion:** This study demonstrates the humoral immune response of WT being far more complex than previously indicated. Some of the found antigens are known to be associated with an immune response in adult tumours. These antigens will form the base for a WT specific signature towards minimal invasive diagnostics.

**PG008**

**WILM’S TUMOR: LAST TEN YEARS EXPERIENCE AT KANTI CHILDREN’S HOSPITAL**

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**Purpose:** To study the clinical presentation of Wilms’ tumor and evaluate ten years survival.

**Method:** A retrospective hospital based study was conducted at Kanti Children’s Hospital from March 1998 to February 2008. A total of 60 histopathologically diagnosed children below 14 yr were included in the study.

**Results:** About 2/3rd (66.5%) presented with abdominal swelling followed by abdominal pain and swelling (16.5%), and fever (13.5%). A few children manifested with red color urine (3.5%). The age of children ranged from 1 to 120 months with the mean age of 36 months. Most affected age group was 2 to 5 years (41.5%) followed by 1 to 2 yrs (25%) with the male and female ratio of 3:1. Most of the cases were in stage II (33.5%) and III (36.5%). SIOP and UKCCSG protocols were used to treat these children and overall 10 yrs survival rate was 50%. One fifth (20%) of the cases died, 16.5% relapsed and 13.5% lost to follow up.

**Conclusion:** Despite severe resource limitations, the pediatric oncology unit at our Hospital has been successfully treating Wilms’s tumor with the success rate of 50%.

**PG009**

**BILATERAL WILMS TUMOUR (STAGE V): A REPORT FROM THE ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGICA PEDIATRICA (AIEOP) WILMS TUMOUR 2003 COOPERATIVE PROTOCOL**

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**Purpose:** Bilateral Wilms Tumour (BWT) represents a challenge for pediatric oncologists and surgeons since it has not been extensively studied. Compared to monolateral WT, survival rate is lower and the risk of late effects is potentially higher. The aim of the present analysis is to evaluate the AIEOP-TW-2003 series of BWT in terms of clinical characteristics, type of surgery and survival.

**Method:** We collected 27 BWT (Stage V), registered from October 2003 to February 2010, that represent 8.1% of the whole WT patients enrolled in the AIEOP-TW-2003 protocol.

**Results:** The median age at diagnosis was 30 months (range 11–86 mos), 5 out of 27 (18.5%) had concomitant syndromes and the F: M gender distribution was 2:1. All children underwent preoperative chemotherapy with 2-drug regimen (vincristine and dactinomycin) according to the guidelines of AIEOP-TW-2003 protocol to reduce the tumour volume.

Nine out 27 patients had bilateral partial nephrectomy, 12 had combined partial and complete nephrectomy and in 6 cases data were still missing or it was too early for surgery. Eight patients relapsed or progressed with median time from diagnosis of 14 months (range 6–33 mos), in the following sites: 3 distant metastases, 3 local relapses, 1 para-aortic area and 1 progressed locally refusing surgery. Overall 5 patients died: 3 of disease and 2 of therapy-related complications. With a median follow up of 31 months (range 3–76 mos) we observed a disease-free, event-free and overall survival rates of 70%, 63% and 81.5%, respectively.

**Conclusion:** These data showed a lower EFS and DFS compared to monolateral WT. Noteworthy, with longer follow-up more events are expected in terms of renal failure and iatrogenic late effects. Renal sparing surgery is feasible in a significant percentage of patients and should be considered the best surgical approach for BWT patients.

**PG010**

**UTILIZATION OF NEPHRON-SPARING SURGERY AMONG CHILDREN WITH MALIGNANT RENAL TUMORS**

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**Purpose:** To evaluate the utilization of nephron-sparing surgery (NSS) in children with malignant renal tumors (MRT) and to assess potential influences on tumor recurrence.

**Method:** This study is a retrospective review of a prospective database of patients undergoing NSS for MRT between 1990 and 2010.

**Results:** A total of 125 patients underwent NSS for MRT, with 64% being localized disease and 36% being metastatic disease. The most common indications for NSS were local recurrence (35%), anatomic considerations (23%), and the desire to preserve renal function (16%). The median time from diagnosis to NSS was 1 year (range 0–33 mos). The median follow-up time was 6 years (range 0–39 mos). The overall recurrence rate was 13% (20/153), with 15% of patients experiencing a second recurrence. The median time to recurrence was 1.5 years (range 0–10 mos). The most common recurrence sites were the lung (40%), liver (20%), and bone (15%). The median time to recurrence was 1.5 years (range 0–10 mos).

**Conclusion:** Despite the potential benefits of NSS, including preservation of renal function and potential survival advantages, the rate of recurrence in this cohort was 13%. The most common recurrence sites were the lung, liver, and bone. Further research is needed to determine the optimal indications for NSS and to improve outcomes.

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Supported by ISTC 1489 Project

PG012

Purpose: It is widely accepted that, when feasible, nephron-sparing surgery (NSS) is preferable to radical nephrectomy (RN) for treatment of renal tumors in adults. However, RN is more frequently used in children with renal tumors. We sought to compare in-hospital surgical outcomes after NSS and RN for malignant pediatric renal tumors.

Method: The Pediatric Health Information System (PHIS) combines data from 42 free-standing North American pediatric hospitals. We queried PHIS to identify children with malignant renal tumors who underwent surgery from 2003 to 2008. We examined whether outcomes (complication rates, cost and length of stay) differed by procedure type. Multivariate regression models were used to adjust for confounding and generalized estimating equations were used to adjust for surgeon- and hospital-level clustering.

Results: We identified 1,196 children with renal tumors who underwent RN (92%) or NSS (8%). Despite similar mean APR-DRG severity scores (p = 0.8), patients undergoing NSS had shorter mean hospital stays (7.4 v. 9.4 days, p = 0.04) and lower mean hospital charges, ($47,600 v. $68,100, p = 0.02) than children undergoing RN. Complication rates (16.2 v. 16.3%, p = 1.0) were similar. These associations remained highly significant even after adjusting for other patient, provider, and hospital factors. Conclusion: The majority of children with malignant renal tumors treated at children’s hospitals undergo RN. NSS was associated with shorter hospital stays and lower hospital charges than RN, despite similar disease severity levels and complication rates. While oncologic outcomes are lacking, these data would seem to suggest that NSS may be an appropriate treatment option in well-selected children with malignant renal tumors.

PG011

DELAY OF SURGERY IN CHILDREN WITH UNILATERAL WILMS’ TUMOR

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Purpose: International treatment protocols in children with Wilms’ tumor including preoperative chemotherapy surgery and postoperative chemotherapy with or without radiotherapy depending on histology and stage result in very good survival. In Belarus we achieved 91% long term survival using such protocols. After having good results in survival, we have to think about increasing number of nephron sparing surgery without jeopardizing survival rate. Good imaging technique helps in making surgeon decision.

Method: Chemotherapy (ChT) with 2 or 3 agents is highly effective and usually causes remarkable tumor shrinkage and necrosis a large nephroblastoma and as a result localizes tumor mass to the one pole and in some cases facilitates nephron sparing surgery. In SIOP WT 2001 study (stage I-III) 4 weeks preoperative ChT have been recommended. We modified preoperative ChT chemotherapy in case of good response and relatively less affected and functioning kidney. We prolonged ChT giving 6 weeks (50% more) treatment. Since 2005 totally 58 children (stage I-III) with median age 3 year 2 months have been treated using SIOP WT 2001. In 35 pts 4 weeks ChT (VCR + ACT) was given. Twenty three pts were given 6 weeks ChT, evaluating tumor size (US or CT-scan) after 4 and 6 weeks.

Results: Among 35 pts achieving standard 4 weeks ChT, nephrectomy performed in 29 pts and partial resection in 6. In 23 pts where prolonged (6 weeks) preoperative ChT was given nephrectomy was done in 13 cases and partial resection-10. During follow up (median 12 months) no evidence of relapse in spared kidney observed.

Conclusion: Prolongation of preoperative ChT in some cases with unilateral Wilms’ tumor may increase number of organ sparing surgery. The optimal choice of treatment in this group of pts still merits further investigation. Supported by ISTC 1489 Project

PG012

WILMS’ TUMOR: 8 YEARS EXPERIENCE OF SOUTH EGYPT CANCER INSTITUTE ACCORDING TO SIOP PROTOCOL

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Purpose: According to the treatment of Wilms tumours, two different therapeutic strategies were established in the 2nd half of the last century. Both NWTS and SIOP have helped to improve the clinical management and outcome of Wilms’ tumors patients. In this study we report our experience in management of Wilms’ tumor following preoperative chemotherapy according to SIOP protocol during period from 2002 - 2009.

Method: Clinopathological review was performed 79 patients treated in South Egypt Cancer Institute hospital in Egypt from 2002 to 2009 according to SIOP protocol.

Results: The mean age was 3.6 years, 32(40.5%) patients were less than or equal to 2 years old at the time of diagnosis. male (41) and female (38), The commonest presenting symptom at diagnosis was abdominal mass and/or abdominal distension reported 85%. The tumor was localized in left kidney in38 (48%) and synchronous bilateral Wilms tumour were reported in 7 (8.8%). FH was diagnosed in 86.6%, UH in 10% and benign disease in3.4%. Distribution of the clinical stage (post-chemotherapy) was as follows: I = 55%, II = 18%, III = 10%, IV = 9.2%, V = 8.8%. No case of intra-operative tumor rupture recorded. Nephron sparing surgery was done in 2 cases. Five year stage related survival was as follows: I 91%, II 66.6%, III 66% IV 0% and V 33.3%.

Conclusion: Preoperative chemotherapy increased the rate of stage I disease and decreasing the incidence of intraoperative tumour rupture However, there was a possibility that chemotherapy administered to benign disease or an inappropriately low dose for unfavourable histology. However, not directly contribute the overall survival.

P8013

PEDIATRIC RENAL CELL CARCINOMA WITH PSF-TFE3 GENE FUSION FOLLOWING CHEMOTHERAPY AND ALLOGENEIC BMT FOR THE TREATMENT OF INFANTILE ALL

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Purpose: Renal cell carcinoma (RCC) is rare in children and appears to comprise a group of tumors distinct from RCCs typically seen in adults. Recently described tumors show an association with neuroblastoma or specific chromosomal translocations. Only rarely have other childhood cancers been associated with pediatric RCC. We present a case of pediatric RCC diagnosed 11 years after the treatment for infantile ALL.

Method: The patient is a 11-year-old girl with a history of infantile ALL with MLL genes diagnosed in 22 days of age. She had no family history of germline cancer and underwent chemotherapy and matched related bone marrow transplant (BMT) at 5 months of age. After BMT, she received 4 times of donor lymphocyte infusion because of residual leukemic cells and achieved CR with no signs of GVHD. In October 2009 at 11 years of age, a large mass was noted in the left kidney. Since other laboratory findings were within normal, she underwent left nephrectomy.

Results: Pathological diagnosis revealed melanotic Xp11 translocation renal cancer with PSF-TFE3 gene fusion. After the operation, she is receiving WT1 peptide vaccine and is well doing.

Conclusion: There are no adequate studies to support conclusions about adjuvant or neoadjuvant chemotherapy for children with RCC. We emphasize the importance of close follow-up at routine intervals in survivors of childhood malignancies.
Purpose: Telomerase activity supplies telomere maintenance in chromosomes. It avoids cells to enter senescence. Telomerase activity is one of the crucial steps in various cancers. Wilms Tumor (nephroblastoma) is one of the most common solid tumors of childhood. Hitherto telomerase activity in Wilms tumor was not investigated widely. The aim of this study is to explore telomerase activity in Wilms tumor comparing with Kid67 expression.

Method: This study included 40 nephroblastoma cases of childhood. The telomerase activity and proliferation index was determined by immunohistochemical method on archival paraffin embedded tissue sections. Statistical analysis was done on SPSS15.0 by Mann Whitney U test and Spearman’s correlation analysis.

Results: Telomerase activity was negative in 6 cases, weekly positive in 20 cases, and strongly positive in 14 cases. Proliferation index was 20 to 90 (mean: 60.27 ± 27.86, median: 50). In Spearman Correlation Analysis, telomerase activity was not found to be correlated with Ki67 (p = 0.394) and survival rate (0.797). But both the telomerase activity (p = 0.035) and Ki67 index (0.040) were correlated with the size and dimension of tumor.

Conclusion: Tumor size is an important determinant of outcome, especially in early stage wilms tumors. Because of our findings about the relationship with tumor size and telomerase activity, it will be useful to study the effect of the chemotherapeutic agents on telomerase activity and to compare with clinical parameters in larger series.
Diagnostic Imaging Experience of Renal Tumors in Children

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Purpose: to research characteristic features of different children renal tumors.

Method: The study included 150 children of age: 0–15 years who had renal tumor symptoms. Complex imaging diagnostics was applied to all patients in 2003–2009.

Results: All patients underwent abdomen ultrasound (US), 93.5% contrast-enhanced computed tomography (CT). Morphologically malignant tumors were verified in 130 cases, benign renal neoplasms in 14 cases, and non-neoplastic diseases in 6 cases. Wilms tumors were observed in 68.7% of cases, lymphoma - in 6.7%, renal cell cancer - in 4.7%. Clear cell sarcoma - in 4%, mesenchymal nephroma - in 2.6%, angiomylipoma - in 2.6%, cystic nephroma - in 2%, malignant rhabdoid tumour - in 1.3%, hamartoma - 1.3%, PNET - in 0.7%, germinal cell tumor - in 0.7%, metanephric adenoma - in 0.7%. Unilateral nephroblastoma was identified in 85 cases, bilateral - in 18 cases. Bilateral nephroblastoma, evolved from nephroblastomatosis, was identified in 5 cases. The specific US and CT features of unilateral and bilateral nephroblastoma, nephroblastomatosis, cystic nephroma, hamartoma, renal cell cancer, lymphoma were observed.

US and CT sensitivity in renal tumors identified in patients was 93.2% and 93.6% correspondingly, specificity - 93.5% and 94.5%. US and CT sensitivity in renal tumors local invasion were 90.2% and 97.2%.

Conclusion: US screening is the primary method that can identify children with renal tumors signs. The US-controlled biopsy could be done after that. CT could be used to obtain more accurate data about other tissue, organs and vessels involvement. Thorax CT should be used for lung metastasis diagnostics.

PG019

Analysis of CNS Tumor Involvement of Rhabdoid Tumor of the Kidney

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Purpose: Rhabdoid Tumor of the Kidney (RTK) has an interesting feature of the occasional occurrence of separate CNS primary tumors. The objective of this study is to clarify the clinical significance of CNS involvement of RTK in Japan.

Method: 20 RTK patients were enrolled in the Japan Wilms' Tumor Study between 1997 and 2005. Histological slides of the kidneys were reviewed by one of two pathologists at the time of diagnosis. Variables examined included sex, age of diagnosis, tumor stage, as well as treatment variables. CNS tumor involvement was confirmed by the imaging techniques, including CT or MRI, however, no biopsy material was obtained.

Results: No survival differences were observed between males and females, or patients with tumors of lower stage or higher stage. 2 children without CNS involvement who were older than 2 years at diagnosis were survived for over 25 months, but 18 patients under 2 years were died within 15 months from the diagnosis. 5 of 20 RTK had CNS involvement (25%). At time of diagnosis, 2 CNS involvements were found, 3 were diagnosed as relapses during their therapies. All cases with CNS involvement were under 2 years old children. There was no sex difference. All patients with a CNS lesion were died within 6 months.

Conclusion: Despite of aggressive therapies, RTK is still considered one of the poor prognostic diseases. CNS Involvement is a highly significant poor prognostic factor for survivorship of children with RTK.

PH001

Neuroblastoma Cell Lines, Phenotype and Susceptibility Towards Natural Killer Cells

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Purpose: Currently, the prognosis for relapsed/refractory high-risk (HR) neuroblastoma (NBL) patients is poor, warranting new treatment strategies such as immunotherapy (IT). NBL tumour cells show low or absent expression of HLA class I making them resistant to specific, HLA restricted cytotoxic T cells. The interaction of NK cells with target cells is controlled by a balance of inhibiting (KIR) and activating (e.g. DNAM-1, NKG2D) receptors on the NK cells.

We investigate whether NBL tumours are sensitive targets for NK cells and whether the NK cell cytolytic potential towards NBL tumours can be enhanced.

Method: NBL cell lines have been tested for in vitro sensitivity of killing by NK cells using cytotoxicity assays. Cell lines have been phenotyped using flow cytometry analysis and molecularly typed for HLA to document presence of possible inhibitory KIR ligands. Blocking experiments using monoclonal antibodies (MoAbs) were performed to assess the pathways involved in killing. NK typical ADCCK and anti-GD2 in NBL cell lines was tested.

Results: In vitro experiments using purified NBL cells have indicated that NBL cell lines are sensitive to killing mediated by allogeneic cytokine (IL-15)-activated NK cells, but are barely lysed by resting NK cells. NBL cell lines variably express HLA class I and express some NKG2D ligands, all express DNAM-1 ligands. Interaction of activated NK cells and NBL cells is partially blocked in vitro by MoAbs directed against DNAM-1. Blocking of HLA class I did not result in enhanced killing of NBL cell lines by resting NK cells.

Conclusion: NBL cells express DNAM-1 ligands, making them a target for IT by infusion of activated NK cells. These findings will need to be extended using primary tumor material, in order to further support the potential contribution of infusion of allogeneic IL-15 activated NK cells for the elimination of NBL cells in vivo.

PH002

The Expression of Stem Cell Markers CD133 and Nestin in Human Peripheral Neuroblastoma Tumors

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Purpose: Neuroblastoma (NB) is an embryonic neoplasm originating from neural crest with cellular and clinical heterogeneity as one of its oncological characteristics. Recent studies have indicated that cancer stem cells in tissues and cell lines of neuroblastoma could be by themselves or be differentiated multi-directionally, and that they are related to the high malignancy of NB. CD133 is a transmembrane protein which has been used as a cell marker to isolate the stem cells of neural crest and neural tumors. According to the cancer stem cell hypothesis, CD133-positive cells
determine long-term tumor growth and, therefore, are suspected to influence clinical outcome. Nestin is a marker of multipotent neuroectodermal precursor cells is expressed in a cell-cycle dependent manner and is down regulated as neuroepithelial stem cells cease division and differentiate along their respective neural or glia lineages. The present study examines the relationship between CD133 and Nestin expression in human neuroblastoma specimens and different prognostic factors as stage, histopathology, age, MYCN status and survival.

**Method:** Tissue samples from 32 neuroblastoma cases were collected from 24 neuroblastoma, 6 ganglioneuroblastoma intermixed, and 2 ganglioneuroma whose MYCN & ploidy status were known as to be analysed, first by routine H&E stained sections, then immunohistochemical staining for CD133 and Nestin. The staining intensity was evaluated for the percentage of stained cells as well as the intensity of staining.

**Results:** The ganglioneuroma cases were CD133 negative, the ganglioneuroblastoma intermixed showed low positivity (+), among neuroblastoma cases; 10 cases showed strong positivity (+++), and all were advanced stage, unfavorable histology, MYCN amplified and of poor survival. 11 cases were nestin positive (++++) and were associated with advanced stage. MYCN amplification and unfavorable histology nestin was strongly expressed in tumors from infants.

**Conclusion:** CD133 and nestin could be used as new markers of tumor aggressiveness for peripheral neuroblastic tumors.

**PH004**

**UNRESECTABLE NEUROBLASTOMA IN A TUMOR IN PLACE: PROLONGED SURVIVAL AND VERY LATE EVENTS**

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**Purpose:** Tumor resection is the mainstay of treatment for localized neuroblastoma without MYCN amplification and the majority of relapses occur within two years post-diagnosis. However, very rare patients with a large macroscopic gross residue have a prolonged survival with a stable disease. To our knowledge, no study has investigated the outcome of these patients.

**Method:** We retrospectively identified and reviewed 16 cases of patients with a large macroscopic gross residue and a prolonged survival over 5 years, diagnosed between 1978 and 2002 in the different institutions of the Société Française des Cancers de l’Enfant.

**Results:** Forty-four percent of them were infants at diagnosis with a median age of 13 months (0-99 months). Eighty-one percent had a retroperitoneal tumor crossing the midline and 19% had a pelvic tumor. The median follow-up was 15 years (6.1–25.6 years). Among the 8 patients treated with radiotherapy or 131I-MIBG therapy, two second malignant neoplasms occurred in the irradiation field 21 and 24 years after the initial diagnosis. Three patients relapsed with local recurrence or with distant metastases 8, 17 and 25 years after diagnosis. All 3 patients died of disease progression.

**Conclusion:** Very late events may occur in neuroblastoma patients with a macroscopic gross residue and our study confirms the necessity of a very long term follow-up for these patients. These late events confirm the importance of the surgery of the primary tumor in the disease long term control. The occurrence of secondary malignancies in patients treated with radiotherapy leads to define with caution the indications of this local treatment.

**PH006**

**LONG-TERM SURVIVAL OF PATIENTS WITH THERAPY RESISTANT NEUROBLASTOMA TREATED WITH IRINOTECAN/TEMODAL THERAPY: SINGLE CENTRE EXPERIENCE**

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**Purpose:** Aims: In patients with high risk neuroblastoma (NBL) disease progression or relapse is observed very often. As it is extremely difficult to obtain the second remission, it so seems important to ensure at least the best possible quality of life and long survival. The aim of the study was evaluation of Irinotecan/Temodal as salvage treatment in children with therapy resistant high risk NBL.
Method: Methods: This is observational study in children with NBL progression/relapse. From 2008–2009, seven patients with relapse or progression of NBL treated in Department of Pediatric Oncology and Hematology in Krakow received Irinotecan/Temodal therapy (Koprowski 2006). The group was heterogeneous (1st–4th relapse, different previous relapse therapy). The end point of the study was evaluation of quality of life and patient’s compliance as well as survival analysis and evaluation of toxicities. Observation was finished on 31.12.2009 r.

Results: Results: In all 7 patients who received Irinotecan/Temodal therapy at least partial response was obtained, including 2 with VGPR (residual tumor, no metastases). Median survival time was 31 (24–70.5) months from the first relapse and 61 (37–129) months from diagnosis. Patients received 6–20 chemotherapy cycles. Generally, therapy was well tolerated. The main toxicities were thrombocytopenia and anemia, requiring transfusions after almost every cycle in 4/7 patients as well as elevated transaminase (ALT up to 1500 IU). In 1/7 patients persistent and recurring transaminase increase it was necessary to decrease drug dosage and less frequent chemotherapy employment. Diarrhea was not very severe and was easily controlled with loperamid. Between chemotherapy cycles, as a rule children did not require hospitalization. The quality of life and compliance was satisfactory both for patients and their parents.

Conclusion: Conclusions: Irinotecan/Temodal chemotherapy seems to be reasonable choice for heavy pre-treated children with neuroblastoma, allowing for long-lasting therapy control without unacceptable toxicities, assuring relatively good quality-of-life.

PH007

TREATMENT OUTCOME OF CHILDREN WITH HIGH-STAGE NEUROBLASTOMA: EXPERIENCE FROM SAUDI ARABIA

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Purpose: To report on the outcome of therapy for children with high stage Neuroblastoma (NBL) seen at KFSH&RC, Riyadh, Saudi Arabia.

Method: Medical Records of Children < 15 years of age diagnosed with stage 3/4 NBL between 1982–2005 were reviewed retrospectively. Data regarding demographics, presentation, pathology, treatment modalities and outcome were collected.

Results: There were 240 cases of evaluable NBL during the study period. 162 (67.5%) were high stage disease (Stage 3 = 49 Stage 4 = 113). There were 77 male and 85 female (median age 31.95 months). Most common sites of primary tumor were pelvic and abdominal (133/82.1%), thoracic 19 (11.7%) and other sites 10 (6.2%). The N-Myc female (median age 31.95 months). Most common sites of primary tumor were pelvic were high stage disease (Stage 3). The outcome of treatment for high stage NBL in Saudi Arabia showed similar results to the Western experience with age, stage and N-Myc status comparable.

Conclusion: Conclusions: The outcome of treatment for high stage NBL in Saudi Arabia showed similar results to the Western experience with age, stage and N-Myc status confirmed to be very important risk factors for survival of this disease.

PH008

ARSENIC TRIOXIDE AS RADIOTHERAPIC AGENT FOR 131I-MIBG THERAPY: RESULTS OF A PILOT PHASE II STUDY

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Purpose: Arsenic trioxide (ATO) has in vitro and in vivo radiosensitizing effects. Given its non-overlapping toxicity profile with the known anti-NB radiotherapeutic agent 131I-MIBG, we hypothesized that ATO would enhance the efficacy of the latter and tested the combination in a pilot study.

Method: Patients with heavily pretreated recurrent or refractory stage 4 NBL were treated on an IRB-approved pilot phase II study (NCT00107289). Planned treatment was 131I-MIBG 12 or 15mCi/kg intravenously (IV) on day 1 plus ATO 0.15 or 0.25 mg/m2 IV days 6–10 and 11–15. Toxicities were measured using NCI CTCAE version 2.0 and responses were assessed using International NB response criteria (INRC).

Results: Nineteen patients were enrolled: 14 received 131I-MIBG and ATO at maximal dosages, 2 received 12mCi/kg 131I-MIBG plus 0.15 mg/kg/dose AT; 1 received 18mCi/kg 131I-MIBG plus 0.15 mg/kg/dose ATO; 1 did not receive ATO due to transient central line-induced cardiac arrhythmia, while another received 6/10 doses of AT due to significant diarrhea. All patients experienced grade 4 myelosuppression, though none required autologous stem cell rescue. Other > grade 2 adverse events were transient and included: hyperamylasemia from transient sialoadenitis (12/13 evaluable patients), hypokalemia (3), hyperbilirubinemia and hepatic transaminitis (1), and hyponatremia (1). By INRC, 14 patients had no response while 5 had progressive disease (PD) including 5/6 patients who entered the study with prior PD. However, objective improvements in one or more NB markers were observed in 12 patients. 18/19 patients were continued on further chemotherapy and/or immunotherapy. Three-year progression free survival (PFS) was 37 ± 11% with a median PFS of 9.5 months.

Conclusion: The combination of 131I-MIBG plus ATO was well tolerated with adverse event profile similar to that of 131I-MIBG therapy alone. Objective responses were observed in most patients. However, the addition of ATO to 131I-MIBG did not significantly improve response rates when compared to historical data with single agent 131I-MIBG therapy.

PH009

MOLECULAR MARKERS APPLICATION FOR BONE MARROW MINIMAL RESIDUAL DISEASE DETECTION IN NEUROBLASTOMA PATIENTS

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Purpose: To assess applicability of PHOX2B, TH, GD2 and ELAVL4 expression for minimal residual disease (MRD) detection in bone marrow (BM) of neuroblastoma patients.

Method: Molecular markers expression was evaluated by real-time PCR (RQ-PCR) in 174 BM samples from 33 neuroblastoma patients on different stages of disease, in 16 BM samples from 16 patients without malignancies, in 3 neuroblastoma cell lines (IMR-32,SK-N-MC,Kelly). RQ-PCR analytical sensitivity (AS) was assessed by 10-fold dilutions of IMR-32 RNA in healthy volunteers’ RNA. Samples were considered as true positive (TP) in case of detectable PHOX2B expression or tumor cells presence in BM smears. For each MRD marker threshold level (TL) was calculated by ROC curve analysis. Diagnostic sensitivity (DS), specificity (Sp), positive and negative predictive values (PPV, NPV), overall correct prediction (OCP) were calculated for every marker.

Results: AS of PHOX2B, TH and ELAVL4 expression detection in IMR-32 achieved 1E-06, while AS of GD2 assessment was 1E-05. PHOX2B and TH expression was not detected in normal BM. GD2 and ELAVL4 expression was revealed in 10 of 16 normal BM samples. PHOX2B and TH assessment showed high PPV (1.000 and 0.942), NPV (0.975 and 0.942) and OCP (0.984 and 0.942 respectively). Due to relatively low OCP (0.774 and 0.816) GD2 and ELAVL4 were excluded from the further analysis. As OCP for both TH and PHOX2B was high, we tested applicability of MRD monitoring approach where samples were defined positive in case of either PHOX2B or TH expression higher than TL. In comparison with single PHOX2B, TH
Tumorigenesis of NB. The expression of NKAP also correlates with the differentiation of NB and predicts an expression to be an independent prognostic factor even in the presence of Notch1.

Method: Analyzed the recurrence pattern of high risk neuroblastoma from the aspect of surgery in our hospital for these 20 years were included in this study. There

Purpose: Notch signaling pathway can regulate neural crest cells development and is related to neuroblastoma (NB) cell differentiation. NF-kB activated protein (NKAP) was recently found to be the transcriptional repressor of Notch signaling pathway and related to neuroblastoma (NB) cell differentiation. NF-kB activated protein (NKAP) was expressed in 35 of 85 (41.2%) NB tumor tissues and its expression was inversely correlated with Notch1 expression (P = 0.001). Positive NKAP immunostaining also strongly correlated with histological grade of differentiation, and early clinical stages (P < 0.001 and P = 0.009, respectively). Kaplan-Meier analysis showed that patients with positive NKAP expression had a better 5-year survival rate than those with negative NKAP expression (75.9% versus 39.0%, P < 0.001, log-rank test). Multivariate analysis demonstrated NKAP expression to be an independent prognostic factor even in the presence of Notch1.

Conclusion: NKAP expression inversely correlates with Notch1 expression in NB. The expression of NKAP also correlates with the differentiation of NB and predicts a favorable prognosis. Further investigation of NKAP regulation may shed light to the tumorigenesis of NB.

Purpose: Although recent advances in multimodal therapy for high risk neuroblastoma, the treatment results remain to be improved. We retrospectively analyzed the recurrence pattern of high risk neuroblastoma from the aspect of surgery and chemotherapy in our hospital for these 20 years were included in this study. There were nine boys and 11 girls. Average age of those patients were 28.5M (7–75M) including six patients under 18M. Of 18 tumors being examined for MYCN status, eight had MYCN amplification. All patients underwent high dose chemotherapy rescued by stem cell transplantation (14; double megatherapy and 14; allogenic stem cell transplantation). Operative findings, chemotherapy, patients' outcome, recurrence pattern were retrospectively analyzed by medical charts. Gross total resection (GTR) was defined as resection that more than 90% of tumor was removed. Results: GTR was performed in 17 cases. Nine patients were alive without recurrence (mean follow up 75.3 months), two were under treatment for recurrence (from the end of primary treatment to recurrence: mean 21.6 months), nine died of disease (from the end of primary treatment to death: mean 38.0 months). All 11 recurrences included distant metastases and local recurrence was combined in six patients. Of 17 cases underwent GTR, there were four local recurrences. All nine patients in CR received GTR.

Conclusion: GTR is necessary but not enough for local control in high risk neuroblastoma. As all recurrences included distant metastasis, development of more effective systemic treatment to prevent distant metastasis is probably on the top of the list of research priority.
RESULTS: Repeated increase of NKCs was achieved in 93% of courses with increase over baseline and/or acceptable outcome for high risk stage 4 disease.

Analysis of risk adapted treatment according to MYCN amplification (MNA), age, stage and response for children with localized or metastatic neuroblastoma investigated with pan- and/or multigenomic techniques. (MNA), age, stage and response for children with localized or metastatic neuroblastoma investigated with pan- and/or multigenomic techniques.

Purpose: To establish a safe dose of subcutaneous (s.c.) recombinant interleukin 2 (rIL-2) with a sustained increase of natural killer cells (NKCs) in an outpatient setting for stage 4 neuroblastoma patients after megatherapy (MGT) and autologous stem cell reinfusion (ASCR).

Method: Between August 1997 and November 2000, 33 patients with stage 4 neuroblastoma entered the study from 6 countries after receiving MGT/ASCR according to national protocols. Median age at registration was 4.1 years (range 1.8–7.4). Dose levels of 3 x 10^6 IU/rIL-2/m² were given s.c. in six 5-day cycles every 2 weeks. Median observation time was 5 years (range 4–9.8).

Results: Repeated increase of NKCs was achieved in 93% of courses with > 100% increase over baseline and/or > 1g/L in 58%. On the basis of efficacy and moderate toxicity profile, dose level 2 was chosen for the confirmation stage. At dose level 2 the median increase of absolute NKCs was 1 g/L of all 87 cycles, corresponding to a median relative NK increase over baseline of 711%. Fever was frequent, but controllable with adequate supportive care. 6.5% of patients were hospitalized. Localized pain was mild and acceptable. Simultaneous radiation during rIL-2 treatment abrogated completely NK increase. Event free and overall survival rates at 5 years were 45% (95%) and 48% (94.9%) respectively.

Conclusion: The use of 6x10^6 IU/m² rIL-2 s.c. is feasible in outpatients and efficacious. The low toxicity profile allows integration in therapeutic settings aiming for immunomodulation.

PHO14
LONG TERM OUTCOME AND IMPACT OF BIOLOGY WITHIN RISK ADAPTED TREATMENT STRATEGIES: THE AUSTRIAN NEUROBLASTOMA TRIAL A-NB94.

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Purpose: Analysis of risk adapted treatment according to MYCN amplification (MNA), age, stage and response for children with localized or metastatic neuroblastoma investigated with pan- and/or multigenomic techniques.

Method: Between July 1994 and January 2002, 164 patients (pts) were registered (87 males; median age 1.37yrs). Depending on stage, age (cut-off 1yr) and MYCN pts were stratified either to surgery only (stages1&2) or a total of 6 cycles of chemotherapy of adapted intensity. All MNA pts > stage1 received local radiotherapy (age adopted 2-40yrs). Stage 4 pts received 1–3 courses of high dose treatment (HDT) followed by autologous stem cell rescue (SCT) based on age and response. The median observation time is 9 yrs (range, 8.3 to 10 yrs).

Results: The 5-yr overall survival (OS) of all pts is 85% ± 0.03. Outcome by age showed an OS of 99% for pts < 1yr, 90% for 22pts between 1.1-7yrs and 77% for 80pts > 1.5 yrs. Pts with localized disease (LD) any age and any biology achieved OS rates of 98% for 63 pts stage1, 100% for 20 pts stage2, 100% for 26 pts stage3. Ten stage 4 pts had an OS of 90%. Stage 4 pts > 1yr had an OS of 46% while pts < 1yr had an OS of 75%. Thirty-two MNA pts had an OS of 63% as opposed to 132 non-MNA with an OS of 90% (p < 0.001). Segmental Chromosome Aberrations (SCA) were seen in 65pts without MNA in increasing frequencies according to age and stage: in localized pts up to 44%, but 93% in stage 4 pts. In pts > 1.5yrs 71% had SCA, but only less than 33% in pts < 1.5yrs. SCA was highly correlated with stage 4 ± 1.5 yrs.

Conclusion: Risk adapted treatment achieved excellent results in LD pts any age and acceptable outcome for high risk stage 4 disease.

PHO15
THE TURKISH PEDIATRIC ONCOLOGY GROUP NEUROBLASTOMA 2003 (TPOG-NB-2003): TREATMENT RESULTS OF THE INFANTS


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Purpose: To evaluate the clinical features and treatment results of the infants with neuroblastoma who were treated according to the TPOG-NB-2003.

Method: The INSS staging and COG risk stratification systems were used. Low risk group (LRG): stage1 received surgery only, stage2 received surgery+chemotherapy (3x[CDP)+VCR+IF0]), stage4S received surgery+chemotherapy (4x[VCR+CYC]). Intermediate risk group (IRG): patients received surgery+chemotherapy (2–4x[VCR+IFO+DTIC+DOXO(CDP+CYC+EETO)]. Maintenance therapy >13 cis-RA was given. Radiotherapy was given to the residual disease.

High risk group (HRG): patients were randomized to the conventional chemotherapy (CCT) and HDCT+ABMT arms. The CCT group received chemotherapy (4x[VCR+IFO+DTIC+DOXO(CDP+CYC+EETO)], then surgery, maintenance chemotherapy. The HDCT+ABMT group received chemotherapy (3x[VCR+IFO+DTIC+DOXO(CDP+CYC+EETO)], then surgery, and conditioning regimen (carboplatin+etoposide+melphalan). Radiotherapy to the primary site was given in most patients. 13cis-RA was given in HRG. Herein we analyzed infants (<24 months).

Results: Eligible 525 patients registered to the TPOG-NB-2003 from 33 centers; 266 of them were <24 months of age, and M/F was 0.85. Of these, 110(21%) were in LRG, 59(22%) were in IRG, 97(17%) were in HRG (CCT:77, HDCT+ABMT:26). The stages were as follows: stage1(n=57), stage2(n=30), stage3(n=52), stage4(n=97), stage4S(n=30). MYCN analysis was done in 37% cases; 24% of them had amplification. Overall response rate was 79% in LRG, 68% in IRG, 67% in HRG. Racco od death was PD in 48% of deaths. The median follow-up time was 24 months(0–82) in LRG; 17 months(0–65) in IRG; 10 months(0–72) in HRG. The 3 and 5-years OS 91%, 83%, 48% in LRG, IRG, HRG, respectively. The 3 and 5 years EFS 81% and 78% in LRG; 74% in IRG, 31% and 25% in HRG.

Conclusion: Survival rates were acceptable. In LRG 5-years EFS was low probably due to refractory tumors in stage4S and high relapse rate in stage1. Additional clinical and/or molecular-cytogenetic risk factors (such as allelic status of 1p, 11q, 17q) should be analyzed for LRG and IRG.

PHO16
DECISION OF TREATMENT REDUCTION IN SELECTED CHILDREN AGED LESS THAN 18 MONTHS WITH A NEUROBLASTOMA WITHOUT MYCN AMPLIFICATION AND A NUMERICAL GENOMIC PROFILE

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Purpose: In neuroblastoma (NB), children aged less than 18 months have a good outcome in the absence of MYCN amplification. It has recently been shown that a genomic profile characterized by numerical chromosome alterations (NCA), without any segmental alterations detected by array-CGH, is associated with an excellent overall survival. For some of these patients treatment reduction might be possible. The aim of this study was to analyse if the knowledge of a favourable genomic profile, characterised by NCA only, influenced the treatment decision for individual children < 18 months. 

Method: This is a retrospective study of children aged less than 18 months with a localised unresectable or metastatic NB, with a genomic tumor profile characterised by NCA only as determined by array-CGH, and treated at Institut Curie between 08/2004 and 07/2008.

Results: Among 17 children, 4 had INSS stage 2, 10 stage 3, 2 stage 4 and 1 stage 4s disease. Twelve of these children had clinical symptoms at diagnosis, including 4 children with spinal cord compression and 2 with respiratory distress. After treatment for life-threatening symptoms when required, in 14/17 children, chemotherapy was reduced with regard to previous treatment protocols or trials. With a median follow-up of 23 months, overall survival was 100%, with 9 children in complete remission, including 4 who did not have surgery, and 5 others in very good partial remission.

Conclusion: The knowledge of a favourable genomic profile was taken into account for treatment decisions in 14/17 children, enabling a reduction of chemotherapy while maintaining the excellent overall survival. Prospective clinical trials are urgently required to confirm these results.

PH1017

INDUCTION CHEMOTHERAPY BASED ON HIGH-DOSE TOPOTECAN IN HIGH-RISK NEUROBLASTOMA: RESPONSE RATE AND SURVIVAL

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Purpose: Topotecan is an active drug in relapsed neuroblastoma. In a pilot study, we investigated efficacy and toxicity of a topotecan-based induction regimen in newly diagnosed high-risk neuroblastoma. The probability of overall survival (OS) and progression-free survival (PFS) was also evaluated.

Method: Forty-one patients older than 1 year with either metastatic or localized stage 2–3 MYCN-amplified neuroblastoma received 2 courses of high-dose topotecan (HD-TPT) 6 mg/m² and high-dose cyclophosphamide (HD-CMP) 140 mg/kg, followed by 2 courses of ifosfamide, carboplatin and etoposide (ICE). After surgery on primary tumors, a further course including vincristine, doxorubicin and CPM was given. High-dose chemotherapy consisting of etoposide/cisplatinum/cyclophosphamide was administered in 33 children, while the last 8 patients received a combination of busulphan and L-PAM. Local radiotherapy (21 Gy) and cis-retinoic acid completed the induction regimen. Response was assessed according to the International Neuroblastoma Response Criteria, while toxicity was recorded according to CTC version 3.

Results: Of these 41 consecutive patients, 38 had metastatic disease. After two TPT/CPM courses, the median tumor volume reduction was 64%(range 0–97%) while after 4 courses was 80%(range 0–97%). Before HDC, bone marrow was in CR in 21/29 evaluable patients. Of these 41 children, 38 had metastatic disease. After two TPT/CPM courses, the median tumor volume reduction was 64%(range 0–97%), whose chemotherapy included: 1) two cycles of topotecan (0.75 mg/m²/day) plus cyclophosphamide (TOPO/CYCLO) (250 mg/m²/day) X 5 followed by four consecutive cycles of: cyclophosphamide (200 mg/m²/day X 7) plus doxorubicin (45 mg/m²) 8th day, vincristine (1.5 mg/m²), days 14 and 28 and carboptalin (200 mg/m²/day) plus etoposide (300 mg/m²/day), days 20 to 22. Patients with no evidence of progressive disease underwent second-look surgery, except the ones with still involved marrow: they were given 2 additional cycles of TOPO/CYCLO, being the surgery performed should the marrow become free of disease. Autologous stem-cell transplantation (ASCT) was performed afterwards for abdominal residual disease and/or previous skull metastases. 4/33 (12%) had I131MIBG, 10 mci/kg, delivered 4 – 6 weeks prior to stem cell collection, as in vivo purging. Overall (OS) and progression-free survival (PFS), as well as post ASCT PFS were analyzed.

Conclusion: The results of this single institution program delivered to children with high-risk neuroblastoma.

PH1019

SILS ADRENALECTOMY IN NEUROBLASTOMA-PRELIMINARY ONE CENTRE EXPERIENCE.

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Purpose: Laparoscopic adrenalectomy was introduced in 1992, since then many studies on adult population evaluating safety and results of laparoscopic surgery have been published. Laparoscopic approach to adrenal surgery in children population, especially in neuroblastoma cases, remains still controversial. During last 20 years we have observed tendency to minimize surgical trauma that challenged many surgeons, especially in neuroblastoma cases, remains still controversial. During last 20 years we have observed tendency to minimize surgical trauma that challenged many surgeons. In the first case of 11 month-old boy with neuroblastoma stage IV, modified SILS adrenalectomy was performed and lesions from both adrenal glands were resected by right adrenalectomy and left partial adrenalectomy. In the second case of 14 year-old girl left sided 4 cm adrenal ganglioneuroma was resected with SILS adrenalectomy. There were no postoperative complications, except of minor wound inflammatory process in the first case. Hospital stay varied from 2 to 5 days.

Results: We used Covidien SILS Port together with articulating instruments, in both cases. In the first case of 11 month-old boy with neuroblastoma stage IV, modified SILS adrenalectomy was performed and lesions from both adrenal glands were resected by right adrenalectomy and left partial adrenalectomy. In the second case of 14 year-old girl left sided 4 cm adrenal ganglioneuroma was resected with SILS adrenalectomy. There were no postoperative complications, except of minor wound inflammatory process in the first case. Hospital stay varied from 2 to 5 days.

Conclusion: The knowledge of a favourable genomic profile, characterised by NCA only, influenced the treatment decision for individual children < 18 months. 

Method: This is a retrospective study of children aged less than 18 months with a localised unresectable or metastatic NB, with a genomic tumor profile characterised by NCA only as determined by array-CGH, and treated at Institut Curie between 08/2004 and 07/2008.

Results: Among 17 children, 4 had INSS stage 2, 10 stage 3, 2 stage 4 and 1 stage 4s disease. Twelve of these children had clinical symptoms at diagnosis, including 4 children with spinal cord compression and 2 with respiratory distress. After treatment for life-threatening symptoms when required, in 14/17 children, chemotherapy was reduced with regard to previous treatment protocols or trials. With a median follow-up of 23 months, overall survival was 100%, with 9 children in complete remission, including 4 who did not have surgery, and 5 others in very good partial remission.

Conclusion: The knowledge of a favourable genomic profile was taken into account for treatment decisions in 14/17 children, enabling a reduction of chemotherapy while maintaining the excellent overall survival. Prospective clinical trials are urgently required to confirm these results.
**Conclusion:** An early experience with SILS adrenalectomy in neuroblastoma children cases appears to be safe and effective, however further studies and bigger series are required to investigate the true benefit of this approach.

**PH020**

**ABC DRUG TRANSPORTER GENE EXPRESSION IN NEUROBLASTOMA**

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**Purpose:** A distinctive type of drug-resistance, multidrug resistance (MDR), is associated with increased ABC gene expression. In neuroblastoma (NB), ABCB1/MDR1, ABCG2 and ABCG2 gene expression can be increased in NB tumors.

**Method:** Untreated NB samples were obtained from 109 patients aged 1 day to 199 months (median, 32 months). Thirty-six patients were at INSS stage 1, 2 or 4S; 73 at stage 3 or 4. MYCN amplification (MNA) was found in 18/109 NBs (17%). Stage 3/4 patients received induction chemotherapy including cyclophosphamide, doxorubicin, vincristine, carboplatin or etoposide. No selection criteria were applied except for availability of frozen tumor tissue. Written informed consent and ethical approval were obtained. Expression of mRNA was analyzed by real-time PCR: the amount of mRNA was expressed as fold change (2∧DD ∆Ct) of each sample compared to dorsal root ganglion, and categorized as high or low using the upper quartile 2∧DD ∆Ct value as cut-off point. In stage 3/4 clinical cases, end point clinical events were response to induction chemotherapy (based on INRC) and overall survival (OS). Patients with CR/VGPR/PR were categorized as responsive; the others as non-responsive.

**Results:** All 4 genes were expressed at variable levels in the 109 NBs, irrespective of age at diagnosis, primary site, stage and MNA. In the 73 stage 3/4 patients, high levels of ABCB1 (p < 0.003), ABCG1 (p < 0.001), ABCG2 (p < 0.001) and ABCG2 (p < 0.001) were associated with non-response to chemotherapy. No association with OS was found, which may reflect the influence of further treatment.

**Conclusion:** High levels of ABCB1, ABCG1, ABCG2 and ABCG2 at diagnosis were indicative of non response to induction chemotherapy, but did not impact on OS. In advanced NB, resistance mechanisms other-than-MDR appear to play a contributory role in adversely affecting outcome.

**PH022**

**POSTTRANSCRIPTIONAL UPREGULATION OF XIAP EXPRESSION AND EFFECT OF XIAP INHIBITION IN NEUROBLASTOMA**

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**Purpose:** Neuroblastoma is the most common extracranial solid tumor during infancy and childhood and more than 50% of the patients initially present with disseminated stage IV disease. Despite intensive therapy including high-dose chemotherapy and autologous stem cell rescue outcome for stage IV patients is still poor. X-linked inhibitor of apoptosis (XIAP) is a major intrinsic cellular suppressor of apoptosis and XIAP overexpression has been shown in several malignancies. XIAP inhibition by SMAC mimetics represents a novel innovative treatment strategy for refractory malignant disease.

**Method:** In this study, XIAP protein and mRNA expression was determined in human neuroblastoma cell lines as well as primary patients samples. Combination of chemotherapy and XIAP inhibition by SMAC mimetics was tested for induction of apoptosis neuroblastoma cell lines.

**Results:** High XIAP protein expression was detected in all neuroblastoma cell lines and primary patient samples. XIAP protein expression was highly increased in murine neuroblastoma compared to normal adrenal gland tissue. In contrast, XIAP mRNA expression was similar in all investigated tissues indicating a posttranscriptional mechanism of XIAP regulation. XIAP inhibition by SMAC mimetics significantly increased induction of apoptosis by vincristine and etoposide in a murine neuroblastoma cell culture model.

**Conclusion:** Posttranscriptional regulation of XIAP expression results in high XIAP protein expression in neuroblastoma cells. XIAP inhibition by SMAC mimetics appears to be a promising novel approach for treatment of neuroblastoma.
**PH025**

**EPIGENETIC SILENCING OF THE NOTCH SIGNALING PATHWAY IN NEUROBLASTOMA TUMOR CELLS**

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**Purpose**: Notch signaling has critical roles in differentiation, proliferation and survival, and has oncogenic or tumor suppressor effects in a variety of malignancies. Loss of heterozygosity at 1p36 can delete the majority of the Notch target HES genes in one common genetic event (HES 2–5), and we have shown that Notch pathway activation results in reduced neuroblastoma tumor cell growth. We hypothesized that a mechanism for Notch pathway regulation would involve epigenetic modifications of the downstream HES gene targets.

**Method**: Methylation of the promoters of the HES2 and HES5 genes was determined by bisulphite sequencing in a panel of 11 neuroblastoma cell lines. Neuroblastoma cell lines LA155N, IMR-32, and NB12 were then treated with the DNA methyltransferase inhibitor decitabine at 10μM for 24 hours and the RNA expression levels of the HES1–4 gene products was determined by RT-PCR. Neuroblastoma cell lines LA155N, IMR-32, and SK-N-SH were then treated with the pan-histone deacetylase inhibitor PIC24781 at 200nM for 24 hours and the RNA expression levels of the HES1–4 genes was also determined by RT-PCR.

**Results**: Significant methylation of the HES5 gene and, to a lesser extent, the HES2 gene, was found in almost all cell lines compared to control cells. Decitabine treatment resulted in consistently enhanced HES5 expression (7–43 fold over baseline), with smaller increases in HES1/2/4 also seen. PIC24781 treatment resulted in dramatic upregulation of HES2 expression (over 100 fold) in all cell lines, with smaller increases in HES1/4 expression.

**Conclusion**: These results suggest distinct mechanisms of epigenetic regulation of the HES genes in neuroblastoma cell lines. With the combination of 1p36 LOH and epigenetic silencing of HES genes, it appears that the HES gene family is selectively targeted for downregulation in neuroblastoma cells and may contribute to neuroblastoma pathogenesis.

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**PH024**

**EFFECT OF RETINOIC ACID AND CHEMOTHERAPEUTIC AGENTS ON ULTRASTRUCTURAL LOCALIZATION OF MYC-N IN NEUROBLASTOMA**

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**Purpose**: Neuroblastoma is an important pediatric tumor that myc-n amplification is a well known poor prognostic indicator. The effect mechanism of pharmacological agents used in neuroblastoma treatment on myc-n expression is still unclear. Myc-N amplification does not change with any agent. The aim of this study is to investigate the effect of chemotherapeutic agents and cisplatin on ultrastructural localization of myc-N in neuroblastoma.

**Method**: We analyzed ultrastructural localization changes of n-myc by immunoelectron microscopy in n-myc positive, Kelly human neuroblastoma cell line using retinoic acid and cytotoxic drugs (cisplatin, vincristine, cyclophosphamide, etoposide, doxorubicin) and their combinations incubated for 24 hours in preoptimised LD50 doses in cell culture compared with control conditions. Cells were fixed in gluteraldehyde fixative and n-myc was applied by immunoelectron microscopy method using colloidal gold for visualization. Results were scored semiquantitatively as negative, mild, moderate, or high positive in nucleus, ribosome and cell membrane.

**Results**: The 5 MNN tumours showed no mutation. ALK variants were found in 2/25 NN (R1275Q and P226as13bp), 3/10 MF (R1275Q, N25 at 3 months, R1192G at 5 months and R1192G at 2 years) and 1/11 syndromic NB (M597T at TA). PHOX2B variants were found in 1/10 MF (676insC), 1 CHS (618insC), and 1/2 Lo/CHS (C17Y); the patient with HSCR had no mutation. Patients with the ALK R1192G and the PHOX2B676insG variants showed neuroblastoma and multiple sub-cutaneous ganglioneuromas. The PHOX2B676insG patient also showed an intestinal ganglioneuroma.

**Conclusion**: ALK and PHOX2B deleterious mutations are rare events (6/52) in neuroblastoma. The intestinal phenotype associated with such mutations is encountered. Sub-cutaneous ganglioneuromatosis is linked to both ALK and PHOX2B alterations. The intestinal phenotype associated with such mutations deserves closer attention. The search for other predisposing genes is warranted.

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**PH026**

**RESISTANCE TO FENRETINIDE IN NEUROBLASTOMA IS ASSOCIATED WITH INCREASED EXPRESSION OF SPHINGOSINE KINASE AND SPHINGOSINE-1-PHOSPHATE RECEPTORS AND TARGETING SPHINGOSINE KINASE REVERSES RESISTANCE**

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**Purpose**: Fenretinide (4-HPR) is a retinoid cytotoxic to cancer cells via increased dihydroceramide levels with clinical activity against recurrent neuroblastoma (NB). Sphingosine kinase 1 (SPHK1) generates the anti-apoptotic sphingosine-1-phosphate (SIP); SIP counters cytotoxicity mediated by ceramides.

**Method**: The 4-HPR-resistant NB line KCNR-FR (IC99 = 19.9 μM) was selected from SMS-KCNR (IC99 = 4.6 μM). Cytotoxicity was by DIMSCAN, RNA expression by TaqMan quantitative RT-PCR, SPHK1 activity by thin-layer chromatography, and cell surface SP1 receptors by flow cytometry.

**Results**: A TaqMan low-density array (TLDA) for 42 sphingolipid synthesis and metabolism genes identified SPHK1 (5.2-fold) and SIP receptor S1PR2 as over-expressed (2.4-fold) in KCNR-FR vs SMS-KCNR. We observed a 3 to 27-fold increase (p < 0.01) in basal SIPK1 expression in 4-HPR de novo resistant (IC99 > 10μM, n = 6) vs sensitive NB lines (IC99 < 5 μM, n = 4). Forced over-expression in SMS-KCNR increased SPK1 enzyme activity by 70-fold and 4-HPR resistance relative to controls (p < 0.05). RNAI decreased SPK1 mRNA expression (36% of scrambled RNAI, p < 0.05) and increased apoptosis in KCNR-FR treated with 4-HPR relative to controls (p < 0.05). S1PR2 receptor levels (RNA and on the cell surface) in KCNR-FR and SMS-KCNR were induced 2.6-fold by 4-HPR. Saliplol, a putative SPHK1 inhibitor in phase I trials, synergized 4-HPR cytotoxicity in 15 of 15 NB cell
The poor outcome is predicted in patients with neuroblastoma (NB) with the MYCN gene amplification. The purpose of this study was to identify new strategies to target the MYCN gene, particularly in advanced NB patients. Myc N-terminal (N-Term) polyamides targeting the MYCN gene in a CHP134 cell line (a human MYCN amplified neuroblastoma cell line) were used. As a consequence of an aberrantly change from hyper to hypo during developmental stage with repression of the expression of MYCN, neuroblastoma may be developed in human.

In conclusion, the anti-MYCN effect of PI polyamides targeting the SP1 site showed neither decrease in cells proliferation nor down-regulation of MYCN gene expression, compared with those in controls. The PI polyamide targeting the E2F site showed 35% down-regulation of MYCN gene expression and 20% decrease in cell proliferation, compared with those in controls. The simultaneous treatment group of both PI polyamides induced 60% down-regulation of MYCN expression and 40% decrease in cell proliferation, compared with those in controls.

Conclusion: We confirmed the anti-MYCN effect of PI polyamides targeting the SP1 and E2F binding sites in the MYCN gene. We were able to down-regulate expression of MYCN in MYCN amplified CHPI34 cells using the PI polyamides. The combination use of these molecules could be a therapeutic strategy in MYCN amplified NB patients.
displayed highest cytotoxicity activity while Nkp30b isoform signals for Th1 cytokines and Nkp30c isoform induce IL-10 secretion with defective cytotoxic activity.

Neuroblastoma (NB) is known to be sensitive to NK cytotoxicity, a true link between innate and cognate immunity

Aim: To evaluate Nkp30 spliceforms in NB patients and their influence on disease presentation and prognosis.

Method: Nkp30 spliceforms were analyzed by Real-time PCR in peripheral mononuclear blood cells from 94 NB patients treated in Gustave Roussy Institut from 1964 to 2010. Unsupervised hierarchical clustering was applied to data obtained and correlated with patient’s clinical data.

Results: Unsupervised hierarchical clustering classified patients in 3 subgroups. Forty-four out of 94 patients (47%) exhibit the predominant Nkp30b spliceform, 28 (30%) the predominant Nkp30c isoform and 22 (23%) the Nkp30a isoform. Among the 39 metastatic NB, 27 (69%) exhibit the predominant Nkp30b, 6 (15%) the predominant Nkp30a and 6 (15%) the predominant Nkp30c isoform while among the 50 localized NB, 15 (30%) exhibit the predominant Nkp30b, 14 (28%) exhibit the predominant Nkp30c isoform and 21 (42%) the predominant Nkp30a isoform (p = 0.001).

Finally, among the 40 localized NB with a follow-up over more than 2 years, 1/12 (8%) with predominant Nkp30a isoform relapsed comparing with 4/28 (14%) with predominant Nkp30b or c isoforms.

Conclusion: Nkp30 profiles appear to correlate with metastatic dissemination of NB. Prospective studies are in progress to confirm the impact of Nkp30 spliceforms on NB prognosis. New drugs that modulate alternative splicing of Nkp30 receptor may therefore represent a new therapeutic approach in NB.

PH031

THE HEDGEHOG SIGNAL IN NEUROBLASTOMA

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Purpose: It has been reported that the hedgehog (Hh) signaling pathway is activated in adult cancer such as gastric cancer, pancreatic cancer and breast cancer. On the other hand, the Hh signaling pathway plays an important role of development of neural crest in embryo. The aim of this study is to show the activation of Hh signaling pathway in neuroblastoma (NB) that is child malignancy arising from neural crest in embryo. The Aim of this study is to show the activation of Hh signaling pathway in neuroblastoma cell line without any agent was used as control. Fold changes converting, expression of 84 custom array genes of tumor metastasis (SABiosciences, PATS028A) was determined by Real Time PCR for each condition. Kelly cell line was cultured and the agents and their combinations were applied for 24 hour in pre-optimized doses. After RNA isolation and cDNA

Conclusion: All high expression genes indicates that allicin additive treatment as a protective agent of chemotherapy toxicity should be very well questioned in neuroblastoma.

PH032

ALLICIN INCREASES METASTASIS RELATED GENES IN NEUROBLASTOMA

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Purpose: Overcoming of toxic effects of cisplatin in neuroblastoma treatment is a current issue. The try of discovering new agents to decrease toxicity of chemotherapeutic agents needs very much careful assessment not to cause tumor progression. The aim of this study is to explore effect of cisplatin, alllicin and their combination on metastasis related genes in neuroblastoma.

Method: Kelly cell line was cultured and the agents and their combinations were applied for 24 hour in pre-optimized doses. After RNA isolation and cDNA converting, expression of 84 custom array genes of tumor metastasis (SABiosciences, PATS028A) was determined by Real Time PCR for each condition. Kelly neuroblastoma cell line without any agent was used as control. Fold changes according to control group of each three condition were calculated at manufacturer’s online free data PCR expression analysis page.

Results: High expressed genes after alllicin application are ITGB3, TNFSF10, HGD, CCL7, CTSL1, ETV4, KISS1R, HHTATP2, IL1B, IL1RB, ITGAV, KISS1, MMP10, MMP3, MMP7, MYC, MYCL1, SYK, TIMP4, MMP13, TRPM1, CDH1, and FXN. The high expressed genes are related with cell growth and proliferation, extracellular matrix proteins, transcription factors. This high expression was not observed alone with cisplatin, but also observed in cisplatin+alllicin combination. Cisplatin alone decreased expression in EPHB2, TIMP3, CDH6, RORB, COL4A2, IL1B, CDH1, MEAT3, CTNNAA1, RBL1, CD44, MTA1, VEGFA; genes related with extracellular matrix proteins, cell growth and proliferation but also cell adhesion molecules.

Conclusion: Allicin showed prominent effect of gene expression related with tumor metastasis after application to neuroblastoma cells alone and in combination with cisplatin application. Our data showing increase effect of allicin on metastasis related genes indicates that allicin additive treatment as a protective agent of chemotherapy toxicity should be very well questioned in neuroblastoma.

PH033

THE CALCIUM-SENSING RECEPTOR GENE IS INACTIVATED BY GENETIC AND EPIGENETIC MECHANISMS IN NEUROBLASTIC TUMOURS AND ITS OVEREXPRESSION REDUCES NEUROBLASTOMA PROLIFERATION

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Purpose: We have previously reported that the calcium-sensing receptor (CaR) is expressed in differentiated, favourable neuroblastomas (NT) and it is up-regulated upon differentiation induction. However, CaR expression is undetectable in undifferentiated neuroblastomas (NB) and CaR promoter 2 (P2) is GC rich. We have analyzed the genetic and epigenetic mechanisms potentially responsible for the inactivation of the CaR gene in NT.

Method: CaR mRNA was analyzed by qRT-PCR in NB cell lines treated with 5-aza-deoxycytidine (DAC) and/or trichostatin A (TSA). Methylation status of P2 was evaluated by bisulfite specific PCR and sequencing of at least 10 clones. A specific probe for CaR locus was generated to perform fluorescence in situ hybridization (FISH). Two cell lines were stably transfected with pcMV-GFP or pcMV-CaR-GFP. Proliferation rate of independent clones was assessed in vitro and in nu/nu mice. Their metastatic pattern was evaluated in a chick embryo model.

Results: CaR mRNA was undetectable in 7/9 cell lines. Increased CaR mRNA levels were seen in all NB cell lines following DAC+/-TSA, except in SH-SY5Y and SK-N-AS, Percentage of methylated cytosines in P2 was < 6% in control tissues, SH-SY5Y and SK-N-AS, and 21–56% in the other cell lines. Hypermethylation of P2 among primary NT correlated with undifferentiated NB (P = 0.002), age at diagnosis > 12mo (P = 0.026), high clinical risk (P = 0.009), MYCN amplification (P = 0.04) and absence of CaR expression (P = 0.002). Allelic losses of the CaR locus and/or the entire chromosome 3 were detected in 70% of NB, ganglioneuroblastomas and ganglioganglioneuromas. The percentages of cells with one chromosome 3 ranged from 10% to 60% of total tumour cells. pCMV-CaR-GFP clones displayed statistically significant decreased in vitro and in vivo proliferation rates compared to pCMV-GFP clones. Their metastatic patterns were similar.

Conclusion: The CaR gene is silenced by genetic and epigenetic mechanisms and it exhibits tumor suppressor properties in NT.

PH034

PATTERNS OF TUMOUR GROWTH AND DISSEMINATION ON METABOLOBENZYLGUANIDINE (MIBG) SCANS SEEM TO CORRELATE WITH GENE EXPRESSION DATA OF STAGE 4 NEUROBLASTOMA TUMOURS
We investigated the effect of the PI3K/AKT/mTOR pathway on neuroblastoma. Probably, different patterns of tumour growth and dissemination in these patients are a reflection of distinct biological processes. The purpose of this pilot study was 1. to identify these patterns on metaiodobenzylguanidine (MIBG) scans; and 2. to test whether these patterns correlate with gene expression clusters.

**Purpose:** Neuroblastomas show a variable clinical course ranging from spontaneous regression to high-risk disease. Probably, different patterns of tumour growth and dissemination in these patients are a reflection of distinct biological processes. The purpose of this pilot study was 1. to identify these patterns on MIBG scans; and 2. to test whether these patterns correlate with gene expression clusters.

**Method:** All patients diagnosed with a neuroblastoma stage 4 from 1996 up till now were considered for this study. Both a MIBG scan, as well as an Affymetrix gene expression analysis of the primary tumour at the time of diagnosis should be available (n = 12). Two independent observers evaluated the MIBG scans. Gene expression data (Affymetrix MA55.0) of the primary tumours, available in the bioinformatical program R2 of the department of Human Genetics, were used for unsupervised hierarchical clustering of the 1500 most differentially expressed genes. Next we correlated the gene clusters with the growth and dissemination patterns on MIBG scans.

**Results:** Unsupervised hierarchical clustering of the gene expression data resulted in two clusters (I and II) that correlated with high and low dissemination patterns on MIBG scans. Cluster II showed more extensive dissemination than cluster I and cluster I patients more often had a MYCN amplification.

**Conclusion:** Stage 4 neuroblastoma tumors show different patterns of tumour growth and dissemination on MIBG scans that seem to correlate with gene expression clusters and especially with MYCN amplification. An extended cohort of all stages is needed to prove the results of this pilot study. The ultimate goal of this project is to identify biological processes that play a role in these patterns.

**PH035**

**PROMISING EFFECTS OF THE PI3K/MTOR INHIBITOR PI-103 WITH CURRENTLY APPLIED CHEMOTHERAPEUTIC DRUGS ON NEUROBLASTOMA CELL LINES**

_odette besançon, godelieve tytgat, rene leen, huib caron, andre van kuilenburg_

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**Purpose:** Neuroblastoma is a childhood tumor with a poor prognosis and therefore, new therapeutic options are needed. The PI3K/AKT/mTOR pathway is a potent survival-signaling pathway that is necessary for the survival and proliferation of tumor cells. Therefore, new therapeutic strategies that target this pathway are needed. In this study, we investigated the effect of the PI3K/mTOR inhibitor PI-103 on the proliferation of neuroblastoma cell lines.

**Method:** We tested the effect of PI-103 on the proliferation of neuroblastoma cell lines. The cell lines were treated with PI-103 at different concentrations for 24 hours. The proliferation of the cell lines was measured using a viability assay.

**Results:** The results showed that PI-103 inhibited the proliferation of the neuroblastoma cell lines in a dose-dependent manner. The IC50 values for PI-103 ranged from 100 to 500 nM for the different cell lines. In addition, PI-103 readily inhibited tumor spheroid growth (IC50 = 400 nM) with a synergistic effect of the combination PI-103 - topotecan.

**Conclusion:** Our results showed that the combination of PI-103 with topotecan is more effective in inhibiting the proliferation of neuroblastoma cell lines compared to PI-103 alone. This suggests that PI-103 could be a promising new strategy in the treatment of neuroblastoma.
(10 samples total). Sera were analyzed using gas chromatography mass spectrometry (GC-MS). Multivariate data analysis was conducted using SIMCA-P (Umetrics).

**Results:** In vitro: Supernatants from NB cells showed a specific metabolic response easily distinguished from other cancers. MYCN status and nBICs were distinguished by their differing metabolic profiles.

Patient Samples: Sera from patients with bulk disease showed a remarkably unique profile compared with the same patient sera with CR/VGPR. Cross validation ANOVA indicates statistical significance of the multivariate model using 96 features (p = 0.003). Identified metabolites are indicative of perturbations in nitrogen, amino acid, and carbohydrate metabolism, as well as ketosis.

**Conclusion:** NB has a characteristic metabolic profile in vitro. In a pilot study of patients with NB, we have detected with high sensitivity a significant alteration in their metabolic profile after treatment. Formal categorization of a metabolic profile for NB may be possible with a larger patient size and comparison with normal age-matched controls. Prospective use of metabolomics may accurately characterize neuroblastoma and enhance monitoring for minimal residual disease.

**PI038 DIFFERENCES IN BIOLOGICAL FEATURES AND SURVIVAL IMPROVEMENT BETWEEN GENETIC SUBSETS OF HIGH-RISK NEUROBLASTOMA INDICATE THE NEED OF ADAPTED TREATMENT**

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**Purpose:** To evaluate the clinical significance of 11q-deletion in high-risk neuroblastoma (HR-NB) using data from 384 children in our national population-based registry over 28 years.

**Method:** All children were characterized according to age at diagnosis, sex, chromosomal aberrations with FISH/aCGH, INRG stage, treatment and overall survival.

**Results:** From 182 tumors analyzed with aCGH 11q-deletion was detected in 34 tumors (8 localized stage, 26 metastatic, none metastatic-special). Children with 11q-deleted tumors were older, median age 41 months (equal for girls and boys) with longer median survival (40 months) as compared to children with MYCN-amplified tumors, median age 22.5 months (boys older than girls, 28vs.20 months) and median survival 16 months, but similar cure rate (~35% eight-year survival). 11q-deleted tumors had more segmental aberrations (median 12) compared to MYCN-amplified tumors (only four) and spread over all chromosomes. The chromosomal instability phenotype gene H2AFX (11q23.3) was deleted in all 11q-deleted tumors.

Five-year survival for all children improved from 57.7% for those diagnosed 1982–1990 to 78.6% 2000–2009 (p < 0.001). Most improved prognosis was achieved in HR-NB (n = 148) from 11.1% (1982–1990, n = 36) to 17.9% (1991–1999, n = 56) and 61.6% (2000–2009, n = 56, p < 0.001). However, among 101 HR-NB outcome improved significantly for children with MYCN-amplification (from 11.1% for 1982–1995 to 48.9% for 1996–2009) but not for those with 11q-deletion (35.7% for 1982–1995, and 42.9%, 1996–2009).

**Conclusion:** Children with 11q-deleted neuroblastomas are older at diagnosis than children with MYCN-amplification, and their tumors are chromosomal instable, develop later and progress slower but with ultimate prognosis as dismal as for children with MYCN-amplification. Children with 1q13-deleted tumors did not benefit from the intensified multimodal therapy those with MYCN-amplification. Our data support stratification of high-risk neuroblastoma therapy on aCGH analysis and a reconsidered therapeutic approach for 11q-deleted tumors taking the chromosomal instable phenotype into account.

**PI001 IMMUNOHISTOCHEMISTRY OF PROTEINS RELATED TO APOPTOSIS IN RETINOBLASTOMA**

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**Purpose:** Retinoblastoma is the most common intraocular malignant neoplasia during childhood and is a result of the partial or total inactivity of two copies of the retinoblastoma genes (RB1). The treatment currently used, is responsible for a good prognosis, but the preservation of eyesight and the cure of retinoblastoma which spreads to the central nervous system are still considered challenges. The study of apoptotic pathways is fundamental because many contemporary forms of treatment result in apoptosis. Blockages in this pathway could be associated with poor prognosis.

**Method:** Related apoptosis proteins (Apaf-1, Bak, Bax, Bcl-2, Bcl-xL, Birin-L, MDM2, p53, pro-caspase-3, PUMA, Smac/DIABLO and cleaved caspase-3) were evaluated using immunohistochemistry on tissue microarrays which contained samples of tumors taken from ninety-three patients without any treatment prior surgery. The immunohistochemistry reactions were evaluated using an optical microscope as well as the ACES III® platform. The apoptotic index (AI) was assessed by counting cells marked with cleaved caspase-3 in 1000 cells.

**Results:** The pro-apoptotic proteins (APAF-1, Bax, p53, PUMA, Smac/DIABLO) were more frequently expressed than the anti-apoptotic proteins (Bcl-2, Bcl-xL and MDM2). The lower p53 expression was associated with extra ocular tumor extension (p = 0.01). The median of the AI was 0.085. There was no correlation between AI and the intensity of pro-apoptotic protein expression, such as p53 (r = -0.16, p = 0.14), PUMA (r = 0.08, p = 0.94) and Smac/DIABLO (r = 0.09, p = 0.41). The protein Bcl-xL had a negative correlation with AI (r = -0.38, p = 0.001). Patients with tumors with an AI > 0.17 presented poorer survival (87%), although with borderline statistical significance (p = 0.057).

**Conclusion:** The tumor cells seemed to be susceptible to apoptosis. Bcl-xL could be implicated in the apoptosis block. Also, apoptosis index had a prognostic role, although with marginal statistical significance, requiring further studies with larger statistical power.

**PI002 HISTONE DEACETYLASE INHIBITORS VALPROIC ACID AND DEPSIPEPTIDE SENSITIZE RETINOBLASTOMA CELLS TO RADIOTHERAPY BY INCREASING H2AX PHOSPHORYLATION AND P53 ACETYLATION-PHOSPHORYLATION**

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**Purpose:** Although retinoblastoma has wild-type p53, it is inactivated by specific proteins RB1 and the pro-apoptotic proteins (APAF-1, Bax, p53, PUMA, Smac/DIABLO) on ionizing radiation (IR)-induced apoptosis in retinoblastoma cells.

**Method:** Human retinoblastoma cell lines Y79 and WERI-Rb1 were cultured with VPA and FK228. Cell viability was evaluated by trypan blue dye exclusion method and flow cytometry with propidium iodide (PI) staining. Cells were also stained with PI and Bsisbenzimidazole Hoechst 33342 to identify apoptotic cells. Effects of VPA and FK228 on the phosphorylation of histone H2AX on Ser139 were examined as a marker of DNA double-strand breaks by using fluorescence microscopy. Effects of VPA and FK228 on the expression of p53, acetylated p53 and MDM2/X and the interaction with p53 and MDM2/X in irradiated retinoblastoma cells were evaluated by western blots and immunoprecipitation/western blots.

**Results:** VPA and FK228 synergistically enhanced IR-induced apoptosis, associated with activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase in Y79 and WERI-Rb1 cells. Both VPA and FK228 enhanced IR-induced phosphorylation of histone H2AX on Ser139 preceding apoptosis. Exposure of cells to IR in the presence of VPA or FK228 induced the accumulation of p53 acetylated at Lys382 and phosphorylated at Ser46 through the reduction of binding affinity with MDM2 and MDMX.

**Conclusion:** Acetylation of p53 by HDAC inhibitors is a promising new therapeutic target in refractory retinoblastoma.

**PI003 ABCR5 IDENTIFIES TUMOR INITIATING CELLS IN RETINOBLASTOMA**
**PI005**

**RETINOBLASTOMA TREATMENT RESULTS OF 30 YEARS FROM A CENTER IN ISTANBUL, TURKEY**

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**Purpose:** In this study, we aimed to describe the survival and clinical characteristics of retinoblastoma cases treated at Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey, between January 1981 and December 2009.

**Method:** We retrospectively analyzed the clinical records of 170 children (76 boys and 94 girls) (213 eyes) diagnosed with retinoblastoma and treated between 1981 and 2009. Patients were divided into three groups: the first period (1981–1991), the second period (1992–2004) and the third period (2005–2009).

**Results:** A total of 127 cases (74.7%) were unilateral and 43 cases (25.2%) were bilateral. The mean age at the time of diagnosis was 26 months; in unilateral cases, 34 months; and in bilateral cases, 10 months. The most common presenting signs were leukocoria (137 cases, 80.5%), strabismus (21 cases, 12.3%) and proptosis (15 cases, 8.8%). Emaciation was performed in 136 cases (81.7%), and orbital exenteration in 12 cases in the early years of this study. A total of 30 cases had orbital extension, 10 patients had cerebro-spinal fluid invasion, and 5 cases exhibited bone marrow involvement. Chemotherapy was used in 89 patients. Eighty three patients received radiotherapy, thirteen cases received laser photocoagulation, and one underwent cryotherapy. In total, 17 patients (10%) had a family history of retinoblastoma. Two cases developed a secondary neoplasm, one osteosarcoma and the other soft tissue sarcoma. In total, 158 (93%) patients remained alive, and 11 patients died. The 5 year cumulative survival rate of 170 patients was 90% (unilateral 90%; bilateral 87% P = 0.9; P = 0.05, log rank test).

**Conclusion:** Despite that most cases in the early years were in advanced stages, the survival in this whole cohort of patients was high. In recent years most patients received chemoreduction and local ophthalmic treatments.

**PI006**

**CHEMOREDUCTION EFFICACY IN NEWBORNS AND SMALL INFANTS WITH RETINOBLASTOMA**

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**Purpose:** The aim was to evaluate chemoreduction efficacy in children diagnosed with retinoblastoma in the first 13 weeks of age.

**Method:** Medical records of 20 patients treated from 1996 to 2010, 10 boys and 10 girls aged from 1 to 13 weeks (median 8 weeks), 14 with bilateral (9 familial), 6 with unilateral disease (2 familial) were evaluated. Thirty four eye globes with number of tumors varying from 1 to 6 (median 2) were treated. Vincristine, Etoposide, and Carboplatin cycles per patient varied from 4 to 10 (median 8). After every 2 courses tumor response was assessed. All patients achieved regression. During first line treatment cerryotherapy in 3, thermochemistry in 1, brachytherapy in 1 eyes were implemented. Four eyes were enucleated (3 due to atrophic features, 1 of progression).

**Results:** In 23 eyes intraocular relapse was observed (14 in after chemoreduction only) with time to relapse after first line treatment cessation from 3 to 11 weeks.
higher recurrence and enucleation rate. Considering the absence of tumor response, patients were alive and none have presented a trilateral retinoblastoma or a second order to preserve vision function without increasing mortality rate due to tumor progression. In bilateral retinoblastoma, a conservative management is mandatory in order to preserve vision.

Results: Out of 44 eyes, 35 were eligible for conservative management while 9 eyes were enucleated at diagnosis. All children received neoadjuvant chemotherapy before PT. Chemotherapy was applied in 52 children prior to PT and, in 45 children concurrently with PT. Total dose of PT ranged from 36 to 75.6 Gy (med. 54.0 Gy). Baseline bone metastases were observed in 4 eyes (9%), lung (3), lymph nodes (2) or both (1). Only 16 patients had complete tumor removal before PT. Chemotherapy was applied in 52 children prior to PT and, in 45 children concurrently with PT. Total dose of PT ranged from 36 to 75.6 Gy (med. 54.0 Gy). Acute toxicity was recorded according to RTOG and CTCAE. Data on tumor control, site of recurrence and fatal events was evaluated.

Conclusion: Seventy-three patients were evaluable aged from 1.4 to 20.1 years. The predominant histopathological diagnosis was RMS in 37 children (51%). The tumor was situated at head/neck in 50, spine in 17 and pelvis in 6 children, respectively. In 33 children initial tumor size exceeded 5 cm. Six children had metastases before PT to lung (3), lymph nodes (2) or both (1). Only 16 patients had complete tumor removal before PT. Chemotherapy was applied in 52 children prior to PT and, in 45 children concurrently with PT. Total dose of PT ranged from 36 to 75.6 Gy (med. 54.0 Gy). Acute toxicity was not exceeding grade 2 except for skin (3; 5), mucosa (3; 2), eye (3; 2) and, bone marrow (3; 30) when concurrent chemotherapy was applied. At a med. FU of 23 (7–124) months, 59 children remained free of disease, 12 experienced local recurrences, and 2 dissemination of disease, resulting in 81.3% PFS and 87.2% OS after 2 yrs., respectively. Ten children deceased, 9 due to tumor progression and one due to multimodality treatment toxicity. Late effects exceeding grade 2 (CTCAE) were reported so far for eye (cataract, 2), CNS (BS re-infection, 1).

Conclusion: Results of proton radiation therapy are promising regarding both tumor control and late effects. Results need to be confirmed with larger cohorts and longer follow-up period. PT should be accompanied by prospective standardized evaluation of treatment outcome.

**P3003**

PROLONGED 14-DAY CONTINUOUS INFUSION OF HIGH-DOSE IFOSFAMIDE WITH AN EXTERNAL PORTABLE PUMP: FEASIBILITY AND EFFICACY IN REFRACTORY PEDIATRIC SARCOMA

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Purpose: Ifosfamide is currently used to treat pediatric sarcomas (at a dose of 6–9 g/m²/courses). Increasing its dosaging up to 12–14 g/m²/course has been associated with a significantly higher toxicity.

**P3004**

ETOPOSIDE AND CARBOPLATIN PLUS FOCAL THERAPY IN BILATERAL RETINOBLASTOMA: LACK OF EFFICACY AFTER THE THIRD COURSES

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**Purpose:** In bilateral retinoblastoma, a conservative management is mandatory due to patient mortality because of tumor progression or second tumor occurrence. The efficacy of a conservative strategy was evaluated.

**Method:** During a seven-years period, 22 consecutive bilateral retinoblastoma were treated with focal ocular therapies plus chemoreduction by courses of carboplatin and etoposide (CarboVP).

**Results:** Out of 44 eyes, 35 were eligible for conservative management while 9 eyes were enucleated at diagnosis. All children received neoadjuvant chemotherapy before ocular therapy. A median of 6 (range 1–9) courses for each patient were administered. Twenty eyes (57%) presented a maximal tumor response before the fourth course of chemotherapy and only one of them was afterwards enucleated. Six eyes presented a response after the fourth course and then one was enucleated. In nine eyes (26%), no response was observed and five of them were enucleated. None response were observed after the fifth course. An external beam radiotherapy (EBRT) was necessary in 2 eyes (6%) in two different patients. Retinoma plaque were used in 3 patients (13%) on 3 eyes (10%). In 5 patients different chemotherapy were administered after recurrence. At a median follow-up from diagnosis of 56 months (range 15–110), all patients were alive and none have presented a trilateral retinoblastoma or a second tumor occurrence. Bilateral enucleation was necessary in 3 patients (9%) while unilateral enucleation in 10 (45%). Nine (41%) patients preserved both eyes.

**Conclusion:** A conservative strategy based on CarboVP plus ocular therapy achieves a satisfactory tumor control with a low need for EBRT and bilateral enucleation. The eyes who presented a tumor response after the third course or no response, have a higher recurrence and enucleation rate. Considering the absence of tumor response after the fifth course, we suggest 3 CarboVP courses in bilateral retinoblastoma and in few cases a fourth course could be considered.

**P3001**

MUSCLE SPECIFIC MiRNAs AS NOVEL BIOMARKERS FOR RHABDOMYOSARCOMA

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**Purpose:** The recent discovery of microRNAs (miRNAs) has provided new insights into cancer diagnosis. Several studies have shown that profiles of miRNA expression vary among tumor types. To exploit this difference, we evaluated the feasibility of using muscle-specific miRNAs (miR-1, 133a, 133b, 206) as biomarkers for rhabdomyosarcoma (RMS).

**Method:** Total RNA was extracted from 16 cell lines (7 RMS, 4 neuroblastoma, 3 Ewing sarcoma and 2 malignant rhabdoid tumor culture), supernatants of the same 16 cell lines and 21 tumor specimens (7 RMS, 1 Ewing sarcoma, 4 undifferentiated sarcoma, 1 osteosarcoma, 1 alveolar soft part sarcoma, 2 neuroblastoma, 2 Wilms tumor, 1 malignant rhabdoid tumor, 1 adrenal carcinoma and 1 retinoblastoma). The supernatants were centrifuged at 17,000xg for 10 minutes to eliminate cultured cells. miRNA was quantified by real-time RT-PCR. The expression levels of miRNAs were calculated utilizing the delta-delta Ct method, normalized to the level of miR-16, and compared using the Mann-Whitney U test.

**Results:** The expression levels of muscle-specific miRNAs in the RMS cell lines were significantly higher (p < 0.01) than those in neuroblastoma, Ewing sarcoma and malignant rhabdoid tumor cell lines. miR-206 was most abundantly expressed and miR-1 was least abundantly expressed among muscle-specific miRNAs in RMS cell lines. The expression levels of muscle-specific miRNAs in the culture supernatants of RMS cell lines were similarly evaluated. The expression levels of muscle-specific miRNAs in RMS tumor specimens were significantly higher (p < 0.01) than those in other pediatric tumors. The difference in the expression levels between RMS and other tumors was largest in miR-206.

**Conclusion:** The expression levels of muscle-specific miRNAs were significantly elevated in RMS cell lines and tumor specimens. Cell-free muscle-specific miRNAs we detected in plasma, demonstrating their potential for diagnosis and follow-up of RMS patients. Muscle-specific miRNAs, especially miR-206, can be potential biomarkers for RMS diagnosis.
better response rate in adult sarcomas. Since the drug has proved stable in solution over a 9-day period, prolonged continuous infusions of high-dose ifosfamide might be an attractive therapeutic option. The aim of the present study was to assess the feasibility of such a regimen and its preliminary efficacy in a subset of relapsing pediatric patients with soft tissue and bone sarcomas.

Method: Ifosfamide 14 g/m² (with mesna) was administered through an external portable pump over 14 days as a continuous infusion, starting every 3 weeks, in 14 patients with relapsing sarcomas (treated in an outpatient setting between June 2005 and January 2010). No hyperhydration was required.

Results: Five patients had recurrent/progressive rhabdomyosarcoma, 4 synovial sarcoma, 3 Ewing sarcoma and 2 osteosarcoma. All patients had previously received multi-chemotherapy with conventional-dose ifosfamide. Sixty-six cycles were administered in all, with a median of 4 cycles per patient (range 2–12); 7 patients received 6 or more cycles. Acute G3 hematological toxicity was observed in 13/66 cycles. Hematuria and dysuria occurred in only 3 cases. There were no cases of G4 toxicity. The response rate was: 5 partial responses, 5 stable disease. The median time to progression was 3 months (range, 2–19 months). The best response rate was seen for synovial sarcoma (2/4) and Ewing sarcoma (2/3).

Conclusion: Prolonged 14-day continuous infusion of high-dose ifosfamide is well tolerated. Potentially interesting preliminary responses in pediatric patients already treated with ifosfamide are reported. While we await for new effective target drugs, an alternative use of classic cytotoxic drugs may be of potential interest.

PJ004

PLEUROPULMONARY BLASTOMA: CHILDREN’S HOSPITAL LOS ANGELES EXPERIENCE

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Purpose: To describe the clinical features, management and outcome of pleuropulmonary blastoma (PPB), a rare primary intrathoracic mesenchymal malignancy that occurs exclusively in early childhood.

Method: Retrospective review of the medical records of consecutively diagnosed PPB patients at Children’s Hospital Los Angeles (CHLA) between 1979 and 2009.

Results: Twelve patients were diagnosed at CHLA in the time period: 1 with Type I, 5 with Type II and 6 with Type III PPB. Median age at diagnosis was 31 months (range 0–39) and 8 were female. Presenting symptoms were cough, respiratory distress, chest pain and pneumothorax. Seven patients had involvement of pleura and/or mediastinum and one had distant metastases to the bone marrow. Upfront complete tumor resection (CR) was successful in 5 of 6 patients. Six patients had biopsy followed by neo-adjuvant chemotherapy; 2 had CR and 2 had microscopic residual disease. Of these, 4 were initially diagnosed with high grade sacral/ rhabdomyosarcoma. All patients received vincristine, dactinomycin and cyclophosphamide chemotherapy. Eight received additional chemotherapy with doxorubicin, cisplatin, etoposide or ifosfamide. Four patients received local irradiation, including one for palliation. The 5-year event free survival and overall survival were 36 ± 15% and 40 ± 15% respectively. Median time to disease progression was 8 months and none survived following relapse. Five of the 9 patients with gross total resection survived while all 3 with gross residual disease died. Three of 5 survivors did not receive radiation.

Conclusion: A high index of suspicion for PPB must be maintained in all patients diagnosed with intra-thoracic sarcoma in early childhood. The prognosis of patients diagnosed with PPB is poor. Gross total resection is necessary for cure. Radiation may be avoided in select patients. Further understanding of the biology may lead to better treatments to improve outcome.

PJ005

SURVIVAL AFTER RECURRENCE OF METASTATIC RHABDOMYOSARCOMA - AN UNPROBABLE, BUT NOT IMPOSSIBLE EVENT IN THE EXPERIENCE OF THE COOPERATIVE WEITEILSARKOM STUDIENGREPP (CWS)

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Purpose: Analysis of prognostic factors predicting the possibility of postrelapse survival in recurrent, primary metastatic rhabdomyosarcoma [RMS].

Method: As of 2010, 215 of 363 patients with metastatic RMS treated in consecutive CWS-protocols between 1980 and 2007 achieved a first complete remission. 127 developed a first recurrence thereafter. Diagnosis was confirmed by reference pathologic review in all cases.

Results: Of 127 relapsed patients, 47 patients had embryonal [RME], 75 alveolar [RMA] and 5 other RMS. Merely 9 of them are currently alive: n = 4 with disease and n = 5 in 2nd CR. The follow-up of the disease-free survivors ranges from 6 to 17 years. Four of the 5 disease-free survivors after relapse had RME, the remaining RMA. All 4 survivors with RME in 2nd CR just had isolated lung metastases at diagnosis. The patient with RMA had lung metastases and a questionable CNS metastasis. Their relapse pattern was local in n = 2, combined in n = 1, and metastatic in n = 2. The metastasis of the 3 patients with systemic relapses were however just restricted to the lungs.

Conclusion: Postrelapse outcome for primary metastatic RMS is dismal. Long-term survival was only possible in case of embryonal histology and primary isolated lung metastases. For the majority of the patients with RMA and involvement of more metastatic sites such as bone or bone marrow, survival after disease recurrence appears to be the exception from the rule with current treatments. We propose to treat recurrences in patients with primary metastatic RME and isolated lung metastases with conventional multimodal treatments including adequate local therapy, because these individuals have a realistic post-relapse survival chance. The remaining patients should be entered in studies investigating new therapeutic approaches.

PJ006

MALIGNANT ECTOMESENCHYOMA TREATED IN THE COOPERATIVE WEITEILSARKOM STUDIENGREPP (CWS)

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Purpose: Malignant ectomesenchymoma [MEM] is a soft tissue tumor with heterologous rhabdomyoblastic components believed to arise from pluripotent migratory neural crest cells. To date merely about 50 cases have been published, mainly as case reports or pathological studies and the knowledge about the course of disease and best treatments is very limited. We therefore analyzed the outcome of MEM-patients registered with the Cooperative Weiteilsarkom Studiengruppe [CWS].

Method: 11 patients from Germany and Sweden were diagnosed with MEM between 1996 and 2009. Their diagnosis was confirmed by central pathologic review.

127/128 patients had embryonal [RME], 75 alveolar [RMA] and 5 other RMS. Merely 9 of them are currently alive: n = 4 with disease and n = 5 in 2nd CR. The follow-up of the disease-free survivors ranges from 6 to 17 years. Four of the 5 disease-free survivors after relapse had RME, the remaining RMA. All 4 survivors with RME in 2nd CR just had isolated lung metastases at diagnosis. The patient with RMA had lung metastases and a questionable CNS metastasis. Their relapse pattern was local in n = 2, combined in n = 1, and metastatic in n = 2. The metastasis of the 3 patients with systemic relapses were however just restricted to the lungs.

Conclusion: Postrelapse outcome for primary metastatic RMS is dismal. Long-term survival was only possible in case of embryonal histology and primary isolated lung metastases. For the majority of the patients with RMA and involvement of more metastatic sites such as bone or bone marrow, survival after disease recurrence appears to be the exception from the rule with current treatments. We propose to treat recurrences in patients with primary metastatic RME and isolated lung metastases with conventional multimodal treatments including adequate local therapy, because these individuals have a realistic post-relapse survival chance. The remaining patients should be entered in studies investigating new therapeutic approaches.
Results: The median age of the 5 girls and 6 boys was 1 year (range: 0–17). Seven had primary localized tumors, 4 individuals presented with metastases. The primary tumor site were the limbs in n = 3, the trunk in n = 5 and the head/neck including the CNS in n = 3 patients. All but one patient received multiagent chemotherapy according to CWS-protocols during their initial treatment, a single patient additional high-dose chemotherapy. Four individuals were irradiated with a median dose of 45Gy. The tumors of 5 of the 7 patients with localized MEM were at least grossly ressected at best surgery and 6 of them achieved a 1st CR. In contrast, only one of the 4 patients with disseminated disease achieved a 1st CR, but developed a recurrence and died. As of 2010, none of the patients with metastatic MEM survived, but 6 of the 7 patients with localized MEM are alive in CR with a median follow-up of 6 years (range: 5–13).

Conclusion: The outcome of localized MEM appears to be fair if the patients are treated with multimodal treatment including chemotherapy and adequate local treatment. Primarily metastatic tumors however have a dismal prognosis. We propose to treat patients with MEM according to pediatric soft tissue sarcoma protocol in the future.

PJO07

VALUE OF PET SCANNING IN SYNOVIAL SARCOMA OF CHILDHOOD

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Purpose: This paper evaluates sensitivity and specificity of PET imaging in children with sarcoma synoviale(SySa) in comparison to other imaging techniques (CT, MRI, Scintigraphy) and the histopathological verification.

Method: 8 patients with Sy Sa were submitted to PET scanning, CT, MRI, usg, X-ray and scintigraphy.

Results: Regarding the primary focus, positive PET results (SUV above 2.5) were observed in 4 patients. In 2 of them histopathological examination was also positive. Negative PET results (SUV below 2.5) were false concerning the pathology of 2 in 4 of patients. CT/MRI were suggestive for malignant origin of the lesions in 6 patients. 3 of them were confirmed by histopathology. Concerning the lymph nodes metastasis the negative PET did not correlate with other imaging (usg/CT/MRI).

Conclusion: In case of SySa the PET scanning is not reliable in the assessment of lung nodules. In case of the primary focus the evaluation is doubtful. In SySa both the primary site (mean SUV = 1.8) as metastases (1.2) show low metabolic activity measured by FDG uptake. So therefore the FDG PET-CT may be suboptimal for SySa imaging.

PJO08

THE TOPOTECAN/CARBOPLATIN COMBINATION IN THE TREATMENT OF RESISTANT RHABDOMYOSARCOMA. A REPORT FORM THE AEOP SOFT TISSUE SARCOMA COMMITTEE

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Purpose: The prognosis for children with resistant/relapsing rhabdomyosarcoma (RMS) remains poor and therefore there is a need to test new drug combinations. Topotecan (T) and carboplatin (C) are known to have activity against a variety of pediatric tumors and the T/C regimen has been proposed as second line chemotherapy for children treated in the STSC protocols. We present the preliminary data of this phase II study.

Method: 37 patients with available data on response have been analyzed: 7 resistant to first line treatment and 20 treated at relapse (local 11, nodal 2, metastatic 5, local and metastatic 2, missing data 1). Treatment: T: 2 mg/m² days 1,2,3; C: 250 mg/m² days 4,5 every 3 weeks. Tumor response has been evaluated after 2 cycles adopting standard criteria: complete response (CR); partial response (PR = tumor size reduction > 50%); minor response (MR = reduction < 50%); no response

(NR = reduction < 25%), progressive disease (PD = increase of tumor size or detection of new lesions)

Results: 13 patients presented alveolar and 14 embryonal RMS. At diagnosis IRS Group was II: 1 patient, III: 18, IV: 6, missing data: 2 and the tumor site was parameningeal 6, head and neck 2, genito-urinary 6, orbit 1, extremities 4, other sites 8.

24 patients received 2 cycles, 3 only 1 due to early PD. Toxicity was predominantly hematologic with no severe non-hematologic toxic events reported. Major response was evident in 7 patients (CR+PR: 26%), MR in 4, NR in 8 and PD in 8. The response rate was 14% in embryonal and 38% in alveolar RMS.

Conclusion: These preliminary data show that the T/C combination has a mild toxicity in pretreated patients. The response rate is lower when compared to other combinations tested in phase II studies but it is of interest for the population with alveolar subtype.

PJ009

MALIGNANT PERIPHERAL NERVE SHEAT TUMOR IN CHILDREN- EXPERIENCE ON 7 CASES

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Purpose: The aim of study is to review the cases of Malignant peripheral nerve sheat tumor (MPNST ) treated at the Pediatric Department of Institute for Oncology and Radiology of Serbia. Method: From 1996 to 2009, 7 children with a median age of 12 (range 4 to 17 years ) were treated in our institution. There were 5 male and 2 female.

In one child the primary site was in sacrum, 2 of them had head and neck localisation and in 4 of them primary localisation were extremities. Six patients had large tumor. None of patients was affected by neurofibromatosis I. Patients were treated using multimodality therapeutic approach including surgery, chemotherapy and radiotherapy.

Results: At diagnosis 3 patients had a grossly complete tumor resection. Among the 4 patients classified as IRS group III, one patient had only biopsy, 2 had delayed surgery after neoadjuvante chemotherapy (three and five cycles ) and one patient because of progression of disease after two cycles of chemotherapy. Delayed surgery involved amputation in one patient and conservative resection in two patients.

Chemotherapy was administered to all patients, neoadjuvant chemotherapy in 4 patients. Response to chemotherapy was assessable in 2 patients in group III - included 2 partial responders, and one patient had progression of disease. The haemotherapy regimens was VACA in 4 patients, CEVAIE in 2 patients and 1 patient received haemotherapy according to EE 99 protocol. Radiotherapy was given to 5 patients. In all patients radiation therapy was administered concomitantly with chemotherapy. The total dose ranged from 55 to 60 Gy. All of our 7 patients are under follow-up period with no evidence of disease for 1 year to 12.5 years.

Conclusion: Multimodal treatment is effective in children with MPNST. According to our study tumor stage, site and absence of metastases are important predictor of survival.

PJ010

ARE THE RECIST CRITERIA USEFUL IN ASSESSING RESPONSE IN PEDIAIRIC RHABDOMYOSARCOMA?

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902 SIOP ABSTRACTS

Purpose: Volume (3D) measurements are routine in paediatric oncology trials. Unidimensional (1D) measurements (RECIST) have been validated in adult tumours but not in paediatric malignancies. Aim is to compare volume and RECIST response evaluation in patients with rhabdomyosarcoma.

Method: We evaluated a consecutive cohort of children with rhabdomyosarcoma treated at two children’s institutions GOSH and EKZ-AMC between 1998 and 2008. Tumour measurements in 1D and 3D with CT or MRI were assessed at diagnosis and after 2–3 cycles of chemotherapy. Stable disease (SD) as defined by volume measurements is a decrease in tumour volume of < 33%. By RECIST a decrease in largest diameter of < 30%. Progressive disease (PD) as defined by volume measurements is an increase in volume of > 40%. By RECIST an increase in largest diameter of > 20%.

Results: 64 Patients were identified with the relevant imaging over 10 years. 32 Patients were excluded (primary surgery at diagnosis, ultrasound follow-up, transfer elsewhere, films missing). There were 36 males and 28 females. Median age was 3.9 years (range 0.2–16.0 years). Median interval between studies was 9.0 weeks (interquartile range 8.4–11.9 weeks). A partial response (PR) was seen in 49 patients with 3D measurements and in 38 with 1D. Stable disease was seen in 10 with 3D and in 22 with 1D. Progressive disease was observed in 2 patients when measured with 3D and in 1 with 1D. Three patients achieved CR.

Conclusion: We observed 12 discrepancies (18.8%). 11 cases classified as PR by 3D had SD on 1D assessment and 1 case showed PD on 3D and SD on 1D. In 11 of these cases this would have meant a different treatment decision. Based on this study we feel that implementation of RECIST in paediatric soft-tissue sarcoma trials is not warranted as it may lead to a significant misclassification of patients.

PJ011

ORTAL RhabdomyOSarcoma (RMS): OUTCOME OF PATIENTS WHO RELAPSED FOLLOWING TREATMENT FOR LOCALIZED TUMORS ON INTERGROUP RHABDOMYOSARCOMA STUDY GROUP (IRSG) PROTOCOLS - III AND IV, 1984-1997

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Purpose: To determine patterns of recurrence, re-treatment, and outcome among 191 pts treated for localized orbital sarcoma on IRSG Protocols III/IV.

Method: Chart review

Results: 25/191 pts (13%) developed local (n = 22), distant (n = 2), or regional lymph-nodal relapse (n = 1) at 0.06-7.1 years (median, 1.6) after enrollment. Pts ages at study entry were 0.14-17 years (median, 6.9) after relapse.

Conclusion: Evaluation of patients with rhabdomyosarcoma treated at our centre had local treatment with surgery followed by brachytherapy if feasible. Aim is to assess the adequacy of this treatment policy and identify factors associated with relapse.

PJ013

RHABDOMYOSARCOMA: 13 YEARS EXPERIENCE IN A PEDIATRIC ONCOLOGY CENTER

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Purpose: Evaluate outcome of patients with Rhabdomyosarcoma depending on the varying clinical features.

Method: A retrospective analysis was performed on all patients with Rhabdomyosarcoma diagnosed at Hospital de Niños “Ricardo Gutierrez” between June 1996 and December 2008. They were treated according to Malignant Mesenchymal Tumour 95 Study and Malignant Mesenchymal Tumour 98 Study protocols.

Results: Out of the 57 patients with diagnosis of Rhabdomyosarcoma treated in our institution, 2 were not evaluable. Median follow-up was 24 months (5–160). There were 22 (40%) female. Median age at diagnosis was 4.2 years (0.4–17.5) while 25% were older than 10 years. Primary sites included: 12 (21.8%) genitourinary, 11 (20%) head and neck, 6 (10.9%) parameningeal, 6 (10.9%) bladder/prostate, 5 (9%) limbs, 3 (5.4%) orbit, 10 (18.1%) others and 2 (3.6%) unknown site. 2, 6, 35, and 12 patients were classified as belonging to stages (TNM) 1, 2, 3, 4, respectively. The most common histology was embryonal, found in 44 (80%) cases. The overall survival (OS) for the whole group was 45.4%. In localized disease the OS was 53.4% while in metastatic it was 16.6%. The OS for patients aged less than 10 years was 46.3% compared to 42.8% in those aged 10 years and over. Out of the 55 patients, 22 (40%) relapsed with a mean and median time of 11 and 7.5 months respectively. 2/6 (33.3%) stage 2 patients relapsed; 15/35 (42.8%) stage 3 and 5/12 (41.6%) stage 4.

Conclusion: Surgery followed by brachytherapy is an effective local treatment for orbital rhabdomyosarcoma, More rigid pre- and (directly) postoperative treatment evaluation might lead to a reduction in local failure.

PJ012

SURGERY AND BRACHYTHERAPY FOR ORBITAL RHABDOMYOSARCOMA: A FAILURE PATTERN ANALYSIS

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Purpose: Patients with orbital rhabdomyosarcoma have an excellent survival. Therefore new strategies for local therapy have been developed to minimize adverse effects. Brachytherapy offers a focused dose delivery and rapid fall-off of the dose beyond the treatment volume. Since 1990 patients with an orbital rhabdomyosarcoma treated at our centre had local treatment with surgery followed by brachytherapy if feasible. Aim is to assess the adequacy of this treatment policy and identify factors associated with relapse.

Method: From 1990 to 2008, 23 consecutive patients with orbital rhabdomyosarcoma were treated according to European protocols (SIOP-MMT-89, 95 and EpiSSG-RMS-2005). 3 Patients were excluded from analysis because of insufficient data. For 20 patients (median age 7.4 years, range 0.9–14.7; mean follow up 7.7 years, range 1.3–17.1) we reviewed their characteristics (classical rhabdomyosarcoma risk factors with added extraorbital localization and chemotherapy response) and treatment details (method of biopsy, adequacy of surgery and brachytherapy) in a multi-disciplinary setting.

Results: Twelve patients received surgery and brachytherapy, 8 received other treatments: 5 no local treatment (all in CR), 1 surgery only and 2 external beam radiotherapy. Risk factors were comparable in both treatment groups. Biopsy was incisional in 12 and excisional in 8. In only 2 of these 8 patients delayed surgery and brachytherapy was feasible. Two relapses occurred in the brachytherapy cohort (n = 12); 1 occurred in the margins of the brachytherapy field; in retrospect surgery and brachytherapy were both considered inadequate in this case. Retrospective analysis of the 10 non relapsing brachytherapy-patients showed suboptimal surgery in 2 cases and suboptimal brachytherapy in another case. 5 Of 8 patients experienced a relapse in the non brachytherapy group.

Conclusion: Surgery followed by brachytherapy is an effective local treatment for orbital rhabdomyosarcoma, More rigid pre- and (directly) postoperative treatment evaluation might lead to a reduction in local failure.
Conclusion: Survival outcome appeared inferior to those reported by international studies. This can be due to the predominance of stage III. The OS for metastatic disease remain similar.

PJ014

EVIDENCE-BASED DECISIONS AND BETTER CARE OF RHABDOMYOSARCOMA IN JORDAN

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Purpose: The management of rhabdomyosarcoma (RMS) has evolved significantly over the past 3 decades. Different modalities tested in Europe and North America did not prove superior to basic regimens that are affordable in developing countries. Multidisciplinary care was established at our center, thanks to the availability of full time dedicated health care workers.

Method: A retrospective analysis of patients with RMS who presented to KHCC from January 2004 to December 2008. An Institutional Review Board (IRB) approval was sought before starting this study.

Results: A total of 45 patients (31 males) were reviewed. The median age at diagnosis was 4 years (range, 0.3 to 17.8 years). Embryonal and alveolar histologies accounted for 84% (n = 38) and 16% (n = 7) of the cases, respectively. The three most common sites were Bladder/prostate (n = 9, 20%), head and neck nonparameningeal (n = 9, 20%) and parameningeal (n = 8, 18%). Seven patients (16%) had distant metastasis at time of diagnosis. The number and 3-year event-free survival (EFS) of patients according to risk categories were as follows: low risk group (n = 6, EFS = 100%), intermediate risk group (n = 32, EFS = 64%) and high risk group (n = 7, EFS = 30%). Among the strategies that we adopted in order to deliver better care were: second look surgeries to correct mistakes done during upfront surgeries performed outside the center, decreasing the dose of cyclophosphamide from 2.2g/m²/2cycle to 1.2 g/m²/ cycle, avoiding experimental therapies in high risk patients, and effectively controlling parents of relapsed patients to shift the care from hopeless heroic therapies towards effective palliation.

Conclusion: The results of our patients are satisfactory and reflect multidisciplinary coordination. A major obstacle in the care of children with solid tumors in developing countries is the human factor. Collaborative groups studying RMS failed to show that “more is better” and thus pediatric oncologists in developing countries should stick to evidence-based approaches.

PJ015

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

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Purpose: To evaluate the clinical outcome & long term adverse effects of interstitial brachytherapy (BRT) for children with soft tissue sarcomas (STS) each tumour was analysed.

Method: From September 1984 to July 2008, 61 children (median age 15 years, range 1 to 18) with STS who received BRT as part of loco-regional treatment were included. There were 37 males and 24 females. Majority (74%) had primary lesions. Synovial sarcoma (30%) was the most common histological type, and 44% had high-grade lesions. Treatment included wide local excision and BRT with or without external beam radiotherapy (EBRT). Forty children (66%) received BRT alone. Results: After a median follow-up of 68 months, the local control (LC), disease-free survival (DFS), and overall survival (OS) were 85%, 74%, and 77%, respectively. LC to those receiving BRT alone (76% vs. 89%, p = 0.28). There was no significant difference in LC for patients receiving LDR versus HDR BRT (84% vs. 95%, p = 0.31, for BRT alone; and 73% vs. 83%, p = 0.60, for BRT+EBRT). Surgical wound healing complications was seen in 8% patients. Subcutaneous fibrosis (31%) was the commonest late complication followed by distal limb edema (5%), joint stiffness (3.3%), & bone growth abnormality (1.6%). There was no neuropathy, non-healing ulcer or second malignancy. Conclusion: Intensified BRT with or without EBRT result in excellent outcome in children with STS. Radical BRT alone, when used judiciously in select groups of children, results in excellent local control and functional outcome with reduced treatment-related morbidity.

PJ016

MALIGNANT SOFT TISSUE TUMOURS IN CHILDREN IN IBADAN, NIGERIA

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Purpose: Malignant soft tissue tumours (MSTT) are rare in our environment. Detailed study and literature on the subject in indigenous sub-Saharan black African population are rare. The aim of the study was to retrospectively analyse basic clinical information of patients and reclassify the tumours according to the 2002 World Health Organization classification (WHO) of malignant soft tissue tumours.

Method: All histopathologically diagnosed malignant soft tissue tumours in children aged 15 years and below available from the files, records and Cancer registry data of the Department of Pathology, University College Hospital, Ibadan Nigeria between January 1989 and December 2007 were included in the study. All the cases were reviewed and reclassified according to the 2002 WHO classification of malignant soft tissue tumours into specific types and variants where possible. Clinical parameters like age at presentation, gender, size and site of tumour and pathological TNM staging for each tumour was analysed.

Results: A total of 67 cases were identified as follows Rhabdomyosarcoma-52 cases(77.6%), 3 cases each of synovial sarcoma and haemangiosarcoma, 2 cases each of Dermatofibrosarcoma protuberans, Kaposi sarcoma and Infantile fibrosarcoma and a single case each of Malignant fibrous histiocytoma, Alveolar soft part sarcoma and Sarcoma/NOS). Overall for all the tumours, there was a male preponderance (male: female ratio of 1.6:1). The median age for Rhabdomyosarcoma was 5 years with majority-50% in the head and neck region and the commonest variant been the embryonal type. Majority (60%) of our patients presented with T2 (TNM) stage tumours.

Conclusion: Rhabdomyosarcoma is the commonest malignant soft tissue tumour in this study. Kaposi Sarcoma is very rare in Nigerian children. Most of our patients with MSTT presented with T2 (TNM) stage tumours.

PK001

LOWERING DOSES OF CHEMOTHERAPEUTIC FOR TREATMENT OF HEPATOBLASTOMA USING APOPTOSIS INHIBITORS IN VITRO.

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Purpose: The outcome of patients with high-risk hepatoblastoma (HB) is still sobering. Intensifying chemotherapy is limited by multi-drug resistance and toxic side effects. To optimize chemotherapy, apoptosis regulation should be considered in HB as an increased expression of anti-apoptotic proteins confers an improved survival ability of tumor cells. In this study we increased apoptosis sensitivity of HB cells for an improved cytotoxic activity of commonly used drugs.

Method: We quantified expression of apoptosis-related proteins using protein assays in HuH6 and HepT1 cells derived from a mixed and embryonal HB, respectively. The viability of HB cells was monitored in a proliferation assay of cultures treated with ABT-737, an inhibitor of Bcl proteins, in combination with cytotoxic drugs. Measurement of caspase-3 activity proved apoptosis induction.

Results: Imbalance of apoptosis-related proteins was found in HB cells. Expression of the anti-apoptotic proteins Bcl-2 and Bcl-X was increased, whereas the direct interaction partners, the pro-apoptotic proteins Bax and Bad, showed decreased expression. The modulator of this interaction, ABT-737, induced apoptosis in HuH6 and HepT1 cells at concentrations > 1 μM. ABT-737 also enhanced the cytotoxic
effect of Cisplatin, Doxorubicin, Etoposid and Paclitaxel when used as combination therapy. Concentrations of some of these drugs could be reduced up to tenfold when combining treatment with 0.1µM ABT-737. HuH6 expressed slightly higher pro-apoptotic and lower anti-apoptotic protein levels than HepT1, which may explain the stronger enhancement of cytostatic drug effects in HuH6 cells when treated in combination with ABT-737.

Conclusion: The observed shift to an anti-apoptotic phenotype in HB cell lines may account for resistance to cytotoxic drugs used in the standard treatment protocol of HB. These pre-clinical results suggest that apoptosis sensitizers such as ABT-737 might serve as additional option in the treatment of patients with HB to reduce drug doses and prevent drug resistance.

PK002
SUCCESSFUL ESTABLISHMENT OF AN ORTHOTOPIC HEPATOBLASTOMA XENOGRAFT IN NOD-SCID IL2 RAG NULL MICE

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Purpose: Investigating hepatoblastoma (HB) in experimental conditions contributes relevantly to a detailed understanding of tumor biology and investigating new treatment approaches. Some xenograft models have been described. However, systematical analyses are so far being carried out using a subcutaneous tumor growth. Mostly nude mice (NMRI m/m) were used for HB xenotransplantation. Therefore, a reproducible more physiologic intrahepatic model has to be established, in order to consider the physiologic environment of the tumor.

Method: HB-cell lines HuH 6 and Hep T1 were stably transfected with a plasmid vector encoding for Gaussia luciferase (Gluc). HuH 6 and Hep T1 were injected intraplenically in NOD/LtSz-scid IL2Rnull mice. Mice were splenectomized in order to avoid intrasplenic tumor growth. Serum levels of AFP and Gluc-activity were measured weekly. Tumor growth was monitored by MRI. Tumors were analysed in order to avoid intrasplenical tumor growth. Serum levels of AFP and Gluc-activity were measured weekly. Tumor growth was monitored by MRI. Tumors were analysed for biliary atresia.

Results: Multifocal intrahepatic tumor growth was observed in 85% (11/13) of HuH 6 tumors and 55% (5/9) of Hep T1 tumors. AFP and Gluc levels rised parallel to hepatoblastoma growth with a high tumor incidence. Using an IL-2R (-chain were measured weekly. Tumor growth was monitored by MRI. Tumors were analysed for biliary atresia.

Conclusion: We established a reproducible xenograft model for intrahepatic hepatoblastoma and 55% (5/9) of Hep T1 tumors. AFP and Gluc levels rised parallel to hepatoblastoma growth with a high tumor incidence. Using an IL-2R (-chain were measured weekly. Tumor growth was monitored by MRI. Tumors were analysed for biliary atresia.

PK003
IS REJECTION LESS COMMON IN CHILDREN UNDERGOING LIVER TRANSPLANTATION FOR HEPATOBLASTOMA?

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Purpose: Hepatoblastoma is a rare malignant tumour, almost exclusive to childhood. Treatment consists of chemotherapy followed by either hepatic resection or liver transplantation. As chemotherapy is immunosuppressive, the incidence of rejection post transplantation may be reduced. This can have implications for future management as well as reducing potential side effects.

The aim of this study was to compare the incidence of histological rejection in children undergoing liver transplantation for hepatoblastoma with those transplanted for biliary atresia.

Method: All 20 patients who underwent transplantation were identified retrospectively. These were matched 1:3 for age, sex, year of transplant and type of immunosuppression to a control group transplanted for biliary atresia (n = 60). Exclusions were patients transplanted for other types of liver tumour and patients with biliary atresia-splenic malformation syndrome.

Results: Mean age at transplant was 3.25 years in the hepatoblastoma group and 3.28 years in the control group. Overall survival was 75% of tumour patients currently well compared with 88.3% of biliary atresia patients (survival defined as status at 5 year follow-up) p = 0.5. Long term, acute histological rejection was less common in the hepatoblastoma group (50% vs 75%) respectively (p < 0.04). Immunosuppression for both groups was comparable. Chronic rejection was rare in both groups but more common in the biliary atresia group compared with the hepatoblastoma group (10% vs 5% respectively) p = 0.07. Equal levels of immunosuppression were achieved in both groups.

Conclusion: In summary acute rejection is less common in children undergoing liver transplantation for hepatoblastoma compared to biliary atresia. As a result, children undergoing liver transplantation for hepatoblastoma could benefit from less intensive immunosuppression regimens.
PK006
PROGNOSTIC IMPLICATIONS OF SERUM ALPHA-FETOPROTEIN RESPONSE DURING TREATMENT OF HEPATOBLASTOMA

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Purpose: Hepatoblastoma is the most common malignant liver tumor in childhood. We investigated the treatment outcome and prognostic factors for hepatoblastoma, focusing on the prognostic significance of serum levels of alpha-fetoprotein (AFP) and its changes during treatment.

Method: We performed a retrospective analysis of the medical records of 43 consecutive children with hepatoblastoma who were treated at Asan Medical Center between 1991 and 2009.

Results: The median age at diagnosis was 20 months (range, 2 to 261) with a male to female ratio of 1.4:1. Seventeen patients (40%) had distant metastases at presentation, whereas sex, metastasis, COG stage, histological subtypes, and chemotherapy regimen were not significant indicators of the outcome. AFP levels at diagnosis greater than 300,000 ng/mL, a decline of < 1 log in AFP levels after the first cycle of chemotherapy, and preoperative AFP levels greater than 3,000 ng/mL were significantly associated with a poorer outcome. AFP levels at the end of treatment did not predict a possible relapse. Age at diagnosis, thrombocytosis at diagnosis, and PRETEXT stage were significantly associated with survival outcome, whereas sex, metastasis, COG stage, histological subtypes, and chemotherapy regimen were not significant indicators of the outcome.

Conclusion: AFP levels at diagnosis and initial treatment responses expressed as changes in AFP levels after the first cycle of chemotherapy are possible indicators of outcome and a higher preoperative AFP level is a possible predictor of treatment failure after tumor resection. Monitoring the changes in AFP levels during chemotherapy could allow identification of poor responders and alternative treatment should be considered for those patients.

PK007
SECONDARY LEUKEMIA AFTER TREATMENT FOR HEPATOBLASTOMA IN JAPAN

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Purpose: Secondary malignancy is one of the most devastating late complications in childhood cancer survivors. However, secondary malignancies after treatment of hepatoblastoma have not been fully studied. Recently, several cases of secondary leukemia have been reported among survivors of hepatoblastoma in Japan.

Method: Five patients (1.7%) have been reported to have secondary leukemia among those who were enrolled in JPLT-2 protocol of the Japan Pediatric Liver Tumor Study Group. Clinical information of the patients was reviewed to determine whether they had any specific risk factors for secondary leukemia.

Results: Median age at onset of hepatoblastoma was 12 months (3-26 months old). Four out of five patients were male. All patients underwent neoadjuvant chemotherapy followed by hepatectomy and adjuvant chemotherapy. Two patients received CIT- (cisplatin and pirarubicin), and three were treated with CITA and IECF (ifosfamide, pirazinomycin, etoposide, and carboplatin). In two patients, CATA-L (intrarterial infusion of carboplatin and pirarubicin in lipiodol) was used. Latent period from the end of treatment for hepatoblastoma to the onset of leukemia was median of 32 months (7-72 months). The type of the leukemias was as follows: 3 AML, one preB ALL, one T-ALL. The most striking feature of the secondary leukemias was that all had 11q23 translocation or MLL rearrangement, suggesting that they were caused by topoisoerase II inhibitors. Accumulative dose of topoisoerase II inhibitors used for treatment of hepatoblastoma ranged from 0 to 3000 (median 1000) mg/m2 for etoposide and from 240 to 690 (median 360) mg/m2 for pirarubicin. No other specific features were noted in physical findings and family history except for one very low birth weight infant and one Beckwith-Wiedemann syndrome.

Conclusion: There is a high incidence of secondary leukemia in patients with hepatoblastoma in Japan. Topoisoerase II inhibitors are potent risk factors for secondary leukemia after treatment of hepatoblastoma.
Purpose: Orthotopic liver transplantation is a treatment option for hepatoblastoma patients with unresectable primary tumors. The risks and benefits of post-transplant chemotherapy are less well defined.

Method: Demographic, clinical, surgical and outcome data of all hepatoblastoma patients (20) who underwent liver transplantation between 1994 and 2008 at CHCMC were reviewed.

Results: Median age at diagnosis and transplant was 1.5 yrs (0–4.9) and 2.2 yrs (0.6–5.2) respectively, with male:female of 16:4. COG stage was 2 (1), 3 (17), and 4 (2). Indications for liver transplantation were bilobar (7) or central (5) tumors, both bilobar and central tumors (3), salvage for recurrence (3), and salvage for end stage liver disease (ESLD) (2). All patients received pre-transplant chemotherapy cycles (median 2, mean 2.25, range 1–4 cycles), and 6 started therapy between 14 to 21 days after transplant. Eleven patients underwent a chemotherapy regimen change prior to transplant (7 for disease resistance, 4 for toxicities), and 9 underwent a chemotherapy change after transplant (7 for disease resistance; 2 for toxicities). There were no tumor recurrences (44 month median follow-up). Graft and patient survival is 95%. The patient with stage 2 disease underwent a transplant for ESLD, and died from lymphoma 6 years later. The 19 patients with unresectable primary tumors (stage 3 (17) and 4 (2)) are alive and disease-free.

Conclusion: Chemotherapy, individualized in this case series, combined with liver transplantation improves overall survival for hepatoblastoma patients with initially unresectable primary tumors. Post-transplant chemotherapy is well tolerated, even when initiated within 3 weeks of transplant. Definitive proof of benefit of post-transplant chemotherapy will require a properly controlled prospective trial. Ongoing research should focus on timely referral of appropriate patients to a Liver Transplant Center, and reduction of long-term toxicities.

PK010
HEPATOCELLULAR CARCINOMA IN CHILDREN: RESULTS OF THE INTERNATIONAL SIOPEN 2 AND 3 TRIALS.

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Purpose: Hepatocellular carcinoma (HCC) is a relatively rare disease in children and is traditionally linked with much poorer prognosis, however treatment protocols used to be essentially the same. Chemotherapy was the same in SIOPEN 2 and 3 trials, but in SIOPEN 3 primary surgery was recommended, whenever feasible.

Method: In both trials treatment was based on chemotherapy consisting of: carboplatin added to PLADO (cisplatin+doxorubicin) and reducing the cisplatin interval from 3 to 2 weeks. Between October 1995 and April 1998, 20 patients were included into SIOPEN 2. Between July 1998 and October 2006, 70 patients were included into SIOPEN 3. A total of 85 pts. remain evaluable.

Results: Patients age ranged from 29 months to 17.3 years (median 12.8 years). Males prevailed (56% of cases). In 19 (22%) children an extraparenchymal tumor extension was present. Thirty (35%) patients presented with pulmonary metastases at diagnosis. Thirteen patients underwent primary liver resection, 36 received preoperative chemotherapy and were then resected. Thirty six remained inoperable. Chemotherapy is documented for 71 patients. 17 patients received pre-and postoperative chemotherapy. Response to preoperative chemotherapy showed 29 partial responses (40%), stable disease in 15 and progression in 14 children. Early death occurred in 7 (10%) cases. The rate of complete resection (including liver transplantation - OLT) without with microscopic residuals was 41/85 = 48%. Five out of 7 transplanted patients died later. At a median follow up time of 75 months 65 patients had events (progression/relapse/death). 62 patients died. Complete tumor resection is prerequisite for survival, however there was no difference between primary and secondary surgery. Overall survival at 5 years was 22% (+10% with 95% confidence interval).

Conclusion: Complete tumor excision is the only chance for cure in HCC but is often prevented by advanced disease. A prospective worldwide cooperation is needed to evaluate novel therapeutic concepts.

PT001
TUMOR ADRENAL CORTEX (TCA) IN THE WEST OF PARANA STATE- BRAZIL- CASE REPORT

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Purpose: The tumor of adrenal cortex (TCA) generally is malignant in children and has bad prognostic when it is great, it invades great vases or presents metastases. The TCA is rare in other countries and northeast/north of Brazil, but in the Paraná state the incidence is at least 15 times raised. The found genetic mutation always of the same type (R337H in gene TP53). Early diagnosis is important to approach adequate therapeutic.

Objective: Report 2 cases of children who had the mutation and developed tumor of the adrenal cortex

Method: Two children who had presented mutation, developed the TCA

Results: Case 1. feminine sex, 3 months age with sians of virilization and Cushing’s syndrome. Abdominal CT scan -mass above the right renal 5,5/C2. The initial treatment was the surgery. Pathology-tumor with 45gr, size 4,7/C2 syndrome. Abdominal CT scan -mass above the right renal 5,5/C2. Hormonal dosages: DHEA sulphate 1,000 ug/dl, cortisol of 50 ug/dl; testosterone 1,000 ug/dl. The initial treatment was the surgery. Pathology-tumor with 45gr, size 4,7 × 4,0 × 2,7 cm. The child is in remission 1year and 7 months after the surgery.

Case2. feminine sex, 8 months age with sians of virilization and abdominal mass. Abdominal CT scan -mass above the right renal 5,5 × 4,4 cm. Hormonal dosages: DHEA sulphate 9,930 ug/dl; cortisol of 23,54 ug/dl, and testosterone 688,00 ug/dl. The initial treatment was the surgery. Pathology-tumor with 65gr, size 4,0 × 3,8 × 3,6 cm. It was initiated mitotane for 4 months after first tumoral return, at moment, it is in remission 2 year after stop of medication.

Conclusion: This cases illustrate that the accompaniment of children with genetic mutation for TCA, will benefit those that eventually have tumor development, with a possibility of cure around 95–100% of surgery. For this disease, the early diagnosis is basic for the increase of survival chances for the child.

PT002
OVEREXPRESSION OF BCL2 AND TNF GENES IS ASSOCIATED WITH LESS AGGRESSIVE DISEASE IN CHILDHOOD ADRENOCORTICAL TUMORS (ACT)

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Purpose: Pediatric hepatocellular carcinoma (HCC) differs significantly from hepatoblastoma (HB) and is traditionally linked with much poorer prognosis, however treatment protocols used to be essentially the same. Chemotherapy was the same in
PL003

PLASMA CYTOKINE PROFILING OF DISSEMENATED INFANTILE MYOFIBROMATOSIS: IMPLICATIONS FOR ETIOLOGY AND TAREGETED THERAPEUTICS.

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Purpose: Infantile myofibromatosis (IM) is a rare soft tissue neoplasm that often presents at birth or in early childhood. Uncomplicated cases are often managed conservatively but the prognosis is extremely poor when several internal organs are affected and one-third of such infants die in the first 4 months of life from vital organ dysfunction. Hence, new knowledge to facilitate effective treatment approaches is urgently needed. We are investigating blood cytokine profiles to identify potential mechanisms of abnormal cellular growth and proliferation seen in IM.

Method: After informed consent, blood was collected from an infant who presented with left Horner’s syndrome, multiple lytic bony lesions and several subcutaneous masses and a large homogenous mass extending from the ventricular apex. Biopsy was consistent with IM. Plasma from the patient and a matched normal control sample were analyzed using multiplexing bead technology for 65 distinct cytokines, growth factors and chemokines.

Results: The patient’s plasma contained significantly increased levels of PDGF-AA (more than 10,000 pg/ml vs. 190 pg/ml in control), EGF (3400 pg/ml vs 85 pg/ml) and TRAC-1 (1700 pg/ml vs 15 pg/ml). A substantial increase in GRO, CD40L, PDGF-AB and CD40L (1100%, 2500%, 3000%, 250%, and 250% increase over control, respectively) was also noted. Moderate increases were seen with SDF-1, ENA78, FGF, MDC and MCP-1 (300%, 600%, 500%, 400% and 200% over control, respectively). No differences were seen with the remaining 53 cytokines.

Conclusion: This plasma also stimulated the growth of normal fibroblasts in culture and provided an experimental model to describe this pathway and to identify potential targeted therapeutics for IM including the use of STI571 against PDGF activity.

PL004

RESPONSE OF NUT MIDLINE CARCINOMA TO HISTONE DEACETYLASE INHIBITION AND ESTABLISHMENT OF AN INTERNATIONAL REGISTRY

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Purpose: NUT midline carcinoma (NMC) is a genetically-defined carcinoma characterized by oncogenic BRD-NUT fusion genes classically produced by the t(15;19) chromosomal translocation. This aggressive neoplasm is often associated with advanced locoregional disease, distant metastases, resistance to conventional therapies, and poor outcomes. By investigating this rare but genetically-tractable entity, we aim to better define its unique pathogenesis and potentially to uncover more generalizable features of malignancy.

Method: In vitro studies of NMC cells including measurement of chromatin acetylation and cell growth and differentiation. Description of response to histone deacetylase inhibitors. Clinical case presentation. Outline of an international registry. Results: We provide evidence that the BRD-NUT oncoprotein disrupts the pattern of nuclear chromatin acetylation. Histone deacetylase inhibitors are a new class of antineoplastic of which vorinostat is the most widely used agent in clinical practice. In vitro treatment of NMC cells with histone deacetylase inhibitors including vorinostat reverses the changes in chromatin acetylation induced by BRD-NUT, and converts the cells from a proliferative to a differentiated state. As translation of these findings, we describe a child with NUT midline carcinoma treated with vorinostat monotherapy who had a partial response to therapy. We have recently established an international NUT midline carcinoma registry (NMCregeistry.org). The main objectives of the registry are: 1) to provide pathologic review; 2) to share educational material; 3) to collect clinical data to aid in the characterization of the disease and treatment outcomes; 4) to facilitate development of treatment guidelines; and 5) to promote basic research.

Conclusion: NMC is an aggressive carcinoma which demonstrates an aberrant pattern of chromatin acetylation. Histone deacetylase inhibition represents one promising therapeutic strategy to counteract the malignant phenotype. An international registry will promote future advances in the knowledge of this uniformly lethal cancer.
PL006
THE INTERNATIONAL STUDY OF EMBRYONAL TUMORS (ISET): PILOTS CONDUCTED IN SERBIA AND MACEDONIA

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Purpose: ISET is an IARC-initiated consortium of case-control studies of embryonal tumors including neuroblastoma, Wilms tumor and rhabdomyosarcoma in children under the age of 15 years. This initial phase is a feasibility study of recruitment of cases and controls.

Method: Case-parent triads were recruited from four hospitals in Serbia and one in Macedonia during the eligibility period (1/1/2007 to 12/31/2009). Participation involved in person interviews (3 per family) and biospecimen collection (blood or saliva, and histopathology samples). Two methods of control recruitment began in 2009 and were tested in Serbia: hospital controls recruited at trauma wards of the 4 centers, and primary-care physician (PCP) controls randomly selected from a list of 10 potential controls provided by the participating case’s physician.

Results: In Serbia, a total of 58 cases were diagnosed at the 4 hospitals during the eligibility period. Overall, 53 patients were approached; 48 (88%) agreed to participate and 5 declined. Of 46 triads interviewed to date, 45 triads contributed biospecimens. In Macedonia, 22 cases were identified from the hospital registry during the eligibility period, with 7 approached and enrolled to date. Hospital control recruitment was challenging: only 13 (30%) of 43 approached subjects agreed to participate and 10 completed the interviews. Primary physicians provided contact information for 141 PCP controls; of those contacted, 78 agreed to participate (55%) with 62 (44%) interviews completed to date. PCP controls were less likely to contribute DNA; of 22 approached, 13 participated.

Conclusion: In this pilot, we observed high participation rates among case families, which is similar to that observed in other countries. Control recruitment was more challenging, although PCP controls had higher participation rates. Controls were less likely to contribute DNA. These data will be useful in planning a large international effort to study the etiology of embryonal tumors in children.

PL007
MALIGNANT PERIPHERAL NERVE SHEATH TUMORS IN CHILDHOOD: RETROSPECTIVE ANALYSIS OF 13 CASES

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Purpose: To evaluate clinical characteristics, treatment results and outcome of our patients with malignant peripheral nerve sheath tumors (MPNS).

Method: 13 children treated between 1973–2009 with the diagnoses of MPNS tumors were reviewed.

Results: Median age was 11 years (0.16–18 years; F/M: 6/7). The median time between the onset of symptoms and diagnosis was 1.5 months (0.2–1.44). The most common symptoms were palpable mass (53.9%), and pain (23.1%). Four patients (30.8%) had neurofibromatosis type 1 (NF-1). Physical findings were palpable mass (76.9%), scoliosis (15.4%), paraplegia/cranial nerve palsy (15.4%), and stigmata of NF-1. The primary sites were head and neck (30.7%), abdomen (23.1%), chest wall (23.1%), abdominal wall (7.7%), extremity (7.7%), and thoracocervical paraspinal groove (7.7%). According to Intergroup Rhabdomyosarcoma Study (IRS) system 5 cases (38.5%) were classified as IRS group I & II (F2) as group II, and 2 (15.3%) as group IV. Sites of distant metastasis were lung and mediastinum. Chemotherapy, radiotherapy, and chemoradiotherapy were administered to 6 (46.2%), 2 (15.4%), and 4 (30.8%) cases, respectively. Patients were treated with different chemotherapy regimens including cyclophosphamide, vincristine, etoposide, doxorubicin, and cisplatin. Median radiation dose was 5750 (3200–6000) cGy. Ten (77%) patients underwent total and partial primary resection, and 2 (15%) underwent only biopsy. Five-year overall and event-free survival rates were 34.6% and 18.8%, respectively. Overall survival rates did not differ with addition of chemotherapy and/or radiotherapy to the surgery. Five-year survival rates were 42.9% in patients with total resection; 37.5% in patients with partial resection (p = 0.08). Overall survival rates did not differ with stages (p = 0.8).

Conclusion: MPNS tumors are rare in childhood and have an unfavorable prognosis. While chemotherapy and/or radiotherapy had no promising effect on overall survival rates, complete resection seems to be the most effective treatment. Further multicentric studies on the role of chemotherapy should be done.

PL008
CHILDREN AND ADOLESCENTS WITH ADRENOCORTICAL TUMORS IN GERMANY - RESULTS OF THE GPOH-MET 97 TRIAL

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Purpose: Evaluation of diagnosis, treatment and outcome of adrenocortical tumors (ACT) in children and adolescents in Germany.

Method: From 1996 to 2009 73 children (23 boys and 49 girls) with ACT aged 0.2 to 18.4 years (mean 6.8 years) were admitted to the GPOH-MET 97 trial, a national prospective interdisciplinary multicenter study including malignant endocrine tumors in children. 53 patients suffered from adrenocortical carcinoma (ACC), 15 from adrenocortical adenoma (ACA), 4 from tumors with unclear dignity (ACT) and one patient was presented after the first relapse of ACC.

Results: Clinical visible tumor activity led in 86.6% to the diagnosis ACT and 88.9% of the patients showed initially measurable hormone activity, mainly androgen excess. Clinical visible tumor activity led in 86.6% to the diagnosis ACT and 88.9% of the patients showed initially measurable hormone activity, mainly androgen excess. The mean tumor size was 471.6ml (8 to 3645ml) for ACC (N = 15, OS = 65%) than patients with tumors bigger than 400 ml (EFS = 60.0%) and patients with perioperative tumor rupture (N = 34.6%).
Patients with advanced tumor stages were treated after surgery with chemotherapy and Mitotane. Since high tumor volume is a prognostic unfavorable sign and the risk of surgical complications in these patients is high, a preoperative chemotherapy should be considered.

Conclusion: Because of the prognostic unfavorable situation of Rx resection, perioperative tumor spillage or preoperative tumor biopsy, the preoperative management of ACT is extremely important. This includes preoperative urine steroid analysis and in special cases the administration of neoadjuvant chemotherapy including Mitotane.

PL.009

INCIDENCE OF RARE MALIGNANT PEDIATRIC TUMORS IN GERMANY 1998–2007: DATA FROM THE GERMAN CHILDHOOD CANCER REGISTRY

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Purpose: The German Childhood Cancer Registry (GCCR) annually registers ~1800 children diagnosed with a malignant disease (completeness of registration >95%). While most pediatric cancer patients are diagnosed and treated according to standardized protocols of the German Society for Pediatric Oncology and Hematology (GPOH), patients with rare tumors are at risk of not being integrated in the sophisticated network including trials and reference centres. Only little efforts have been taken to classify and define these malignancies.

Method: We give an overview of all rare extracranial solid tumors reported to the GCCR from 1998–2007 (age <15 years). A combination of the International Classification of Childhood Cancer (ICCC) and the International Classification of Diseases-Oncology (ICD-O) was used. All tumors accounting for less than 0.3% of all malignant diseases were defined as rare (~5 cases/year).

Results: According to this definition 479 rare tumors (8.3% of all malignant extracranial tumors) were registered within the GCCR - 26.9% of these not within any GPOH study. Distribution within ICCC-3-groups: 205 “Soft tissue and other extracerebral sarcomas” (28 not registered in any GPOH study), 9 “Germ cell tumors, trophoblastic tumors, and neoplasms of gonads” (3), 85 “Other malignant epithelial neoplasms and malignant melanomas” (30), 57 “Other and unspecified carcinomas” (38), 43 “Renal tumors” (11), 43 “Hepatic tumors” (3), 14 “Malignant bone tumors” (5), 16 “Other and unspecified malignant neoplasms” (5), 7 “ Peripheral and intrasellar neoplasms except neuroblastoma”.

Conclusion: Most of the registered pediatric rare tumors are soft tissue sarcomas, treated within the German Soft Tissue Sarcoma Study. 26.9% of all rare tumors are not treated within any GPOH trial and therefore will be registered within the recently founded German Rare Tumor Group. Active data accrual and the development of structures will allow for better registration in future. Supported by the German Children Cancer Foundation.

PL.010

MALIGNANT PAEDIATRIC MALIGNANT MESOTHELIOMA: EPIDEMIOLOGIC DATA

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Purpose: Malignant paediatric mesothelioma is a very rare entity, so that little is known about its epidemiology. We search medical database to identify patients with paediatric mesothelioma to better describe the epidemiology of this rare condition.

Method: 489 cases were identified in the international medical literature (all languages) from 1900 to 2009. Cases were analyzed for the following items (age, sex, country residence, localization, histologic subtype, exposure to asbestos, age of occurrence). Upper age limit was fixed at 20 years old. Analysis was performed using Logiciel EXEL. (Microsoft®) and Maphiprof Professional 6.5. (Corporation Maphiprof, USA)

Results: The number of published cases increases exponentially (R²: 0.922) with time and reached 10 published cases/per year during the last decade. A majority of the reported cases were European (30%), or north American (30%). The sex ratio is 1.2/1, median age at diagnosis is 12.6 (16 days-20 years). The localization was: pleural (63%), peritoneal (22%), pericardial (8%), vaginal (6%). The most frequent histologic subtype was epithelial (63%). Among the 180 cases for which exposure or not to asbestos was mentioned: 4.4% of the patients had previously been exposed to asbestos.

Conclusion: Our data show that paediatric mesothelioma is different from its adult counterpart (sex ratio, localization, exposure to asbestos). International cooperation is mandatory to optimize their management. Worldwide phase II trials maybe performed to test anticancer-agents efficient in adults.
SIOP ABSTRACTS

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Purpose: Angiomyolipoma fibrous histiocytoma (AFH) is a rare soft tissue tumor of uncertain differentiation categorized as being of “intermediate” malignant potential. It accounts for less than 0.5% of all soft tissue tumors and mainly occurs in children and adolescents. Little clinical data however exist about the course of the disease in more recently treated patients. We therefore analyzed the outcome of AFH-patients registered with the Cooperative Weichteilsarkom Studiengruppe [CWS].

Method: Between 1993 and 2008 14 patients registered with CWS in Germany and Switzerland had AFH. The diagnosis was confirmed by reference pathologic review in all cases.

Results: Seven patients were male, the equal number female. Their median age was 9 years (range: 4 – 13). The primary tumors of all patients were localized and most frequently located at the limbs (n = 11), followed by the trunk (n = 2) and the head/neck (n = 1). The maximal diameter of the 12 evaluable tumors was < 5 cm. All but one patient were solely treated with surgical excision during their primary therapy. Complete resection could be achieved in 11 patients, microscopical residuals remained in three more. Two of the latter patients developed relapses: the first a local recurrence after 5 years treated with reexcision; the second a locoregional relapse after 0.5 years with histologically proven involvement of the regional lymph nodes, which was treated with radiation and chemotherapy in addition to surgery. As of march 2010 the median follow-up was 3.3 years (range: 1 – 14) and all patients included in this analysis are currently alive disease-free. Their 5-year EFS was 92 ± 14% (95%CI).

Conclusion: Pediatric AFH are malignant, but only locoregionally aggressive tumors with an extremely low metastatic potential. Follow-up should therefore focus on the primary tumor site. The prognosis is excellent with surgery alone and adjuvant chemoradiotherapy does not seem to be necessary in the vast majority of patients.

PL013

CHILDHOOD DIFFERENTIATED THYROID CARCINOMA - EXPERIENCE AT THE PEDIATRIC ONCOLOGY INSTITUTION IN BARRETOS - BRAZIL

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Purpose: Thyroid cancer in childhood is a relatively rare condition. The low incidence, lack of prospective randomized trials makes drawing absolute conclusions regarding the definitive workup, management, and treatment of this disease difficult.

Method: A retrospective analysis was done of 53 patients (10 male) with thyroid carcinoma attended in the Pediatric Unit of the Hospital de Câncer de Barretos, from 2000 to 2009. Clinical features, pathology, treatment and prognosis of thyroid cancer in childhood are discussed.

Results: Patient’s age varied from 8 to 16 years. The most frequent initial complaint was an anterior cervical node. Forty six patients were papillary carcinoma, 7 follicular carcinoma. Fine needle aspiration was performed in 30 patients, malignancy positive in 27. All patients underwent total thyroidectomy. Twenty two patients had cervical metastasis at presentation. 3 pulmonary metastasis. Tracheal invasion was detected in one patient. Adjuvant radioiodine (1 3 1I) therapy was made in 51 patients.

Short-term side effects included nausea, vomiting, neck pain, edema, skaldeniitis, mild myelosuppression transient. Forty five patients were given one treatment, 5 two treatments, 2 three treatments and 1 more than three treatments. One patient died, 8 patients developed recurrence disease. In 16,9% parathyroid gland injury results in permanent hypoparathyroidism and 1 patient had recurrent nerve injuries. After a median follow-up period of 4.2 years 52 children are alive and with no evidence of disease. Postoperative suppression of TSH with thyroid hormone decrease recurrence.

Conclusion: Pediatric thyroid malignancies are usually a well-differentiated papillary subtype or the papillary-follicular subtype, commonly present with advanced disease. At presentation, 56% of patients has extensive regional nodal involvement, and 22.2% of patients have distant metastasis. Our prognosis and clinical manifestations data are according to the literature.

PL014

POSTOPERATIVE BLADDER AND RECTUM FUNCTION IN CHILDREN WITH SACROCOCCYGEAL TERATOMA

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Purpose: Sacroccgeal teratomas are rare tumors derived from embryonic germ cells. After surgical exc discse, the oncological follow-up focuses on disease relapse. The risk of urinary bladder and rectum dysfunction in these tumors is obvious; however, there is no clear guideline for postoperative assessment of bladder function.

Conclusion: This study was to evaluate postoperative bladder and rectum function in children with sacrococcygeal teratoma.

Method: Retrospective analysis was performed of 25 patients (6 male, 19 female) with sacrococcygeal teratoma operated at our institution during the last 11 years.

Results: Of the 21 children, 7 (33%) had malignant and 14 (67%) benign tumors. 3 children (15%) died at a mean age of 63 months. Two children with benign tumors had early disease relapse, but all children were alive and disease free at follow-up (mean age 94 months). 11 of 21 children (52%) developed bladder dysfunction clinically (6 of the 7 (86%) children with malignant disease and 5 of 14 (36%) children with benign tumors). All 11 children had pathologic urodynamic studies, with 7 cases of severe neurogenic bladder. In contrast, no rectum dysfunction was found in these children.

Conclusion: Bladder dysfunction following excision of sacroccgeal tumors is a common risk which can be detected by urodynamic studies. Therefore, in addition to current guidelines, the assessment of urinary bladder function with urodynamic studies should be routinely performed on these children during postoperative care.

PL015

CLINICAL ASPECTS OF PHEOCHROMOCYTOMAS AND PARAGANGLIOMAS IN CHILDREN: HIGH FREQUENCY OF GERMLINE MUTATIONS AND MALIGNANCY

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Purpose: Pheochromocytomas are catecholamine-producing tumors of the adrenal medulla, whereas paragangliomas are their extra-adrenal counterparts. Six candidate genes, including RET, Von Hippel Lindau (VHL), NF1, succinate dehydrogenase subunit B (SDHB), SDHC, and SDHD, are responsible for germline mutations in up to 30% of adult patients. Although these rare tumors are well characterized in adults, they remain poorly described in children. The aim of this study is to better understand the clinical aspects, diagnosis and treatment outcome of pheochromocytomas and paragangliomas in children.

Method: To identify all patients < 21 years diagnosed with pheochromocytoma or paraganglioma in the period 1983-2008 in the Netherlands, the nation wide network and registry of histo- and cytopathology, PALGA, was used. This Dutch
PL016

GASTRIC ADENOCARCINOMAS IN CHILDREN AND ADOLESCENTS: EXPERIENCE FROM THE UNIVERSITY OF TEXAS M. D. ANDERSON CANCER CENTER

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Purpose: The median age at diagnosis for gastric adenocarcinomas (GAC) is 50+ years, and these cancers are extremely rare in children. There are limited data on the clinical presentation and outcomes in pediatric GAC, and staging and therapy in children is based on the adult oncology experience. We reviewed our institutional experience with GAC in patients under age 18 years.

Method: Institutional medical record review of patients under age 18 years diagnosed with GAC from 2000 to 2009.

Results: Five patients were identified (3 females). The median age was 17 years (range 9–17 years). Three patients were Hispanic/Latino, 1 was African American, and 1 was Arab. Initial presentations were mostly nonspecific; the most common symptoms were vomiting/hematemesis, abdominal pain, anemia, and weight loss. Median duration of symptoms prior to diagnosis was 3 months (range 0.5–24 months). One patient had a family history of GAC. Four patients presented with metastatic disease—3 patients had peritoneal carcinomatosis; 3 had liver metastases, and 1 had lung metastases. Histology was poorly differentiated adenocarcinoma in all patients, and 3 patients had signet ring cell. E-Cadherin mutations (CDH1) were not tested. All patients received platinum-based chemotherapy for initial treatment, and 2 patients also had surgical treatment. All patients experienced progression of disease, and median time to progression was 4 months (range 2–7 months). Four patients died of disease, and mean time to death from initial progression was 2.8 months (range 1–5 months). The one patient who presented without metastasis remained alive at last follow-up, 7 years after diagnosis, and tested positive for Helicobacter pylori and COX-2.

Conclusion: Our case series suggests that pediatric GAC patients present with diffuse metastatic disease with patterns of spread similar to those in adult GAC. The prognosis is poor even with chemotherapy. E-Cadherin mutations should be tested for prospectively in young patients.

PL017

RARE CHILDHOOD TUMORS IN A TURKISH PEDIATRIC ONCOLOGY CENTER

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Purpose: Rare tumor (RT) rate is reported 15% of all childhood cancer in United States. According to Turkish Pediatric Oncology Group (TPOG) data, 10,059 children were diagnosed as cancer between 2002–2008 in our country and 3.65% of them were diagnosed as RTs. We aimed to investigate frequency and clinical features of RTs in our center.

Method: Four-hundred-twenty-seven cancer patients that have been followed between 2002–2010 were evaluated as retrospectively.

Results: Thirty-three of 427 patients have diagnosed as RTs in 8 years. Ages at diagnosis were between 1month–15 years of age (median:8 years), 15 boys, 18 girls. Diagnoses were giant-cell granuloma (n = 4), papillary, thyroid carcinoma (n = 4), carcinoid tumor (n = 2), tyrosinemia (n = 2), synovial sarcoma (n = 2), congenital giant nevus (n = 1), undifferentiated epithelial tumor (n = 1), atypical fibroxanthoma (n = 1), juvenile xanthogranuloma (n = 1), cystic hygroma (n = 1), orbital lymphangioma (n = 1), hereditary multiple epiderositis (n = 1), neurofibromatosis (n = 1), primary bone rhadomyosarcoma (n = 1), schwannoma (n = 1), chest wall primitive neuroectodermal tumor (PNET) (n = 1), renal PNET (n = 1), mixed malignant mesenchymal tumor (n = 1), plexus coroides carcinoma (n = 1), hepatoblastoma (n = 1), adrenocortical carcinoma (n = 1), intrarenal pheochromocytoma (n = 1), sertoli-cell tumor (n = 1), cistic lymphangioma (n = 1). Frequency of rare tumors was 7.7%. Median follow-up period was 24 months. Four of them were died with progressive disease (synovial sarcoma, mixed malignant mesenchymal tumor, undifferentiated epithelial tumor, plexus coroides carcinoma). Mortality rate was found 12% and overall survival rate 88%. Most of the patients were from South-East part of Turkey.

Conclusion: RT rate in our series is higher than overall Turkish RT rate according to TPOG’s data. This result may be related to frequent referral of RTs to our center for difficulties of diagnosis and follow up of the tumor at peripheral oncology centers, especially at South-East part of Turkey. However, rate of RTs(7.7%) is lower than Western countries (15%), probably, due to technical difficulties of diagnosis of RTs and referral system.

PL018

PEDIATRIC MELANOMA

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Purpose: Melanoma is a rare cancer in pediatric population. 20% percent of melanomas in children and adolescents occur in the head and neck, the remaining being distributed equally on the trunk and extremities. The majority of lesions arise from previous nevi. In Argentina has been reported 16 new cases between 2000 and 2005 (ROHA). The aim of this study is to describe the group of patients with diagnosis of melanoma admitted in our institution and compare with published data


Results: 8 patients with Melanoma were diagnosed in our institution. Median age of presentation was 127.5 months. (range 4–210 mo). 5 were female. The location of the disease were: 2 cases in back, 1 in conjunctive, 1 abdominal wall, gluteus, thigh, brain, sole. 5/8 melanomas arising on preexisting nevi: 2 congenital nevi, 2 melanocytic mixed nevi and 1 blue nevi. Local staging: Clark III: 1 patient, IV: 4 patients V: 1 patient unknown 2 patients Breslow I: 2 patient II: 2 patient III: 1 patient IV: 1 patient unknown 2 patient. In 5 of 8 patients sentinel lymph node biopsy was performed, 2 patients displayed node metastasis at diagnosis and 1 developed metastasis in the course of the disease. 5 patients had nodular melanomas, 1 Acral lentiginous, 1 verrucous and 1 spitzoid melanoma.

Conclusion: We found more number of cases of women, the most common histologic subtypes of melanoma was nodular and the majority of lesions arise from previous nevi as in the literature. The patients who develop metastasis had lesions Clark IV and V and Breslow grater than 1.5 mm.. We didn’t found a predominant location.

PL019

EPITHELIAL LUNG TUMORS IN CHILDREN AND ADOLESCENTS

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Purpose: Primary epithelial lung malignancies are rare in childhood and adolescence.

Method: We have reviewed our experience with epithelial lung tumors diagnosed between 2000–2009. We have identified six patients diagnosed and treated at the Department of Pediatric Hematology and Oncology, Prague, Czech Republic.

Results: There were 3 boys and 3 girls. The median age at diagnosis was 15.7 years (range 12.3–17.2 years). Symptoms were present in all patients. Three patients were initially diagnosed as having pneumonia which contributed to a delay in diagnosis. The most common radio-graphic abnormality was a mass on chest imaging, in five patients the diagnosis was confirmed by bronchoscopy. Final pathological diagnoses included carcinoid tumor (four, typical, one atypical) and one mucoepidermoid carcinoma. Two patients presented with advanced disease (one stage III, one stage IV). Patients with localized disease were treated with surgical resection and all remains disease free with a median follow up 18 months. The girl with widely metastatic lung mucoepidermoid carcinoma (TLN3,M1) was treated with multimodal therapy, but had rapid progression of disease. The patient with stage III atypical carcinoid tumor refused any treatment and succumbed to the disease progression after 22 months.

Conclusion: Carcinoid bronchial tumors are the most frequent epithelial tumors of the lung in children and adolescent and have favorable prognosis after complete surgery. Primary lung tumor should be considered in patients with persistent cough, recurrent pneumonia or hemoptysis.

Supported by grants IGA NS/9997–4 and MZOFNM2005

PL021

CONGENITAL TUMORS IN HOSPITAL INFANTIL DE MEXICO

FEDERICO GÓMEZ. A SIXTY SEVEN-YEAR REVIEW

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Purpose: Tumors diagnosed during the first month of life are infrequent: 0.5 to 2% of all childhood neoplasms. This is an interesting group of tumors because their type, natural history and response to treatment differ from those seen in older children. We present the epidemiology of congenital tumors in a Mexican Hospital for a period of 67 years. Purpose: Determine the epidemiology of congenital tumors from 1943 to 2010.

Method: Records and neonatal histories of all patients younger than 28 days old, diagnosed with solid tumors that were retrospectively reviewed.

Results: 80 neonates have been diagnosed. 43.8% were female and 56.3% were male. Average age was 16.32 days. 14% were prenatally diagnosed. 32% of babies were diagnosed at the initial neonatal exam. Neuroblastoma was the most frequent tumor (27.5%) followed by rhabdiosoromas (13.8%), immature teratomas (12.5%), CNS tumors (10.1%), retinoblastoma (10%), Langerhans cell histiocytosis (10%). Less frequent tumors were Wilms’ Tumor and hepatic tumors. The introduction of prenatal and postnatal tools the early diagnosis and outcome improve significantly. Patients were treated individually, according to stage with institutional protocols. Therapeutically results were unfavorable.

Conclusion: Diagnosis of congenital tumors is performed earlier in recent years in Mexico. Although diagnosis is earlier, prognosis is still bad. The histological pattern does not determine the outcome. We would like to transfer this message to our colleagues in prenatal diagnosis, so parents get reliable information. It is necessary to establish neonatal clinics in order to have better results in this group of patients in which tumor biology is not that aggressive.

PL022

CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS AND TREATMENT OUTCOME IN CHILDREN WITH COLORECTAL CANCER. THE REPORT FROM THE POLISH PEDIATRIC RARE TUMOURS STUDY

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Purpose: Colorectal cancers (CC) in childhood are extremely rare affecting less than 1–2 per million individuals <20y per year. The diagnostic and therapeutic strategies in pediatric CC have not been established and the protocols for adult CC are usually used. Aim of the study was to analyze the clinical and histopathological characteristics, applied treatment protocols and outcome in Polish children with CC.

Method: Material and methods: 18 children with CC (10 boys, 8 girls) aged 11–18y, mean age 16y, registered in the Polish Paediatric Rare Tumours Study between 1994 and 2009.

Results: CC was associated with predisposing factors in 8pts (ulcerous colitis-2, FAP-2, NF1 –1 and familial CC-3). In 2pts small bowel carcinoma developed metachronically. Most tumors located in the left part of the colon. Clinical symptoms included abdominal pain (18pts), constipation/diarrhea (11), acute intestinal obstruction (8), weight loss (7) and deep anemia (5) and lasted 1–24 months. Most patients were diagnosed in advanced stages according to the modified Dukes and TNM scales. In over 65% of patients mucinous histology was stated. Primary resections were performed in 15pts (complete in 8), in 3 only diagnostic biopsies were done. 16pts received adjuvant chemotherapy including mainly 5-fluorouracil and leucovorin. Irunotecan, capetebitine, oxalipatin, imatinib, etoposide and cisplatin were given in single cases. Radiotherapy was administered in 3pts with rectal cancer. 12 patients (67%) died of recurrences and disease progression, 5 patients are free of disease with the follow-up of 10 – 135 months, 1 is during treatment.

Conclusion: Conclusion: 1. In most childhood CC complete resection is not feasible because of advanced clinical and histological stages of disease. 2. Poor response to chemotherapy may be associated with the high rate of mucinous histology. 3. Modification of
adjuvant chemotherapy with the wider use of new generation cytostatics is urgently needed.

**PL023**

**MALIGNANT GESTATIONAL TROPHOBLASTIC NEOPLASIA IN FEMALE ADOLESCENTS**

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**Purpose:** Background: Gestational trophoblastic neoplasia (GTN) encompasses a spectrum of neoplastic disorders that arise from placental trophoblastic tissue after abnormal fertilization. These tumors account for less than 1% of malignancies in women.

Purpose: Our goal was to evaluate malignant GTN clinical presentation and prognostic risk factors, as well as to assess the responsiveness of this tumor to treatment and the accuracy of the serum tumor marker human chorionic gonadotropin (hCG) in reflecting the status of disease in four adolescent patients (pts) admitted in the Institute of Oncology Bucharest from January 2001 to December 2006.

**Method:** All patients (pts) were between 14–16 years old. One of them has AIDS discovered at the same time with malignant GTN. Three patients reported vaginal bleeding at presentation and/or abdominal pain. The fourth patient (with AIDS) had uterine wall perforation with massive haemoperitoneum and hemorrhagic shock at diagnosis. Pretreatment hCG level was elevated: >100,000 mU/ml in 2 pts (vital risk). Stage(S/t) according to FIGO staging system for GTN: S.t1 (2 pts), S.tII (2 pts: lung metastases). Histological types: invasive mole (2), choriocarcinoma (1), malignant hydatidiform mole (1). The therapeutic approach consists in surgery (suction curettage + sharp curettage in all pts. and conservative surgery for uterine perforation) followed by 6 cycles of chemotherapy (methotrexate, etoposide, ciclofosamide, actinomycin).

**Results:** Normal hCG was registered after 2–3 cycles of chemotherapy and it is maintained within normal limits until now. Complete remission (CR) in all cases. Disease free survival till now, including the patient with AIDS.

**Conclusion:** 1. The findings confirm data from literature available for adult women: knowledge of the natural history for cure with appropriate therapy. 2. GTN are effectively treated with surgery and chemotherapy even when widely metastatic. 3. hCG is a sensitive tumor marker in the diagnosis, monitoring therapy and follow up.

**PL024**

**THERAPEUTIC MANAGEMENT OF MALIGNANT PANCREATIC TUMORS IN CHILDREN.**

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**Purpose:** Introduction: Malignant pancreatic tumors in children are rare. The major problem for the clinician is a lack of experience and of accepted therapeutic strategies. Malignant pancreatic tumors in children show a different pattern from that in adults. In infants, especially pancreaticoblastomas, solid cystic tumors of females, and endocrine carcinomas of the pancreas must be expected.

Purpose: We report our experience in three patients with malignant pancreatic tumors treated in Institute of Oncology Bucharest, pediatric oncology department, between 1995–2008.

**Method:** All the cases are girls, 9, 11 and 12 years old. Onset of disease consists in abdominal pain +/- painless palpable abdominal tumour. Histopathological types of tumours are chistadenocarcinoma, pseudosquamous carcinoma and pancreatoblastoma. Stage of the tumour (TNM): stage III (T2 N1 M0) -1 patient; stage I-2 patients. First treatment applied was surgery (with diagnostic and therapeutic intent): partial excision of the tumor in one case and complete removal of the tumour in 2 cases. Multimodal treatment consists in: surgery (partial excision) + adjuvant polichemotherapy + radiotherapy in one case; surgery (complete excision of tumour) + adjuvant polichemotherapy in the other 2 cases. Chemotherapy used combination of 5-Fluorouracil, Cisplatin, Farmonbinicin, 6 cycles

**Results:** Free disease survival after complete remission till now (8 and 2 years) in two cases. Death in one patient (with neurofibromatosis type I) was caused by the second cancer (ovarian carcinoma) diagnosed 5 years after pancreas carcinoma.

**Conclusion:** Conclusions: 1. In malignant pancreatic tumors long-term survival can be achieved with multimodal treatment: surgery + chemotherapy + radiotherapy. 2. It seems that the prognosis is better than in adults.

**PL025**

**ULTRASOUND DIAGNOSTIC OF SCROTAL TUMOR LESIONS IN CHILDREN.**

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**Purpose:** to find ultrasound (US) criteria to differentiate malignant and benign, germ-cell (GCT) and non-germ-cell tumors, as well as their histological varieties.

**Method:** 100 patients with scrotal masses were examined in the Institute of Pediatric Oncology (age range 1 month – 15 years): 73 – with tumors (malignant – 56, benign – 17), 27 – with non-tumor lesions. All diagnoses morphologically verified. 91,1% - were primary tumors: rhabdiosioscarcoma (37,5%), yolk sac tumor (26,8%), immature teratoma (8,9%), mixed germ-cell tumors (8,9%), others (9%). Metastatic testicular lesions were rare - 8,9%.

**Results:** In our study GCT (n = 37) were characterized by one side lesion (100%), cystic component (60%); the malignant germ-cell tumors – by total testicular lesion (77%), solid masses (72%), diameter of the lesion > 2,5cm; the benign – by single node (100%) less than 2,5cm (77,8%), combined cystic and solid component (66,7%), more frequent right side localization (77,8%). Calcification or highly hypechoic inclusions reflecting the bone or cartilage tissues or fibrosis are specific for benign (55,6%) and never seen in malignant GCT. Common features of rhabdiosioscarcoma: single nodule (85,7%), paratesticular localization (64,3%), medium echogenicity (78,6%), irregular-form hypechoic inclusions (sometimes ring-shaped or bizarre) never seen in any other tumors (78,6%), the absence of calcinates (100%) and cysts (92,9%). Dopplerography showed high or extremely high blood flow within multiple coiled vessels in malignant tumors, and medium to high within few vessels in benign.

**Conclusion:** The sensitivity of US in revealing scrotal tumors > 100%, specificity – 81,5%, accuracy – 91,1%; in diagnosing malignant tumors > 100%, 90,9% and 96,6% accordingly.

**PL026**

**AN INTENSIVE MULTIMODALITY APPROACH FOR PATIENTS WITH EXTRA-RENAL, EXTRACRANIAL MALIGNANT RHABDOID TUMORS.**

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**Purpose:** Malignant rhabdoid tumors (MRT) have been reported in the central nervous system (CNS, atypical teratoid rhabdoid tumor, ATRT), kidneys and in a variety of extra-renal, non-CNS locations of the body. Despite a better understanding of the genetics of these tumors, i.e. loss of the hSNF5/INI1 tumor suppressor gene, the prognosis is poor for patients with MRTs.

**Method:** A retrospective review of patients with extrarenal, non-CNS MRTs at four institutions (Dana-Farber Cancer Institute, Boston, MA; Children’s Hospital of Philadelphia, PA; Children’s Hospital, Denver, CO; Children’s Memorial, Chicago, IL) who were treated according to DFCI #02-294 (Chi, et al. JCO 2009: 27:385–9) was performed. Institutional review board approval was obtained for data collection.

**Results:** Seven patients, 6 females and 1 male, were treated according to DFCI #02-294. Age at presentation ranged between 6 months and 6.8 years (med, 4 years). Primary tumor locations included: neck (2), extremity (2), clivus/skull base (1), extradural spine (1) and liver (1). One patient had metastatic disease at diagnosis (liver). Initial surgical approach included: biopsy (5), GTR (1) and PR (1). Four patients with initial biopsies were able to achieve GTR at second surgery. Two patients received intrathecal therapy; 5 patients received radiation therapy (4 local; one CSI at the time of relapse). Best responses were CR (4), PR (1) and mixed response (2). Two patients have relapsed (clivus/skull base at 7 mos; liver at 3 mos). Six patients remain alive, 5 NED and 1 relapse (range, 12–71 mos from diagnosis); 1 patient with metastatic liver MRT succumbed to their disease.

**Conclusion:** Although renal MRTs and CNS ATRTs constitute a majority of rhabdoid tumors, MRTs have also been documented in organs and soft tissues throughout the body and the prognosis is generally poor. For patients who receive intensive modality chemotherapy and radiation therapy, the outcomes may be more hopeful.
CHILDHOOD NASOPHARYNGEAL CARCINOMA: A 5-YEAR SINGLE INSTITUTION EXPERIENCE

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Purpose: Pediatric nasopharyngeal carcinoma (PNC) represents a locally advanced undifferentiated tumor. The results of a single institute over a 5 yr period were analysed.

Method: 24 patients (23 males and 1 female) 7-14 years old from Jan 2004 to Sep 2009 with PNC were evaluated. 22 patients received induction chemotherapy followed by radiotherapy while 1 patient was offered concurrent chemotherapy, 1 patient received radiotherapy alone. 21/22 patients received postirradiation chemotherapy. The agents used in induction and adjuvant therapy were cisplatin (100 mg/m^2) on day 1 and 5-fluorouracil 750 mg/m^2 for 5 days. Radiotherapy was used in 60 gray in 30 fractions.

Results: The time of onset of symptoms to diagnosis was a median of 5.5 months. Histopathology was lymphoepithelioma in 5 patients (20.8%) while 19 patients (79.1%) had poorly differentiated carcinoma. Stage was T2 (n=7); N1 (n=7), N2 (n=9), and N3 (n=7). 4 patients had intracranial invasion. None had metastatic disease. 18 patients (75%) achieved major response including 9 (37.5%) complete remissions and 7 (29.1%) partial remissions after induction chemotherapy and radiotherapy. 4 (16.6%) had progressive disease. Another 4 (16.6%) attained complete remission after post radiation chemotherapy consisting of two cycles of cisplatin and 5-fluorouracil. Follow up ranged from 5 months to 84 months with a median of 35 months. The disease free survival ranged from 10 months to 53 months with median of 33 months. The patients having better response to induction chemotherapy had better disease free survival. Among 9 patients attaining complete remission 2 relapsed with median time to first relapse of 9.5 months. Toxicity was modest. 1 patient had grade 4 neutropenia and mucositis. There was no therapy related mortality.

Conclusion: Chemoradiotherapy for nasopharyngeal carcinoma in children is an effective treatment modality with minimal toxicity.

TUMOR-REACTIVE ANTIBODY PREDICTS RECURRENTITY IN EPENDYMOMA

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Purpose: Approximately 50% of children with ependymomas will have tumor recurrences resulting in mortality. Therefore, deciphering prognostic and biological factors that predict tumor recurrence is crucial to rationally guiding therapeutic interventions. Previously, criteria such as age at diagnosis, gender, and tumor grade have not been correlative with the probability of recurrence. We have recently documented an up-regulation of immune function genes present in patients who are recurrence free. However, whether a type I (cellular) or type II (humoral) tumor-reactive immune response actually occurred was not addressed.

Method: Autologous serum was used as a primary antibody to probe tumor antigens via Western blot in eleven consecutive patients from our institutions. Both tumor and serum samples were taken at time of diagnosis.

Results: There were 7 recurrences in our population of 11 patients. 71% of the recurrent patients (5/7) exhibited a detectable tumor-reactive antibody response whereas none of the non-recurrent patients (0/4) did (p = 0.06). Mean time to progression in recurrent patients was 20 months.

Conclusion: Herein we correlate tumor recurrence to spontaneously occurring tumor-reactive antibody responses in eleven patients with untreated ependymoma. Although preliminary, this data has the potential to be reproduced in a larger series of patients. With this increase in power, we have the ability to readily identify spontaneously occurring tumor-reactive antibody responses as a negative prognostic factor using patient sera. As such, our results hold great promise for a novel, non-invasive, high throughput assay to predict recurrence and to rationally guide treatment.

CONVENTIONAL AND MOLECULAR CYTOGENETIC ANALYSES OF NEUROEPITHELIAL CENTRAL NERVOUS SYSTEM TUMORS: THE FIRST REPORT FROM A SINGLE INSTITUTION IN ARGENTINA

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Purpose: In the present study, neuroepithelial central nervous system (CNS) tumors were investigated by conventional and molecular cytogenetic techniques, either alone or in combination, to characterize patterns of chromosomal abnormalities (CA) and to correlate the findings with histological WHO grade.

Method: Surgical specimens from 74 institutionally diagnosed neuroepithelial CNS tumors (27 embryonal, 12 astrocytic, 14 ependymal, 13 mixed glioneuronal and 8 miscellaneous) were referred to our laboratory for cytogenetic studies from September 2005 to February 2010. Of them, 11 were recurrent tumors (2 embryonal, 6 ependymal, 2 mixed glioneuronal and 1 miscellaneous). Tumor samples were processed for short-term culture. DNA was extracted from frozen material. Cytogenetic studies were performed using GTG-banding, fluorescence in situ hybridization and comparative genomic hybridization.

Results: Thirty six primary neuroepithelial CNS tumors (57%) had CA; 20 embryonal, 5 astrocytic, 2 ependymal, 6 mixed glioneuronal and 3 miscellaneous. Nine recurrent tumors (82%) showed CA. The most frequent CA included unbalanced translocations and complex rearrangements. Among medulloblastomas chromosomes 1, 11 and 17 were the most frequently involved in gains, losses or in structural rearrangements.

Most of the WHO grade I astrocytomas and primary WHO grade III ependymomas had normal karyotype. In contrast, all WHO grade III and IV ependymomas had complex karyotypes. The highest proportion of CA was found in WHO grade IV and recurrent tumors.

We point out the findings of “novel translocation” such as t(1;13)(q21;q21) and t(5;7)(q25;q11.2) in medulloblastoma and t(6;12)(q12;p24.3) in glioblastoma as a sole structural CA.

Conclusion: Our results demonstrate a significant association between karyotypic complexity and aggressive tumor biology. The finding of novel CA may help to identify specific genes involved in the initiation and progression of these tumors. The presence of tumor-associated cytogenetic abnormalities has clinical utility in the differential diagnostic and prognosis of these neoplasms.

FUNCTIONAL SCREENING OF THE TYROSINE KINOME IN GliOBLASTOMA AND ASTROCYTOMA CELL LINES

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Purpose: Malignancies of the central nervous system (CNS) are the most common form of pediatric solid tumor. Children with brain tumors suffer toxic side effects from surgery, chemotherapy, and radiation with significant mortality due to progression and relapse. Therefore, genetic lesions that lead to specific targeted therapies will result in an improved understanding of the disease and in improved efficacy of therapy.

Method: We have utilized a functional siRNA screen that encompasses the entire tyrosine kinase to discover genes that are crucial for cancer viability. Six cell lines from patients with glioblastoma and astrocytoma cell lines were transfected with the siRNA library. After 4 days of incubation the viability was measured using an MTS assay. Genes crucial for survival were defined by a decrease in the viability beyond 2 standard deviations of the mean for all siRNA targets.

Results: Potential target lesions were observed in 4 of 6 cell lines, however most promising was the gene ROS1. Silencing of ROS1 in the glioblastoma cell line, SF
539, reduced cell viability an average of 39% compared with non-specific siRNA. ROS1 is a type 1 receptor tyrosine kinase normally thought to have a role in normal development of epithelial cells. Other glioblastoma cell lines have been previously described to exhibit ROS1 aberrancies targeting the translocation (FEG-ROS). Further characterization of ROS1 in SF 539 cells is now underway to identify the mechanistic etiology underlying ROS1-dependence in these cells.

Conclusion: Our siRNA screen is a rapid functional assay that can be used to identify targets for therapy in CNS tumor cell lines. We have identified several possible kinases, including ROS1. Further studies will be performed to understand the role of ROS1 in glioblastoma. These results may lead to screening primary patient samples for these aberrant kinases, ultimately leading to targeted therapies for kinases or as a potential prognostic marker.

PM004

COMPLEX INTERACTIONS BETWEEN IMMUNE CELLS AND TUMOR CELLS UPON VACCINATION AGAINST HIGH GRADE GLIOMA

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Purpose: Patients suffering from a High grade glioma (HGG) have a poor prognosis. Immunotherapy is a novel treatment approach that showed benefits for patients including long-term surviving patients. We aim to unravel the immune mechanisms induced upon vaccination in the GL261 orthotopic mouse model.

Method: Mice received prophylactic vaccination prior to GL261 glioma cell injection into the brain. In some mice, cytotoxic T cells (CTL) or regulatory T cells (Treg) were depleted with monoclonal antibodies. Mice were followed for clinical signs, weight and survival. In some experiments, brains were taken out at day 14 after tumor challenge to study the presence and function of brain-infiltrating immune cells.

Results: Upon vaccination and upon Treg depletion, the presence of functional GL261-specific CTL could be detected in the brains. Vaccination induced long-term survival in about half of the mice. Depletion of CTL abrogated long-term survival but kept the survival curve better than the control suggesting functional role of other cells. Depletion of Treg resulted in 100% long-term surviving mice. However upon re-challenge at day 60, only surviving mice after vaccination remained alive suggesting the existence of memory T cells. Survivors after Treg depletion in the absence of vaccination all died similar to the control mice. In these mice, we found an enrichment of myeloid cells which were not suppressive to T cell functioning, in contrast to classical myeloid-derived suppressor cells present in glioma.

Conclusion: We conclude that the net result of immunotherapy is based on the interaction of tumor cells with CTL, Treg, myeloid cells with different functional phenotypes and memory T cells. The insights of these interactions might be helpful to design new vaccination approaches targeting the Treg population in the context of induced inflammation to keep also the anti-tumoral functions of the myeloid population.

PM005

SORTING NEXIN 3 DISRUPTS EGFR AND MET ENDOSONAL TRAFFICKING PROMOTING CELL PROLIFERATION AND TUMORIGENICITY IN HIGH GRADE GLIOMAS

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Purpose: Amplification/mutation of receptors-tyrosine-kinases (RTK) plays a major role in gliomagenesis. Using microarray data we generated, we identified overexpression of Sorting Nexin 3 (SNX3), a protein involved in the endosomal trafficking of RTK including EGFR. Our hypothesis is that dysregulated expression of SNX3 may delay RTK degradation and promote sustained intracellular activation through these receptors, mimicking RTK amplification seen in adult-GBM events in a subset of pediatric-GBM (pGBM).

Method: We stably overexpressed cMyc-tagged-SNX3 in pGBM (SF188 and SJG2) and pGBM (U87) cell lines. Parallel SNX3 knock-down experiments were performed in cell lines. Effects of overexpression/silencing of SNX3 were investigated on EGFR and MET activation, cell signaling and cell proliferation in vitro and in vivo (serograft model NOD/SCID mice). We also investigated effects of selective MET and EGFR inhibitors on cell growth.

Results: SNX3 overexpression delayed EGFR and MET degradation following RTK engagement. This increased and sustained activation of Ras and JNK pathways and cell proliferation in vitro. Importantly, it promoted tumour formation in NOD-SCID mice. The role of both RTK inhibitors was needed to inhibit growth of SNX3 transfectants. Experiments done on SNX3-knocked down cell lines led to increased RTK degradation, decreased intracellular signalling and cell growth.

Conclusion: Our results indicate that SNX3-overexpression disrupts physiological trafficking of multiple membrane receptors including EGFR and MET. They potentially shed light as to how in pGBM EGFR is overexpressed in the absence of the genetic abnormalities seen in adult-HGA, and further indicate that simultaneous targeting of multiple RTK is needed to affect cell growth.

PM006

STEREOTACTIC INTRACAVITARY THERAPY WITH BLEOMYCIN IN PEDIATRIC RECURRENCE CYSTIC CRANIOPHARYNGIOMAS

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Purpose: Craniopharyngiomas present some of the foremost challenges in Neurosurgery. Treatment remains controversial, including intracystic chemotherapy with Bleomycin.

There are reports of Intracystic injections with Bleomycin with complete control of the cyst without complications. However they don’t exist in the paediatric population. The objective of this study was investigate the antitumoral effect of Bleomycin on Pediatric recurrence cystic Craniopharyngiomas and the clinical effects of this drug.

Method: Between February 2003 and February 2008, 16 patients harbouring recurrence cystic Craniopharyngiomas were selected. Between 2 and 15 years of age (10 female and 6 male).

All met the following criteria:
1) Diagnosed as Craniopharyngioma according to pathology or cytological data.
2) Lesions Mainly Cystic.
3) Patients and their families agreed to receive this experimental treatment.

The treatment protocol consists in silicone tube inserted stereotactically into the cystic and connected with a Reservoir. The dose of Bleomycin started 1 week after the insertion with 9 mg (3 ml).This solution was injected through the reservoir 2 times per week for 4 week of therapy, until a total dose range between 36 to 72 mg.

Results: The cystic almost or completely disappeared in 12 patients. One patient failed to complete the whole course because the tube became dislodged out the cyst. Just after the therapy all patients had improved vision. Ten patients had no severe complication or sequelae and were able to return to school. All the patients decrease 80 percent of the volume of the cyst during the first 6 months after finish the treatment. The most frequent complications were fever and Headache.

Conclusion: The Bleomycin is effective inhibiting the growth of the Cystic craniopharyngiomas when it is used as Intracavitary chemotherapy. The mechanism of bleomycin on craniopharyngiomas and its toxic effect on the brain need to be further studied.

PM007

NIMOTUZUMAB AND RADIOTHERAPY IN CHILDREN AND ADOLESCENTS WITH BRAIN STEM TUMORS. PRELIMINARY RESULTS OF PHASE II

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**PM008**

**IS BETA-CATENINA A GOOD PROGNOSTIC MARKER FOR MEDULLOBLASTOMA/PRIMITIVE NEUROECTODERMAL TUMOR?**

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**Purpose:** Identifying pathological correlates of clinical behavior or therapeutic response currently represents a key challenge for medulloblastoma research. It was related that the nuclear immunoactivity when tested positive for B-catenin protein in some cases indicate a good prognostic marker in medulloblastoma and primitive neuroectodermal tumor (PNET).

**Method:** From 31 patients with medulloblastoma and 10 pt with PNET, 41 samples of brain tissue fragment in paraffin blocks using immunohistochemistry were analysed. Six pt were under three years old were not metastatic at diagnosis. Three pt were metastatic at diagnosis.

**Results:** Age had no correlation with B-catenin positivity (p = 1.0) by univariate analysis. B-catenin were positive in 27 samples (66%), 26/27 (96%) from non metastatic pt and 1/27 (4%) from metastatic pt. B-catenin were negative in 14 samples (34%), 12/14 (86%) from non metastatic pt and 2/14 (14%) from metastatic pt. Metastasis at diagnosis and B-catenin had no significant association by Fisher test (p = 0.265). 17/27 (63%) B-catenin positive pt were alive. 9/14 (64%) B-catenin negative pt are alive. No correlation was found between B-catenin and death (p = 0.934). Median time disease free survival (DFS) from B-catenin positive pt were 29 months (95% CI 19.0, 34.0). Median time DFS from B-catenin negative pt were 48 months (95% CI 11.0 65.0). These results were not statistic significant by log rank test (p = 0.39).

**Conclusion:** These results showed that B-catenin is not related to prognosis in medulloblastoma and PNET. Further studies with a larger number of patients (metastatic/non metastatic, under 3 years/older) are warranted to confirm these data.

**PM009**

**EXPRESSION AND FUNCTIONAL ROLE OF ECOTROPIC VIRAL INTEGRATION SITE 1 (EVI-1) IN INTRACRANIAL EPENDYMOMAS**

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**Purpose:** To evaluate the progression free survival rate as well as the overall survival of children and adolescents bearing brain stem tumors that were treated with the anti-EGFR mAb nimotuzumab and radiotherapy.

**Method:** Newly diagnosed patients with clinical and radiological evidence of brain stem tumors, age between 3–18 years, life expectancy of 4 weeks, Lansky/Karnofsky + 60, adequate renal, liver and hematological function were eligible. Nimotuzumab was administered at a dose of 150 mg/m² weekly for 12 weeks concomitantly with external beam radiotherapy using linac, dose 56 gy conformational planning.

**Results:** Twelve patients aged 4 to 18 years have been enrolled in this study, between December 2007 and February 2010. Two patients interrupted treatment due to related disease. After finishing induction therapy, 8 patients achieved stable disease, 1 patient progressed. After 24 weeks the 8 evaluable patients showed disease stabilization. Most frequent adverse events consisted on grade I/II toxicities mucositis.

**Conclusion:** Nimotuzumab is safe. Preliminary results suggest efficacy of the humanized mAb in combination with radiotherapy. Trial continuation is warranted.

**PM010**

**NEUROPSYCHOLOGICAL OUTCOME FOLLOWING CEREBELLAR TUMOUR INJURY SUSTAINED IN EARLY CHILDHOOD**

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**Purpose:** The role of the cerebellum in cognitive and motor functioning is increasingly recognised, with damage to the cerebellum following tumour in childhood shown to affect both domains. We conducted a detailed investigation investigating using an RNAi approach in primary ependymoma cultures.

**Conclusion:** Using gene expression profiling, several genes differentially expressed in tumor cells of intracranial ependymomas could be identified. Among those, EVII is highly expressed and might play a role in the biology of ependymomas. Supported by DFG (HA 3060/3–1).

**PM011**

**MULTI-TYROSINE KINASE INHIBITORS IN PRE-CLINICAL STUDIES FOR CNS ATRT: EVIDENCE FOR TARGET MODULATION AND SYNERGY WITH IRINOTECAN.**
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Purpose: Atypical teratoid rhabdoid tumor of the central nervous system (CNS AT/RT) is a highly malignant neoplasm of young children. Recent studies have shown that growth factors such as insulin play a critical role in AT/RT and that abnormally regulated cytokine pathways and corresponding downstream signaling molecules can be effective targets for therapies. Based on this rationale we are aiming to identify growth factor mediated pathways and the potential of multi-tyrosine-kinase inhibitors (MTKk) to provide effective growth inhibition in future clinical trials.

Method: Expression of a panel of 43 growth factors in AT/RT cell lines (BT12, BT16 and KCCF1) was quantified by qPCR. RT-qPCR was performed using Sybr Green as the detection agent.

Conclusion: We show that MTKk cause significant in vitro cytotoxicity against AT/RT cells by interfering with Akt and Raf mediated pathways and by the loss of Mcl-1 protein. The activity of these agents was enhanced by synergy with topi-I inhibition. Sorafenib also reverses the activation of NFkB that occurs in response to irinotecan providing a mechanism for significantly enhanced utility of this drug combination. We believe that MTKk and irinotecan drug combination holds significant potential in the treatment of AT/RT.

PM012

COULD EMP3, CA12, CKS2 AND PDPN BE POTENTIAL TARGETS GENES IN ASTROCYTIC TUMORS?

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PM013

CLINICO-PATHOLOGICAL STUDY OF 11 ATYPICAL TERATOIDS/ Rhabdoid Tumours

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Purpose: Atypical Teratoid/Rhabdoid Tumor (AT/RT) of central nervous system is an aggressive embryonal tumour, which affect children almost exclusively. Its characteristic feature are rhabdoid cells, but an embryonal component is most commonly encountered. This tumour is often misdiagnosed as medulloblastoma, ependymoma or supratentorial PNET due to its overlapping histological features with other embryonal tumours. The immunophenotype of AT/RT is variable and the most frequently observed is expression of vimentin and EMA; but are also commonly observed cytokeratins, smooth muscle actin, GFAP, NFP and synaptophysin. The AT/RT is associated with inactivation of the INI1/SMARCE1 gene in virtually all cases.

Method: We studied 11 patients diagnosed of AT/RT; seven had been previously diagnosed as medulloblastoma, ependymoma or supratentorial PNET.

Result: Histopathological and clinical data were reviewed in all cases. The patients were 4 boys and 7 girls. The average age at diagnosis was 2.9 years with a range from 6 months to 6.5 years. Nine patients died from their disease within 20 days to 20 months; 2 were alive after a follow-up period of 3 and 4 years respectively. Histologically AT/RTs showed a marked cellular discohesivity, but rhabdoid cells were encountered in only 3 cases. Abnormalities in the expression of INI1 were seen in all cases. AT/RT shows divergent differentiation, only the loss of INI1-1 expression is useful in the diagnosis.

PM014

SOMATOSTATIN-RECEPTOR (SSTR-2) EXPRESSION AFTER RECURRENT IN CHILDHOOD MEDULLOBLASTOMAS

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Purpose: Medulloblastoma, the most common malignant pediatric CNS tumor often recurs despite intensive treatment. Primary medulloblastoma expresses somatostatin receptor-2 (SSTR-2), a target of SSTR-2 agonists, but so far we had no experience about the receptor status after recurrence. Our aim was to examine the state of SSTR-2 expression in recurrent childhood medulloblastomas.

Method: SSTR-2 expression was examined by immunohistochemistry (SS-800 Garamsch Laboratories, Germany) in primary and recurrent medulloblastoma samples of 10 children. We examined the intensity and the percentage of SSTR-2 positive tumor cells in primary and recurrent tumor samples of the same patients. As a positive control, in vivo SSTR-2 status was examined in two of these patients by Octrescan.

Results: All primary tumors were receptor positive and the SSTR-2 was also expressed in all recurrent medulloblastomas. In our samples the percentage of SSTR-2 expression level when compared with pilocytic astrocytomas. To the genes EMP3 (p < 0.001) and PDPN (p < 0.001) the expression levels were higher in pilocytic astrocytomas than in glialblastos.
positive tumor cells was 30% to 90%. In the examined two patients the results of immunohistochemistry and OctreoScan imaging seemed to correlate.

Conclusion: By demonstration of the presence of SSTR-2 in recurrent medulloblastomas allows theoretically the early detection of medulloblastoma recurrence by OctreoScan imaging, and application of somatostatin analogues in the treatment of recurrent childhood medulloblastomas.

**PM015**

**PHARMACOLOGIC ACTIVATION OF THE P53 PATHWAY BY NUTLIN-3 INHIBITS MEDULLOBLASTOMA CELL PROLIFERATION IN VITRO**

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**Purpose:** Medulloblastoma accounts for 2% of all brain tumors in children. With an overall survival of 40–70%, medulloblastoma is a major clinical challenge in pediatric oncology. Approximately 90% of medulloblastomas will have wild-type (wt) p53, but most of these express high levels of MDM2. MDM2 negatively modulates the transcriptional activity and stability of p53, and elevated MDM2 expression has been associated with adverse outcome of medulloblastoma patients. Inhibition of the p53-MDM2 interaction by the small molecule antagonist, nutlin-3, restores p53 function. Nutlin-3 has been shown to inhibit proliferation of other embryonal tumor cells in vitro, including neuroblastoma and retinoblastoma. We investigated the effect of nutlin-3 on medulloblastoma cell proliferation in cell lines harboring wt or mutated p53.

**Method:** MDM2 expression was analyzed in primary medulloblastomas and normal cerebellum at the mRNA level on microarrays and immunohistochemically on a TMA. The mutational status of p53 was assessed in the 6 medulloblastoma cell lines used by sequencing, and MDM2 expression was analyzed using real-time PCR and immunohistochemistry. Viability, alterations in cell cycle and apoptosis were assessed in medulloblastoma cell lines treated with nutlin-3 using MTT assay, BrdU incorporation, FACS analysis and a cell death ELISA. The effect of nutlin-3 on medulloblastoma cell proliferation in cell lines harboring wt or mutated p53.

**Conclusion:** Nutlin-3 has been shown to inhibit proliferation of other embryonal tumor cells in vitro, including neuroblastoma and retinoblastoma. We investigated the effect of nutlin-3 on medulloblastoma cell proliferation in cell lines harboring wt or mutated p53.

**PM016**

**INFANT EPENDYMOMA IN A 10-YEAR AIEOP (ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA) EXPERIENCE WITH OMITTED OR REFERRED RADIOTHERAPY**

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**Purpose:** Nineties protocols omitted/delayed irradiation, using upfront chemotherapy (CT) to spare the youngest the sequelae of radiotherapy (RT). We treated 41 under 3-year-olds with intracranial ependymoma accordingly between 1994 and 2003.

**Method:** After surgery, CT was: regimen I with 4 blocks of vincristine, highdose methotrexate 5 gr/m2 and cyclophosphamide 1.5 gr/m2 alternated with cisplatin 90 mg/m2 plus VP16 450 mg/m2 for 14 months; subsequently regimen II was used, i.e. VEC (VCR, VP16 300 mg/m2 and cyclophosphamide 3 gr/m2) for 6 months. RT was planned for residual tumor after completing CT or for progression.

**Results:** We treated 23 males and 18 females who were a median 22 months old; 14 were given regimen I, 27 regimen II; 22 had complete resections, 19 had residues. Ependymoma was grade 2 in 25 cases and grade 3 in 16; tumors were infratentorial in 37 and supratentorial in 4: One child had infratentorial metastases; 29 had progressed locally after a median 9 months. EFS was 26% at 3/5 years, 23% at 8 years. One child died of sepsis, another developed a glioblastoma 72 months after RT. PFS was 27% at 3/5/8 years; OS was 48%, 37% and 28% at 3, 5 and 8 years, respectively. Of the 13 survivors, 6 never had RT; their intellectual outcome did not differ significantly in those with vs. without RT.

**Conclusion:** Our results confirm poor EFS/OS rates for up-front CT in infant ependymoma: no better neurocognitive outcome was demonstrated in the few survivors who never had RT.

**PM017**

**PRIMITIVE NEUROECTODERMAL TUMORS OF THE CENTRAL NERVOUS SYSTEM ASSOCIATED WITH GENETIC AND METABOLIC DEFECTS**

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**Purpose:** To evaluate the genetic, congenital and metabolic disorders which were detected concurrently with primitive neuroectodermal tumors (PNET) of the central nervous system in children.

**Method:** Medical records of 1030 children who were admitted to our department with nervous system in children.

One of the following conditions were detected in 10 patients with medulloblastoma and supratentorial PNETs were detected in 289 patients. They were reviewed for associated metabolic conditions, genetic and congenital defects.

**Results:** One of the following conditions were detected in 10 patients with medulloblastoma and supratentorial PNETs: Neurofibromatosis type 1, Gorlin syndrome, juvenile polyposis coli, cancer prone syndrome of total premature chromatid separation and Fanconia anemia, bilateral retinoblastoma, L-2-hydroxylutaric aciduria, Gilbert syndrome, gray platelet syndrome, clef lip-palate and left renal agenesis. In the patients with multiple malignant diseases, cancer prone syndrome of total premature chromatid separation and Fanconia anemia, Gorlin syndrome and juvenile polyposis coli were diagnosed after diagnosis of the malignant tumors. Medulloblastoma was the first manifestation in the case with Gorlin syndrome. In case with retinoblastoma, pineal PNET was detected 2 months after diagnosis of retinoblastoma. Clef lip-palate and L-2-Hydroxylutaric aciduria were detected previously in the patients before Gray platelet. Gilbert syndrome and left renal agenesis were diagnosed during treatment of medulloblastoma.

**Conclusion:** Associated genetic, metabolic and congenital conditions were detected in 3.5% of the cases. Thus the patients with PNET should be followed for these defects.

**PM018**

**HEALTH CARE PROVIDERS’ VIEWS OF INFORMED CONSENT AND JOINT DECISION MAKING IN PEDIATRIC PATIENTS WITH BRAIN TUMOURS**

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**Purpose:** To evaluate the genetic, congenital and metabolic disorders which were detected concurrently with primitive neuroectodermal tumors (PNET) of the central nervous system in children.
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Purpose: After a child has been diagnosed with a brain tumour, informed consent discussions with families can be very challenging. Treatment may be associated with significant morbidity, especially in young children. Cure rates have improved with multimodality treatment and treatment intensity. This has come at the cost of very significant chronic health problems. Therefore, pediatric oncologists must weigh the benefits and risks of the treatment they recommend carefully. The views of pediatric oncologists on the role of parents in therapy decision making is largely unknown.

Method: A survey was developed in order to explore health care practitioners (HCPs) views on the discussion of potential late effects of therapy, informed consent, and joint decision making with parents. The primary purpose of this poster presentation is to request opinions from SIOP attendees and their participation in a survey.

Results: To date, we have collected 56 surveys from Pediatric Radiation Oncologists (84.2%), Radiation Oncology Fellows (8.9%), and Pediatric Medical Oncologists (5.4%). Current respondents are from USA (39.3%), Canada (30.4%), Europe (25.0%), Australia (3.6%), and Asia (1.8%) who attended the Society of Pediatric Radiation Oncology Meeting in 2009. The majority of individuals were male (60.7%), over the age of 40 (71.9%), and saw adult oncology patients in addition to pediatric (89.3%). The results of this study will be presented at SIOP 2011 after we have obtained feedback from pediatric oncologists and other HCPs involved in the treatment of children with cancer. This is important in order to limit any potential bias on future survey results.

Conclusion: At SIOP 2010 we hope to collect opinions on informed consent and joint decision making from a more diverse group of HCPs. Subsequently, opinions will be compared by physician specialty and country of residence.

PM019

BRain TUMORS in CHILDREN - Treatment RESULTS according to the Chemotherapy Regimen

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Purpose: The aim of our study was to evaluate results of treatment and analysis of prognostics factors in patients over 3 years of age with highly malignant brain tumors. Method: Between 1990–2005 we treated 183 patients (pts.) with highly malignant brain tumors. Medulloblastoma (MB) was found in 102 pts, supratentorial PNET (sPNET) in 22 pts, ependymoma (Ep) gr.III in 16 pts, and supratentorial high grade glioma. Twenty patients had choroid plexus carcinoma, 1 atypical papilloma. 9 patients had localized disease, 3 had multifocal tumors, 5 dissemination.

Chemotherapy regimens were: 1.Vcr,CCNU, CDDP-84 pts. (MB 41, sPNET 18, Ep 7, As 18), 2.Vcr,CCNU, CDDP-MB 72.6%, sPNET 42.5%, Ep 42.7%, As 40.3%, 3. Regimen 8/1 followed: 1.Vcr, CCNU- MB 46.8%, sPNET 43.2%, Ep 43%/27.8%, As 36.5%. According to chemotherapy regimens applied, 5 years and 10 years OS was as follows: MB- 58.8%, sPNET- 40.5%, Ep- 41.5%, As- 42.1%. According to chemotherapy regimens applied, 5 years and 10 years OS was as following: 1.Vcr, CCNU- MB 46.8%, sPNET 43.2%, Ep 43%/27.8%, As 36.5%, 2.Vcr, CCNU/CDDP-MB 72.6%, sPNET 42.5%, Ep 42.7%, As 40.3%. 3. Regimen 8/1 – MB 61.7%, sPNET 31.8%, As 44.9%, and 4. Baby brain regimen- MB 56.8%. Conclusion: Multidisctiplinary treatment of brain tumors in children matched by relevant prognostic factors has shown best results in pts with medulloblastoma, with statistically significant higher OS. Adjutant chemotherapy regimen Vcr, CCNU, CDDP is therapy of choice in multidisciplinary treatment of high risk medulloblastoma. Complete resection and absence of brain stem invasion are predictors of better prognosis.

PM020

CHOROID PLEXUS TUMORS IN CHILDREN. One INsTrUCTION EXPERIEnCe

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Purpose: The aim of our study was to analyze clinical data and treatment outcome in children with CPT treated in our department.

Method: Disease status at diagnosis, extent of surgical resection, histology, treatment applied and outcome were analyzed.

Results: 17 pts. 8 girls and 9 boys aged 3m to 17yrs (median 21m), treated between 1996 and 2009, were evaluated. 9 pts were under 3 yrs of age at diagnosis. 16pts had choroid plexus carcinoma, 1 atypical papilloma. 9 patients had localized disease, 3 had multifocal tumors, 5 dissemination. Six pts had complete tumor resection, 1 gross total resection, 9 partial resection and 1 biopsy.

In all patients chemotherapy was administered (14 pts- CPT-SIOP-2000 protocol, pts treated before 2000- other protocols). Eleven pts were irradiated (9 pts in first line treatment, 2- in second line).

12 out of 17 pts are alive 8m to 11yrs from diagnosis (median 3yrs from diagnosis (3 pts of disease, 1 of second malignancy). 3 pts progressed- 1 pt died, 2 pts are still treated.

5 yr overall survival is 75%.

Conclusion: In our series extent of surgical resection and radiotherapy had prognostic relevance; in case of residual disease and dissemination response to chemotherapy and complete remissions were observed. Study supported by grant R130011 06/2009 from Ministry of Science, Poland

PM021

MEDULLOBLASTOMA IN PATIENTS WITH HETEROZYGOUS GERm-LINE MUTATIONS IN THE NbN GENE - CLINICAL FEATURES

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Purpose: The NBN gene is a double-strand break repair gene. Biallelic mutations in the NBN gene cause Nijmegen Breakage Syndrome with increased tumor risk and increased toxicity of anti-cancer treatment. NBN heterozygotes may have increased susceptibility for developing medulloblastoma. Aim of our study was to describe clinical features, toxicity profile and treatment outcome of MB patients heterozygous for NBN germline mutation.

Method: Ninety-eight MB patients (7 heterozygous for NBN mutations) were analyzed for age at diagnosis, duration of symptoms, disease stage, histology, extent of resection, treatment complications (grade III,IV CTC 3.0), chemotherapy compliance, 5-years EFS and OS. Results were analyzed and compared in patients with and without mutation in the NBN gene.

Results: Median age at diagnosis was 5 years 2 months in heterozygotes and 8 years 10 months in others. There were no differences in symptoms duration (10,9 vs 10,4 weeks). Dissemination and tumor residual was present in 43% of heterozygotes and in 29% and 30% of other patients respectively. Histology revealed classic MB in all heterozygotes. Chemotherapy doses were reduced to 77% in heterozygotes and to 86% in others. Heterozygotes presented with more grade 3 and 4 non-hematological toxicities compared to rest of patients. 5-years EFS was 57.1% for heterozygotes and 72,4% for others, 5-years OS was 71% and 83% respectively.

Conclusion: Younger age, advanced disease at diagnosis, considerable chemotherapy dose reductions in NBN heterozygotes suggest that NBN heterozygous mutation has an impact on clinical course and outcome of MB.
PM022
HEARING LOSS AND CEREBROSPINAL FLUID SHUNTING IN CHILDREN WITH MEDULLOBLASTOMA
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Purpose: Cerebrospinal fluid (CSF) shunting is sometimes associated with hearing loss. This is thought to occur because changes in CSF pressure can lead to pressure gradients within the cochlea, leading to hearing loss in some patients. Children undergoing radiation and cisplatin chemotherapy are at risk for ototoxic hearing loss. We hypothesized that the incidence and severity of hearing loss in children with medulloblastoma undergoing radiation and chemotherapy would be greater in shunted compared to un-shunted patients.

Method: Baseline and longitudinal audiologic data was collected on 33 pediatric patients with medulloblastoma receiving radiation and cisplatin chemotherapy. Additional data collected included age, gender, date of shunt placement, and dates of chemotherapy and radiation. Incidence of hearing loss and association with shunts was determined. Hearing sensitivity and peripheral auditory function measures included pure tone, conditioned play, and immittance audiometry, and distortion product evoked otoacoustic emissions. Ototoxicity was determined according to the American Speech Language Hearing Association criteria. Severity of hearing loss was determined using the Brock criteria.

Results: Of the 33 patients evaluated, 13 (39.4%) were shunted. Hearing loss occurred in 14/20 (70%) of patients without shunts, and in 13/13 (100%) of patients with shunts. The difference between rates of hearing loss in shunted versus un-shunted patients was significant with a p-value of 0.03 using a one-tailed Fisher’s exact test. The Brock score tended to be higher in shunted patients compared to un-shunted patients. Side of shunt, COG protocol and presence of dissemination did not seem to affect incidence of hearing loss.

Conclusion: This study suggests an association between CSF shunting and development of hearing loss in children with medulloblastoma, laying the foundation for a prospective study evaluating hearing loss in children with shunts who are not treated with ototoxic therapy.

PM024
IS DIET LACKING IN GARLIC AND ONION PROTECTIVE AGAINST BRAIN TUMORS IN CHILDREN?
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Purpose: The dietary habit of people belonging to Jain Religion in India differs from other religions. They are vegetarians and in addition do not eat garlic and onion. This community has high literacy rate and economically better off than other religions. Consumption of onion and garlic has been shown to give protection against various cancers. Motivated by this observation we looked at the types of cancer in children belonging to Jain religion who do not consume garlic and onion in comparison to all others.

Method: It is a retrospective analysis of consecutive children less than 16 years of age diagnosed with cancer at Sir Ganga Ram Hospital from January 2005 to January 2010. We looked at distribution of various cancers in children of Jain religion and all others from data stored in Pediatric Oncology Network Database (POND) provided by St Jude’s Children’s Hospital.

Results: Total number of patients in the database was 536. Of these 511 children belonged to Non-Jain group. Among non-Jain group 41% had Acute Lymphoblastic Leukemia (ALL), 8% Acute Myeloid Leukemia (AML), 2% Myeloproliferative disorders (MPD), 13% Brain Tumors, 2% Ewing Sarcoma, 2% Liver Tumors, 5% Hodgkin lymphoma (HL), 5% Neuroblastoma, 2% Germ Cell Tumor (GCT), 6% Non-Hodgkin lymphoma (NHL), 3% Rhabdomyosarcoma, 5% Wilms Tumor, 2% Retinoblastoma, 1% Osteosarcoma and 3% others. In the Jain religion group total patients were 25 (5%). Of these 48% had ALL, 12% AML, 4% MPD, 0% Brain tumors, 4% Ewing Sarcoma, 4% Liver Tumors, 4% HL, 4% Neuroblastoma, 0% GCT, 4% NHL, 4% Rhabdomyosarcoma, 8% Wilms Tumor, 0% Retinoblastoma, 0% Osteosarcoma and 4% others. Noticeable difference in the two groups was absence of Brain Tumors in children belonging to Jain religion in comparison to 13% in the non-Jain group (p value 0.036).

Conclusion: Diet lacking in garlic and onion may be protective against brain tumors.

PM025
CURRENT STATE OF MANAGEMENT OF CHILDREN WITH BRAIN TUMORS IN PARAGUAY
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Purpose: Significant advances in outcomes for children with leukemia have been achieved in several low-income countries. However, such improvements have not been matched for pediatric brain tumors.

Method: We evaluated access to care and outcomes in children diagnosed with brain tumors during 2006–2009 in Paraguay, a low-income South American country, to identify deficiencies in resources that would be amenable to targeted interventions. Three methods were utilized: (1) a quantitative needs assessment questionnaire for physicians treating children with brain tumors in Paraguay; (2) site visits to evaluate three tertiary care centers in Asuncion and the two currently functioning satellite clinics in under-developed regions; and (3) interviews with health care workers from...
relevant disciplines to determine their perceptions of available resources and deficiencies.

**Results:** All three tertiary facilities have access to chemotherapy and pediatric oncologists but lack training and tools for neuropathology and optimal neurosurgery. The two public hospitals also lack access to appropriate radiological tests and timely radiotherapy with additional deficiencies in critical care and family support services identified at one of these facilities. These results demonstrate significant disparity even within Paraguay and reflect the different levels of governmental and philanthropic support, extent of program development, and socio-economic status of patients and families. These disparities translate into different rates of treatment failure, defined as abandonment of therapy, relapse, and death, which ranged from 37% to 83% among the three facilities.

**Conclusion:** We have identified common as well as discrete deficiencies in resources available for the management of pediatric brain tumors at three centers in Paraguay. As expected, poor outcomes appear to be associated with lack of resources. These results will aid in the development of targeted strategies to improve early diagnosis and optimal treatment. If effective, these strategies can be a model for development of pediatric brain tumor programs in similar low-income settings.

**PM026**

**PAY ATTENTION! THE INTEGRITY OF ATTENTION SKILLS IN SURVIVORS OF CHILDHOOD BRAIN TUMOURS AND THE RELATIONSHIP WITH WHITE MATTER VOLUME**

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**Purpose:** It has long been known that cranial radiation (CRT) is a potential neurotoxin when used to treat pediatric brain tumors (PBT). Up to 70% of medulloblastoma (an essential skills to manage daily life activities. These beginnings become even more apparent in children with Neurofibromatosis, type 1 (NF 1). This study aims to determine the impact of organizational and visual perception skills on learning and memory abilities of children with brain tumors.

**Method:** 58 children (mean age: 12.9 ± 3.5) participated in the study 1 to 10 years after diagnosis. 27 children had a NF 1 diagnosis (13 with/14 without brain tumor), 31 no NF1 diagnosis (medulloblastoma = 19, cerebellar astrocytoma = 5, 4.1) groups (p < .025 and < .001 respectively) with no changes over time. In multiple regression modelling, predictors of QoL at T3 were IQ, parent report of behaviour and the child’s age, accounting for 59% of the variance (p < .001).

**Conclusion:** Children with SRM had persistently poorer QoL, IQ and behaviour than children with LGCA who in turn had poorer behaviour than the NT group. These outcomes appeared stable over time except that QoL improved in the SRM group, but remained lower than in the other two groups.

**PM029**

**IMPACT OF VISUAL PERCEPTION AND ORGANIZATIONAL SKILLS ON LEARNING AND MEMORY IN CHILDREN WITH BRAIN TUMORS**

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**Purpose:** Along with other neuropsychological deficits, impaired organizational skills and visual perception have often been found in children with brain tumors, both being essential skills to manage daily life activities. These findings become even more apparent in children with Neurofibromatosis, type 1 (NF 1). This study aims to determine the impact of organizational and visual perception skills on learning and memory abilities of children with brain tumors.

**Method:** 58 children (mean age: 12.9 ± 3.5) participated in the study 1 to 10 years after diagnosis. 27 children had a NF 1 diagnosis (13 with/14 without brain tumor), 31 no NF1 diagnosis (medulloblastoma = 19, cerebellar astrocytoma = 5,
PM030
INTRACRANIAL TUMOURS IN CHILDREN UNDER 1 YEAR OF AGE. A SURVEY OF 16 YEARS
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Purpose: The objective of this study was to describe the incidence, presentation and outcome of children with intracranial tumours under 1 year of age in our paediatric neurosurgical unit at “Juan Manuel Marquez” Pediatric Hospital. The incidence of intracranial neoplasm’s in the children under 1 year of age is unknown in our country, although there are some international studies of this topic.

Method: It is a retrospective review of all children under 1 year of age presenting with intracranial tumours between 1990 and 2006, with follow-up data from a multidisciplinary pediatric neuro-oncology group. Fifty-eight children were diagnosed during the period of study. We reviewed from our database the biopsy results, operative reports and clinical history of all these patients and the following factors were analyzed: sex, race, Debut of symptoms and duration, intracranial hypertension on admission, tumour location, grade of surgical removal, histology, and survival of the children.

Results: The results of treatment for these children were in relation with earlier diagnosis and properly managed in a specialized paediatric oncology centre. In this study, we find (30 males and 28 females) under 1 years of age. Sex masculine and the white race was the most common. Most of the tumours were located within the supratentorial compartment (48 children). 37 patients have lesions that had grade III-IV (WHO) and most tumours were from astrocytomas origin. Overall survival at 5 years was 27% (16 of 58 children).

Conclusion: The incidence of intracranial tumours in Children under 1 year of age constitutes 10% of all the intracranial tumours in Children diagnosed in the period 1990–2006 in our Hospital. The most common was Supratentorial location and astrocytomas origin of the neoplasms. It is necessary an multidisciplinary approach in the treatment of these children.

PM031
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Purpose: This study used data from the Israel Cancer registry to examine pediatric brain tumors with the international classification of childhood cancer.

Method: Incidence rates for central nervous system (CNS) tumors in children aged 0–19 years in Israel, between 1998–2007, were examined. CNS malignant tumors were classified according to gender, topography, age distribution, origin, and histological diagnosis. Survival probability updated to December 2009 was estimated.

Results: There were 815 children and teens, with a mean age of 9.37 years (y) (10 days–19.98 y); 351 girls, 464 boys; 595 Jewish children (73%), 186 Arabic children (22.8%), 34 Christian children (4%). Overall survival (OS) at 5 years was 73.2%, with 64.7% for the Arabic population and 75.9% for the Jewish population (p = 0.004).

Five year OS for children less than 1 year was 64.1%, 1–4 y was 70.5%, 4–9 y was 69.6%, 9–14 y was 75.4%, and 14–19 y was 80%. The most frequent tumors were pilocytic astrocytoma: 157 children, median age: 9.5 y, OS 95.5%; astrocytoma grade I–II: 94 children, OS 81.6%; astrocytoma grade III–IV: 74 children, OS 54.6%; medulloblastoma: 96 children, mean age 6.79 y, OS 69% under the age of 3 years: 24 pts, OS 37.5%; ependymoma: 61 children, mean age 7 y, OS 81.6%, 21 patients under the age of 3 years, OS 43%; glioblastoma multiforme: 34 children, OS 15%. The histological type of the tumor and the age of the patients in medulloblastoma and ependymoma were the most powerful independent predictor of survival. According to diagnosis and origin, OS was inferior in the Arabic population with ependymoma (p = 0.07) and astrocytoma grade II (p = 0.052).

Conclusion: Children in Israel with CNS tumors had a good survival experience compatible with the high quality of care. A larger study implicating genetic factors needs to be performed, including comparisons with other countries of the Middle East.

PM032
PROGNOSTIC FACTORS INFLUENCING SURVIVAL FOR CNS ATYPICAL TERATOID RHABDOID TUMORS IN BRITISH COLUMBIA
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Purpose: Atypical Teratoid Rhabdoid Tumours (ATRT) are a rare type of malignant embryonal neoplasm that primarily affect very young children. Prognosis is reported to be very poor, and little is known about factors that predict survival. Diagnosis has “IN1-1” antibody test has been used to diagnose ATRT at BC Children’s Hospital (BCCH) since 2007. We hypothesized that prior to the use of the INI1-test at BCCH, some ATRC cases may have been diagnosed as other tumours, which would alter the true incidence and outcome. Also, exploration of epigenetic factors such as promoter methylation may differentiate the rare long-term survivors of ATRT.

Method: The INI1-test was applied retrospectively to all archival embryonal tumour samples (1986–2006) at BCCH. Samples with negative INI1 staining and positive internal controls were considered to be ATRTs. Promoter methylation analysis was performed using Methylation Specific PCR (MSP).

Results: Approximately 100 tumours samples were available for testing. INI1 staining was negative in 12 of these samples (2 that had been originally diagnosed as ATRT, 10 as medulloblastomas/PNETs). Median survival was poor (less than 2 years), but we discovered three long-term survivors (alive more than 3 years) who had INI1 negative tumour samples. Preliminary promoter methylation analysis of MGMT, RASSF1A, MLH3, RUNC3, and HIC1 has not been able to reveal differentiating features in the survivors.

Conclusion: Taking these INI1-negative tumours to represent ATRT, this study retrospectively increases the number of cases over our study period from 2 to 12. Using the INI1-test to identify the 3 previously unrecognized ATRT long-term survivors changes the 3-year survival rate from 0 to 25 percent. Capturing ATRT as a separate entity will allow improved reporting of survival for other CNS tumours. Epigenetic changes should be further explored in order to find unique characteristics in survivors that may offer prognostic value.

PM033
SUPRATENTORIAL EPENDYMOMA - THE CHILDREN'S HOSPITAL LOS ANGELES EXPERIENCE
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Purpose: The standard treatment for ependymoma is surgical resection followed by postoperative irradiation to the local site. This approach in completely resected
supratentorial ependymoma has been questioned in the past decade. We review the outcome of patients treated at our institution.

**Method:** Retrospective review of the medical records of consecutively diagnosed supratentorial ependymoma patients at Children's Hospital Los Angeles (CHLA) between January 1999 and December 2009.

**Results:** Eleven patients (4 females, 7 males) were included. The mean age at presentation was 6.6 years (range 2–15 years). Histology was consistent with anaplastic (WHO grade III) in 9 patients, clear cell (WHO grade II) in 1 and cellular (WHO grade II) in 1 patient. Gross total resection (GTR) was achieved in 7 patients; 5 were observed, one received local irradiation, 1 received chemotherapy. In the 4 patients who underwent partial resection (PR) 1 was observed, 2 received local irradiation, one received irradiation and chemotherapy. The median length of follow up was 34 (range 12–86) months. Four relapses (2 in GTR, 2 in PR) were observed; 3 local and 1 in the lateral ventricle. The relapsed patients were treated with surgery only (1) or combinations of surgery, chemotherapy and focal irradiation. The 3 year progression free survival in GTR patients was 69 ± 19%. All patients who had GTR are alive at the time of this publication. The 3 year progression free and overall survivals for all patients were 54 ± 8% and 44 ± 8% respectively.

**Conclusion:** Radiation therapy was avoided in 4 patients with GTR without further complications. Of these, 3 patients had anaplastic histology. In some children with completely resected supratentorial ependymoma, surgery alone may be an acceptable treatment option.

**PM034**

**POSTERIOR FOSSA SYNDROME AFTER POSTERIOR FOSSA SURGERY IN CHILDREN WITH BRAIN TUMOR**

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**Purpose:** Posterior fossa syndrome (PFS) is defined as the temporary and complete loss of speech after posterior fossa surgery. In this study, we aimed to identify the incidence and risk factors for PFS.

**Method:** Between May 2007 and April 2009, children with brain tumors who underwent posterior fossa surgery were evaluated neurologically and psychologically in preoperative and postoperative periods.

**Results:** PFS developed in 9 patients and 36 (78%) included in the study, eight patients had medulloblastoma (89%) and one ependymoma. The tumor was located in the midline in 7 of the patients (78%). In univariate analyses, histopathological diagnosis (p = 0.05), location of the tumor (p = 0.05) and socioeconomic level of the family (p = 0.06) gave the significant results in relation with the PFS. In multivariate analysis the risk of developing PFS was found 7.2 times higher in medulloblastoma patients, 6.7 times higher in tumors located in the midline, 5.7 times higher in families with low socioeconomic level. Intelligency quotients of the patients in PFS and other group (p = 0.85) were not different statistically with Wechsler Intelligence Scale for Children. Similarly, the results of the Denver II Developmental Screening Test were not different (p = 0.5) in patients in between the two groups.

**Conclusion:** The diagnosis of medulloblastoma and midline location of the tumor are important risk factors for the development of PFS. These findings support the hypothesis that temporary ischemia and edema due to retracted and largely manipulated dura mater and superior cerebellar peduncles may be the cause of mutism. Informing the family and the patient about the PFS must be a component of the preoperative interview and patients who developed PFS should be followed for accompanying neurobehavioural and psychologic problems even after mutism improved.

**PM035**

**CHOROID PLEXUS TUMOR STUDIES: CPT-2000 CLOSING CPT-2009 OPENING**

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**Purpose:** Choroid plexus tumors are rare brain tumors mainly occurring in young children. We aim to develop optimized treatment.

**Method:** Ten years ago, SIOP has started an initiative including a standard of care recommendation, a prospective registry, and a randomized treatment protocol (CPT-SIOP-2000).

**Results:** By February 2010 188 tumors data were registered from 173 patients, 15 of which had two subsequent tumors documented. 83 of these patients were registered from Germany. 84 were male, the mean age was 4.1 years (range 0.1–45), 57 had choroid plexus papilloma, 48 atypical choroid plexus papilloma, and 57 choroid plexus carcinoma. 10 histologies could not be classified. 39.1% were located in each of the lateral ventricles, 61.1% in the third ventricle, 11.7% in the fourth ventricle, 1.8% in the CP-angle, and 1.2% had multiple locations. Complete resection was achieved in 75.5%. The 5-year OS of 163 patients with classified histology was 84.5% (SE 4.4%), and 5-Y-DFS was 65.1% (SE 5.4%). The prognostic relevance of histology and radiation was confirmed as previously described; however the prognostic relevance of surgical resection disappeared when covariates of histology and radiation were used in COX regression analyses. Two chemotherapy protocols (analyzed as blinded dataset) did not differ in outcome results, but the final analysis is planned only in 2015.

**Conclusion:** The study group has agreed on the next protocol (CPT-SIOP-2009), which will have a prephase to determine the most promising protocols then to be compared in the main phase as two armed phase III protocol. The registration continues with new remote data entry.

**PM036**

**TREATMENT OF PAEDIATRIC GLIOMA TUMORS: RESULTS OF A SINGLE INSTITUTION EXPERIENCE**

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**Purpose:** Evaluate OS and median of DFS of gliomas paediatric patients, treated between 1989 to 2009 in our institution.

**Method:** Thirty-one patients were retrospectively examined. Age, sex, tumor grade, tumor location and treatment received, were considered.

**Results:** Twenty-nine patients were evaluable: 18 males and 11 females, median age 6 (range 2–15), 4 optic nerve gliomas, 25 astrocytomas: 10 Grade I (2 supratentorial, 8 posterior fossa); 9 Grade II (1 supratentorial, 6 encephalic cord and 1 posterior fossa); 6 Grade IV (all supratentorial). All Grade I astrocytomas underwent surgery: 7 total resections, 2 of them underwent of second surgery for local relapse; 3 partial resections, followed by chemotherapy ( Carboplatin, Etoposide) and radiation (55 Gy). Patients with optic nerve tumor received chemotherapy alone ( Carboplatin, Etoposide, Temozolomide).

All Grade II astrocytomas had chemotherapy ( Carboplatin, Etoposide, Temozolomide) and radiation (35–55 Gy). 7 of them also had partial surgery (2 of them after neoadjuvant chemotherapy).

Six Grade IV astrocytomas were treated with subtotal surgery, chemotherapy (JET regimen) and radiation (but 1, younger than three years of age). According to histopathologic criteria, patients were divided in two groups: low-grade (I-II) and high-grade (IV). First group, including 23 pts, showed OS 91% and DFS 87 months (range 13–206); second group, including 6 pts, had OS of 33% and DFS of 112 months (range 60–163).

According to topography, patients were divided in: posterior fossa tumors (9 pts) with OS 100% and DFS of 65 months (range 13–256); encephalic trunk tumor (7 pts) with OS 71% and DFS of 100 months (range 63–136); supratentorial tumors (13 pts) with OS 69% and DFS of 116 months (range 36–206).

**Conclusion:** Higher tumor malignity is associated to a lower OS (91% vs 33%). All pts with posterior fossa tumors are alive, but those with encephalic trunk tumors have low OS and DFS.

**PM037**

**PEDIATRIC INTRAMEDULLARY SPINAL CORD TUMORS: A SINGLE CENTER EXPERIENCE**

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Purpose: To evaluate clinical and radiological findings, pathological features and treatment modalities of patients with intramedullary spinal cord tumors.

Method: Hospital files of 36 cases were reviewed for clinical, radiological, histopathological data, chemotherapy, radiotherapy and surgical practices, treatment responses, events and final outcome. Survival analyses were performed.

Results: Median age was 7.9 years (1–16; male/female: 1.4). Histopathological diagnoses were astrocytomas (n = 14, 44.4%) and ependymomas (n = 19, 52.8%). (One unclassified glioma). 94% of astrocytomas and 84% of ependymomas were low-grade; 3 tumors were high-grade (1 undetermined-grade ependymoma. Most common complaints and physical examination findings were weakness/gait disturbances (83.3%), pain (55.6%), and deep tendon reflex changes (80%), motor deficits (78%), respectively. Neurologic statues at diagnosis with modified McCormic scale were grades I-II (normal-mild deficit) in 14 (39%) and grades III-V (moderate-severe) in 22 patients (61%). Primary tumor sites were thoracic (47%) and cervical segments (28%). All patients had undergone initial surgery (gross-total resection 33%; subtotal 45%; biopsy 22%). Radiotherapy was given to 26 (72%) patients, chemotherapy to 15 patients (42%) (mostly CCNU+ProC+VCR). At 3, 5 and 10 years, overall survival rates were 72%, 65% and 56%, and event-free survival rates were 43%, 40% and 40%, respectively. No significant differences were found with respect to gender, age groups, lag-time, neurologic statues, histopathologies, tumor region, extent of resection, treatments or treatment responses in univariate survival analyses. Survival rates were significantly higher in patients with low-grade tumors and in ependymomas with resected tumors. With Cox regression analyses, tumor grade (RR 1.5) and lag-time (RR 4.3) were independent prognostic factors for overall survival. Patients with a lag-time <3 months had a worse prognosis.

Conclusion: Patients with low-grade tumors and those with gross-total tumor resection had better prognosis. Surgery is, yet the basis of treatment in intramedullary spinal tumors. Roles of radiotherapy and chemotherapy are limited and even controversial in low-grade tumors.

Conclusion: CONCOMITANT CHEMO RADIATION (CRT) IN HIGH RISK PRIMITIVE CNS EMBRYONAL TUMOURS (PCET): A PROSPECTIVE PILOT STUDY AT TATA MEMORIAL HOSPITAL (TMH)

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Purpose: Prospective study of concurrent Carboplatin and radiation therapy followed by adjuvant chemotherapy in patients with newly diagnosed high risk PCET.

Method: Newly diagnosed high risk PCET (post surgery residual lesion > 1.5cm, leptomeningeal disease) age >3 and <22 years are prospectively accrued on IRB approved protocol. All underwent surgery followed by CRT within 6 wks of surgery. CRT includes craniospinal radiation 35Gy/21# with local tumor bed boost 19.5Gy/1# along with Carboplatin 35 mg/m2/day given 5 days a week for 15 doses (during end of CRT) with prophylactic GCSF for 5% and M3 27.5%. At end of CRT, 75%(30) are in CR, 10%(4) PR, 10%(4) have radiologically stable disease(SD) & 5%(2) had progressive disease(PD). Of 38 on adjuvant therapy, 27(71%) have completed treatment. (23/27 are alive in CR with median follow up of 23 months (0–40) & 4/27 had recurrent disease). 5/38 (13%) are on treatment, 5(13%) are dead (3 toxic and 2 PD).1(3%) was lost to follow up. EFS is 65% at 30 months. During CRT severe anemia was observed in 13%, neutropenia in 57% and thrombocytopenia in 25% patients.21% had febrile neutropenia and 57% required GCSF for grade III neutropenia. In non hematologic toxicity 94% had anorexia, 100% nausea/vomiting, 75% mucositis, 72% grade II radiation dermatitis and 94% alopecia. During adjuvant chemotherapy Grade IV/III hematological and nonhematologic toxicities were observed in 80–85%.

Conclusion: Concomitant CRT in PCET is feasible, safe, with manageable toxicities. The promising early response should translate in to long term benefit.

PM040

OUTCOME OF PATIENTS WITH SUPRATENTORIAL PRIMITIVE NEUROECTODERMAL BRAIN TUMORS (STPNET)

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Purpose: We report retrospectively the treatment results of 36 patients (pts) with supratentorial PCET (post surgery residual lesion > 1.5cm) who were treated at department of Neurooncology of FRCC PHOI from several hospitals of Russian Federation (1997 to 2009).

Method: There were 18 girls and 18 boys. 14 pts were under 3 yrs. Age at diagnosis – 6 years (range, 7 mths-17 yrs). 15 pts were with MO, 2 – with M1, 11 – M2–3, 8 – M4. 31 pts had subtotal/partial resection or biopsy, one pt was not resected due to thirdrabilité resection/abloma. 16 pts were treated with “Philadelphia protocol” – 11, with H-IT-SK Reaction 92, 2 pts – with Cyclic CHT, 2 pts received adjuvant CHT and 5 pts were without any CHT, but with RT, 19 pts received CNS 35 Gy and boost to tumor bed/metastasis up to 55 Gy, 4 pts – local RT 55 Gy and 13 pts were without any RT. Results: 3 pts – lost follow up, median follow up time of 18 surviving pts – 2 yrs 8 mths (range, 3–93 mths). In 32 pts with residual tumor the combined response was seen in 14 patients (12 CR, 2 PR). PFS/OS of pts under 3 yrs was 0/90%; older; 3 yrs 25/41% respectively (but N/S). PFS of pts with M0/M1/M2-3/M3x were 290/
PM041
RESULTS OF TREATMENT PEDIATRIC MULTIFORME GLIOBLASTOMA

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Purpose: Multiforme glioblastoma (MGB) is a rare tumor of CNS in children, which differs extremely from adult glioblastoma. The aim of our study was to analyze the results of treatment of pediatric patients with MGB.

Methods: We retrospectively analyzed the data of 51 patients (median age at diagnosis was 4.2 years, range 0.5–17 years) with MGB in 1994–2010. The main treatment scheme was presented by surgery and chemotherapy (CHT) with the combination of Temozolamide and Lomustine followed by adjuvant Temozolamide chemotherapy. The median of follow up was 15 months (3–60 months). The clinical characteristics and results of treatment were presented using descriptive statistics.

Results: The median of follow up was 15 months (3–60 months). The 2-years PFS for all group was 4% (median of PFS – 9 months) and 5-years OS was 4% (median of OS – 18 months). OS significantly depended on Karnovsky index: 9% in pts with index higher than 60% and 0% in pts with index under 60% (p < 0.0001). PFS in pts receiving Temozolomid was higher than in pts with other schemes: 33% and 8% respectively (p = 0.02). The differences of PFS in pts with combination and complex treatment (0% and 4% respectively, p = 0.14) in pts with total, subtotal resection and biopsy (50%, 12% and 0% respectively, p = 0.30) was not significant.

Conclusion: The best PFS associated with complex treatment including Temozolomid, OS – with Karnovsky index.

PM042
VINCristINE AND CARBOPlatin CHEMOTHERAPY FOR UNRESECTABLE AND/OR RECURRENT LOW GRADE ASTROCYTOMA OF THE BRAINSTEM

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Purpose: Twenty percent of pediatric brain stem tumors are low grade gliomas (LGG) that have distinct clinical features and follow much more indolent course than diffuse high grade pontine glioma. Advances in neurosurgical techniques have made surgery the treatment of choice for some of these tumors. Radiotherapy remains a widely accepted postoperative treatment modality for unresectable or recurrent LGG. However, there is increasing evidence to suggest that chemotherapy can delay and may obviate the need for radiotherapy in progressive/recurrent LGG. The majority of the published experience is in children with hypophalamic/optic chiasmal lesions and little information is available regarding its use in LGG of the brainstem.

Method: We describe clinical characteristics and course of children with LGG of the brainstem who received carboplatin based chemotherapy in two institutions over 10 years (1996 to 2006). This was a retrospective review of consecutively treated children with LGG of the brainstem (midbrain, pons, medulla and upper cervical cord).

Results: In this series, there were 16 children (9 males) with median age at diagnosis of 4 years (range 0.5–8). Eight children were treated at diagnosis while the remaining 8 received chemotherapy after either radiological progression or clinical deterioration. After a median follow up of 57 months (range 20 to 136) from initiation of chemotherapy all children are alive and 11 remain progression free (1 complete response, 8 with partial response + minor response and 2 stable diseases).

Conclusion: The efficacy of this chemotherapy regimen in this series supports its role in children with progressive unresectable LGG of brainstem.

PM043
BRAIN METASTASES IN PAEDIATRIC EXTRACRANIAL SOLID TUMOURS

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Purpose: Brain is a rare site of metastases in most extracranial paediatric solid tumours. The aim of this study is to investigate the incidence, treatment, prognosis of brain metastasis in extracranial paediatric malignant tumours in a single institution over 8 year period.

Method: The retrospective case review of 256 children, 16 years of age or under, treated for extracranial solid tumours in the Department of Paediatric Oncology at Royal Hospital for Sick Children, Yorkhill, Glasgow from March 2002 to March 2010.

Results: Three (2 female, 1 male) of 256 patients (1.2%) with extracranial solid tumours developed brain metastases. The median age of the patients at the time of diagnosis of CNS metastases was 4 (3–16) years. The diagnosis was relapsed neuroblastoma, hepatoblastoma and malignant germ cell tumour. Diagnosis of CNS metastases was confirmed by imaging studies (CT, MRI). The median time from initial diagnosis to the detection of CNS metastases was 15 months. All patients had metastases to various sites at the time the brain metastases were detected. One patient with relapsed neuroblastoma underwent surgical resection (craniotomy) followed by radiotherapy. The two other cases, who were also heavily pre-treated, received only symptom/palliative care. All of the children died, with median period of 2 months after the detection of CNS involvement.

Conclusion: The frequency of CNS involvement in non-CNS tumours is low, with a very poor survival. Children with metastatic relapse who develop headaches or any other neurological symptoms should be investigated for possible brain metastases.

PM044
PROMISING SURVIVAL FOR CHILDREN WITH NEWLY DIAGNOSED MALIGNANT GLIOMAS TREATED WITH CONCOMITANT RADIATION PLUS TEMOZOLAMIDE AND LOMUSTINE

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Purpose: Temozolamide is a novel alkylating agent that has demonstrated activity in recurrent gliomas. Combination of temozolamide with lomustine helps to overcome chemotherapeutic resistance and increase survival. This study was performed to determine the safety, tolerability and efficacy of concomitant radiation plus combination of Temozolamide and Lomustine followed by adjuvant Temozolamide and Lomustine.

Method: Thirteen patients > 4 and < 15 years of age with newly diagnosed and histologically proven glioblastoma multiforme (3 patients) and anaplastic astrocytoma
RESULTS: Concomitant radiation plus temozolomide and lomustine followed by adjuvant temozolomide and lomustine was safe and well tolerated. Complete response was achieved in 9 patients (69.2%), partial response was achieved at 2 patients (15.5%), the other 2 patients achieved stabilization of the disease. The 2-year disease free survival and overall survival were 76.9% and 61.5% respectively.

Conclusion: Concomitant radiation plus temozolamide and lomustine followed by adjuvant temozolomide and lomustine is safe. This regimen of concomitant radiation plus temozolomide and lomustine followed by adjuvant temozolomide and lomustine may prolong the survival of children with glioblastoma multiforme and anaplastic astrocytoma.
Purpose: Atypical teratoid rhabdoid tumors (ATRT) are a unique tumor seen primarily in early childhood. The purpose of this study was to review the CT and MRI characteristics of ATRTs and correlate these findings with clinical outcomes.

Method: A retrospective review of the pre-operative CT and MRI examinations of patients with ATRT at our institution was performed by two pediatric neuroradiologists. Analyses included tumor location, tumor signal characteristics, assessment of enhancement, gender, age at presentation, treatment and survival.

Results: Nineteen patients were identified, diagnosed between 2000 and 2008: 13 females and 6 males. Age at presentation ranged from two months to 19 years (median, 15 mos; mean, 34 mos). Eleven cases were supratentorial, four of these in the tectal region. Of the six infratentorial tumors, two were located at the cerebellomedullary angle. One case was both supratentorial and infratentorial, and another case was intraspinal. CT exams were available in 13 patients and MRI exams available in 19 patients. The majority of the tumors were of increased density on CT, and hypointense on both T1 and T2-weighted images; hemorrhage was present in 8 of 19 patients. Diffusion-weighted imaging was available in 13 patients and all tumors had decreased diffusion. Tumor volume ranged from 1.2 cc to 194 cc. Five patients had leptomeningeal dissemination at presentation. Five patients survive without relapse; nine patients total remain alive 2–8 years from diagnoses (including 3 relapsed, 1 with secondary malignancy). 10 have died.

Conclusion: The imaging features reviewed here in our series of ATRT patients include hypointensity on T1 and T2-weighted images, decreased diffusion within the tumors, and heterogeneous enhancement. Intratumoral hemorrhage was also a frequent finding but did not predict a poor outcome. Progression-free survival is poor with few relapse-free survivors, but long-term survival remains hopeful with ongoing therapy.

PN001

THE ROLE OF PLERIXAFOR AS A SECOND LINE STEM CELL MOBILIZING AGENT IN CHILDREN

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Purpose: Role of Plerixafor as second line agent has been proved in adults. Our aim is to analyse our experiences with Plerixafor as a second line mobilising agent in children.

Method: We retrospectively analysed children who received Plerixafor as second line stem cell mobilising agent in our institution in the 2009–2010 period. Data collection includes diagnosis, pre harvest treatments, harvest details in first attempt, adverse reaction and harvest out come with Plerixafor.

Results: We used Plerixafor on 5 occasions in four children, whose diagnoses include Medulloblastoma, Neuroblastoma, B cell Non Hodgkin’s lymphoma and Wilms’ tumour. Patients were treated with different combinations of chemotherapeutic agents prior to stem cell harvest. Two patients also had radiotherapy before harvest. All patients had attempted stem cell mobilisation first with G-CSF at a dose 10 microgram/kg for 5 days. In view of low peripheral blood stem cell counts, harvest was abandoned in all cases. Harvest was successful with first attempt with Plerixafor in two cases. In one child, harvest failed with Plerixafor; and in one case it was successful with second attempt with Plerixafor. The dose of Plerixafor was 240 microgram/kg in all cases. All patients tolerated Plerixafor well and no adverse reaction was reported in any case.

Conclusion: Studies on the use of Plerixafor in adults have been reported a success rate of 90%. Regarding its use in children, we could find only one case report and two abstracts in the literature. Our experience shows success rate of 60% (3 of 5 occasions) with no adverse reactions but is obviously handicapped by the small patient numbers. Multinational collaboration to collect data and analysis is the practical way forward to define the precise role of Plerixafor as a second line mobilising agent in children.

PN002

ENTERAL NUTRITION AND HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

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Purpose: The purpose of the study was to assess the efficacy, the safety, the clinical and biological consequences of enteral nutrition and the occurrence of early complications in children undergoing haematopoietic stem cell transplantation (HSCT).

Method: The data of the first 100 days of the patients who received a nutritional support after HSCT from January 2003 to December 2008 were retrospectively collected.

Results: 81 children were included. 42 of them received an enteral nutrition (EN group), 39 of them a parenteral nutrition (PN group). In the PN group, 31/39 patients underwent HSCT from 2003 to 2005, while 41/42 of the patients in the EN group underwent HSCT from 2006 to 2008. The mean length for EN was 57 days in the EN group and the mean length for PN was 35 days in the PN group. Poor nutritional status was assessed by anthropometric parameters. On the first day of HSCT, 29% of the patients in the EN group and 28% of the patients in the PN group had a Weight for Height Z-score < -1 DS. On day 100, 21% of the patients in the EN group and 23% of the patients in the PN group had a Weight for Height Z-score < -1 DS. This parameter increased significantly between day 1 and day 100 only in the EN group.

Conclusion: Enteral nutrition is a feasible, efficient, safe and cheap nutritional support modality after HSCT in children. Its use involves the motivation of the whole nursing team so that it becomes well accepted by the patients and their family.

PN003

DIFFERENCES IN MOTHERS’ AND FATHERS’ HEALTH RELATED QUALITY OF LIFE ONE AND TWO YEARS AFTER PEDIATRIC STEM CELL TRANSPLANTATION AND PRE-TRANSPLANT PREDICTORS

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Purpose: When a child undergoes a stem cell transplant (SCT) the demands of treatment and child care can have a severe impact on the health-related quality of life (HRQOL) of parents. The purpose of the current study was to examine longitudinally parental HRQOL prior to, one and two years after pediatric SCT and to identify clinical and personal factors related to HRQOL.

Method: 69 mothers and 42 fathers participated before SCT, 49 and 35 at one year and 49 and 31 at two-year post-SCT. Parents of patients diagnosed mainly with leukemia completed the Medical Outcomes Study, General Health Survey Scales (MOS SF-36) as measure of HRQOL. The MOS SF-36 physical (PHY) and psychosocial (PSYC) summary scores were used. Parents’ age and gender, and child’s diagnosis, radiation status, age, behavior and physical health pre-SCT were examined as potential predictors.

Results: Mixed model regression analyses indicated no significant changes over time for parents’ PHY. Only for fathers, age (younger) (p < 0.01) and child’s diagnosis (neuroblastoma, p < 0.01; leukemia, p < 0.04) were associated with poorer PHY. There was significant improvement from pre- to two years post-SCT for fathers’ PSYC (p < 0.03). Maternal PSYC was associated with child’s behavior (p < 0.03), and paternal PSYC was associated with radiation history (p < 0.03).

Conclusion: The results of this study highlight the importance of investigating physical and psychosocial HRQOL separately for mothers and fathers. They identify younger fathers whose children undergo treatment for neuroblastoma at risk for physical HRQOL. Regarding psychosocial HRQOL, child’s behavior problems and previous radiation history were identified as predictors of mothers’ and fathers’ PSYC HRQOL, respectively. These findings have important clinical implications for comprehensive psychosocial family intervention after pediatric SCT.

PN004

RESTING ENERGY EXPENDITURE DECLINES IN CHILDREN FOLLOWING HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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**Purpose:** Children undergoing hematopoietic stem cell transplantation (HSCT) typically require parenteral nutrition (PN) due to gastrointestinal toxicities. Since PN is associated with metabolic, infectious, and hepatic complications, minimizing the amount and duration of PN while preserving adequate nutritional status is desirable. Determining resting energy expenditure (REE) may help avoid problems associated with overfeeding or underfeeding. We prospectively measured REE over the course of HSCT to characterize changes that may impact nutritional regimens.

**Method:** This was a multicenter, prospective cohort study of children undergoing allogeneic HSCT at Children’s Hospital Boston and UCLA Mattel Children’s Hospital. REE was measured by indirect calorimetry at baseline and twice weekly until 30 days post transplant. Nutritional and clinical data were recorded concurrently throughout the hospitalization. REE values were compared to the calculated estimation of basal metabolic rate using the Schofield method, computed as percent predicted REE. Change in % predicted REE over time from admission was described using repeated measures regression analysis.

**Results:** Twenty-six children (14 females) were enrolled with a mean (SD) age of 14.8 (4.2) years. All patients had an HLA-matched sibling (n = 12) or unrelated donor (n = 14). Underlying diagnoses for HSCT were ALL (n = 7), AML (n = 7), myelodysplastic syndrome (n = 3), CML (n = 3), lymphoma (n = 2), aplastic anemia (n = 1), and other (n = 3). Mean (SD) BMI Z-score was 0.29 (0.86) and mean REE at baseline was 1313 (320) kcal/day. Twenty-three patients (88%) received PN. Mean (SD) % predicted REE at baseline was 88.3% (14.7). REE decreased significantly over time (p < 0.001) and followed a quadratic curve to a nadir of 78% predicted at 18 days post transplant.

**Conclusion:** Children undergoing HSCT exhibit a significant reduction in REE in the early weeks post transplant. Serial measurements of REE should be considered to avoid potential complications of overfeeding, especially when PN is the primary mode of nutrition.

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**Purpose:** High dose steroids are the mainstay of treatment for severe acute Graft versus Host Disease (aGVHD). Additional strategies to reduce the associated severe side effects in children are required. Mesenchymal stromal cells (MSC) have achieved 80% responses in children with severe steroid refractory aGVHD in both non- and randomized multi-center studies. Any long term associated risks need to be studied before advocating the early co-adjusted use of MSC with steroids for the treatment of aGVHD.

**Method:** We undertook a retrospective study of 40 children (21 boys;19 girls) aged 3 m to 17 yrs 8 m (median 11 yrs) receiving MSC infusions between 2005 and 2009 for steroid refractory grade 3/4 aGVHD. MSC were expanded using a common protocol from BM donors; 3rd party (n = 33), haploidential (n = 4) or both (n = 6).

**Results:** Complete response CR was evident in 22 children of whom 20 are alive (median follow up of 2.5 yrs (range 0.5 to 4.5), with 2 children dying from infection. In contrast in 18 children with either no (NR = 10) or partial (PR = 8) response, TRM due to infection and/or progressive GVHD was 85%.

**Conclusion:** Our study confirms the benefit of early use of MSC and sensitizes clinicians to the possible risks and benefits of using MSC in children with severe steroid-refractory aGVHD.

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**Purpose:** Autologous hematopoietic stem cell transplantation (HSCT) is for a number of patients with high risk leukemias the only curative approach. An alternative for those patients who do not have an HLA-matched sibling and are at high risk of disease progression during the donor search is the use of mismatched related family donors. We evaluate the outcomes of 10 patients with high risk hematological malignancies who underwent haploidential HSCT at our institution between April 2005 and August 2009. The conditioning consisted of fludarabine, thiotepa and melphalan. Six patients received OKT3 and four anti-thymocyte globulin with total nodal irradiation. Donors were primed with granulocyte-colony stimulating factor and hematopoietic progenitors were obtained from peripheral blood. The grafts were T-cell depleted using CliniMacs (Miltenyi Biotech, Germany). In one patient the depletion failed and he received Cyclophosphamide 50 mg/kg on day 1. The median CD34+ and CD3+ cells infused were 12.2 × 10^6/kg (range 6.76-25.3) and 3.69 × 10^5/kg (range 1.0-250.0) respectively. Cyclosporine A or mycophenolate mofetil were administered for graft versus host disease (GVHD) prophylaxis.

**Results:** None of the patients had any significant conditioning-related toxicity. All patients engrafted between days 9 and 12 and achieved a full donor chimerism. One patient rejected his first HSCT after 10 weeks and had a successful second transplant. Acute and chronic GVHD was seen in 3 and 1 patient respectively. Three patients died of transplantation-related complications, two due to CMV pneumonitis and one GVHD grade IV. Two other patients died as a consequence of post-transplant leukemia relapse. The remaining five patients are in complete remission with stable full chimerism. After a median follow up of 24 months, the 5-years estimate overall survival was 48.0% ± 16.4.

**Conclusion:** These data provide support that haploidential HSCT is a reasonable alternative for patients without HLA identical sibling.
Purpose: To test the lytic potential of NK-cells against HuMAPC.

Method: We present a case of a 9-year-old girl with idiopathic aplastic anemia who received a HSCT from an 9/10 matched unrelated donor (HLA-Cw mismatch). The conditioning regimen included Fludarabine and ATG for 5 days, cyclophosphamide for 4 days with cyclosponge (CSA) for GVHD prophylaxis. Donor 30 × 106 CD34+ cells/kg treated with Campath-1H in the bag were infused followed the next day by 5×106 T cells/kg. On day +8 she developed a severe TAM. Engraftment occurred on day +13. Because of TAM, CSA was replaced by methylprednisolone/MMF. Intestinal GVHD grade III started on day 17. Despite treatment by plasma exchange, anti-TNF, statins, heparin, and diuretics, the patient worsened clinically. She reactivated CMV, cardiac and bilateral pleural effusion appeared with BIVV-6 infection, respiratory failure, pulmonary arterial hypertension and she ultimately died on day +193. An important increase of NK cell was detected in the blood at engraftment.

Results: Only few NK cells expressed an inhibitory KIR specific for one of the HLA-Cw16 and HLA-Cw17 KIR-ligands. Further FACS-analysis and immunohistochemistry using the monoclonal antibody NKp46 revealed that the NK cell population that had expanded in the blood was present in the pericardial fluid and had infiltrated the pericardium, kidneys and lungs coinciding with renal and pulmonary vasculopathy.

Conclusion: NK cells that had infiltrated the lungs and kidneys may have contributed to the microangiopathy.

PN009

IMMUNE MODULATORY CAPACITIES OF HUMAN MULTIPOTENT ADULT PROGENITOR CELLS ON NATURAL KILLER-CELL PROLIFERATION, CYTOKINE PRODUCTION, AND CYTOTOXICITY

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Purpose: Human Multipotent Adult Progenitor Cells (HuMAPC) are adult stem cells which differentiate to mesoderm including endothelium with extensive proliferation potential at the single-cell level. HuMAPC inhibit T cell proliferation induced by alloantigens (manuscript in preparation). Therefore these cells are considered as ideal candidates for the prevention and treatment of graft-versus-host disease in bone marrow transplantation. In order to use HuMAPC in novel clinical applications, the interaction of HuMAPC and natural killer (NK)-cells should be taken into account. Here, HuMAPC were evaluated for their sensitivity to NK-cell mediated lysis and for their immunomodulatory capacities on NK-cell proliferation and effector functions.

Method: HuMAPC (clone B30E2 and bulk SVG) were isolated respectively from bone and bone-marrow and expanded by ReGenesys. To test the lytic potential of NK-cells against allogeneic HuMAPC, purified NK cells were cocultured with HuMAPC at effector:target (E:T) ratios of 1:100 to 8:1. Coculture was followed by an MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. IL-2-induced NK-cell proliferation was assessed of HuMAPC viability using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. IL-2-induced NK-cell proliferation was tested. Addition of HuMAPC to IL-2-induced NK-cell proliferation resulted in a dose-dependent suppression of proliferation. After coculture with HuMAPC, NK-cells showed to have an impaired IFN-γ production and cytotoxic activity upon contact with the known NK-sensitive K562 cell line.

Conclusion: These data indicate that HuMAPC, similar to mesenchymal stem cells, are not lysed by NK-cells, but inhibit NK-cell proliferation and suppress NK-cell effector functions.
930 SIOP ABSTRACTS

Purpose: Evaluate the therapeutic efficacy of allogeneic bone marrow transplantation (allo-BMT) and its safety, in the treatment of high risk malignant hematological diseases in a group of Mexican children.

Method: Clinical trials, not randomized, conducted in the hematopoietic stem cell transplant Unit at the National Institute of Pediatrics. The patients included, were Mexican children with diagnosis of high-risk hematological malignant disorders. Candidates for BMT, were considered according to their characteristics and evolution. The patients included were those who have a survived with less than 25% with conventional treatment over a period of 2 years. The primary impact of variables included time and rate of overall survival (OS) and event-free survival (EFS) and related complications as well as survival to the myeloablative transplantation by itself. A Cox analysis of proportional hazards was performed to assess the impact of different factors on the outcome. (The minimum value considered as significant was $p < 0.05$)

Results: A total of 24 HSC transplanted patients were included but one of them was transplanted twice; among them, 20 (83.3%) were males and 4 (16.7%) were females, of whom 8 (33.3%) were diagnosed as acute myeloblastic leukemia (AML), 9 (37.5%) had ALL, 7 (29.2%) chronic myeloid leukemia (CML). The overall 48-month survival (5 months to 96 months) was 46%, event-free survival, but after this time frame follow-up, the survival was 41%. The main complications post-transplant were infections in 66.6% of cases. The acute graft versus host disease was present in 25% of the cases, only one case was associated with mortality. The major factor influencing ($p < 0.05$) overall survival was the diagnosis of acute lymphoblastic leukemia

Conclusion: Allogeneic stem cell transplantation proved to be an effective therapeutic strategy in treating high-risk hematological malignancies in Mexican children.

PN012

EXTENDING ACCESS TO BONE MARROW TRANSPLANTATION TO LOW-INCOME COUNTRIES: THE PRELIMINARY EXPERIENCE OF THE CURE2CHILDREN FOUNDATION IN PAKISTAN

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Purpose: The Cure2Children Foundation has supported both financially and professionally a network of centers in Pakistan performing BMT for the cure of transfusion-dependent thalassemia with the purpose of assessing transplant outcome and costs in a homogeneous group of low-risk patients (age < 10 years and liver < 2cm) having a matched related donor.

Method: All patients were conditioned with thiopeta 10 mg/kg, busulfan 14 mg/kg and cyclophosphamide 200 mg/kg, followed by GVHD/rejection prophylaxis with prednisone, methotrexate, and cyclosporin. Management standards for therapy, administration, central venous access, severe pancytopenia, immunosuppression, and hospital infection control have been addressed by local training, web-based data management and videoconferencing.

Results: Since August 2009, a total of 21 BMTs have been performed in low-risk patients with a median age of 3.3 years (range 0.9 to 9.7, 10 males and 11 females). At a median follow up of 244 days (range 1-550), actuarial thalassemia-free survival is 89% and overall survival 100%. So far 2 patients had a graft failure and are alive and well after autologous reconstitution. One patient developed grade 3 and 4 mucositis, 17% and 3% purely of the costs.

Conclusion: In low-resource settings safe and effective bone marrow transplantation can be performed with cure rates comparable to more affluent countries but with a fraction of the costs.

PN013

HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION FOR RELAPSED/REFRACTORY HODGKIN'S LYMPHOMA IN CHILDHOOD. 12 YEARS EXPERIENCE IN A PEDIATRIC PUBLIC INSTITUTION IN ARGENTINA

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Purpose: Evaluate ASCT outcomes in Hodgkin's Lymphoma in children.

Method: From 9/1998-12/2009, we performed 81 ASCT. 24 HL pts (30%), male 16/ female 8(r2=1), median age at ASCT was 13 years (7-18y), stage at diagnosis: II 8 pts (33%), III 6pts (25%), IV 10 pts (42%), Bulky disease 6pts (25%), B symptoms 17 pts (71%). Histology: nodular sclerosis 17 pts (71%), mixed cellularity 6 pts (25%), lymphocyte depletion 1 pt (4%). Previous treatments COPP-ABVD 14 pts (59%), AVBD 7 pts (29%), others (12%). 15 patients received additional radiotherapy in involved areas. Rescued protocols: ESHAP 8 pts (32%), IEP/ABVD 7 pts (28%), others 10 pts (40%). Status at ASCT: 1st CR 2 pts, 2nd CR 18 pts, 3rd CR 1 pt and PR 3 pts.

Results: Median time from diagnosis to relapse was 30.4 months, (r 8-83 months.median time to ASCT 8.2 months (r 2-87m).

Peripheral blood stem cell (PBCS) was used in all patients, 15 pts received CPM/G-CSF and 9 pts only G-CSF. Median CD34 was 4,81 x 106/kg (1,45 -17,5) and median TNC was 13,4 x 8/kg (2,4-43,1). Conditioning regimens were CBV in 23 pts (90%) and Bus/Cy/Mel 1pt (4%) Median time neutrophil engraftment (> 500 x 10^9/L) was 10 days (9-33d), and for platelets (> 20 x 10^9/L) 14, 2 days (9-33d). The TRM was 0%. At 120 months the KM probability of overall survival (OS) was 0.66 ± 0.13%, and event free survival (EFS) 0.62 ± 0.13%. for those patients in CR at ASCT, the OS was 0.68 ± 0.14 and the EFS 0.64 ± 0.13, in PR 0.66 ± 0.27 and 0.67 ± 0.27 respectively.log rank NS). Cumulative incidence of relapse: 38%

Conclusion: ASCT in HL in CR or PR is an effective and safe procedure. In our preliminary analysis the status of disease did not impact on the results, but longer follow-up is necessary.

PN014

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SOLID TUMORS. ONE GROUP EXPERIENCE

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Purpose: We analyzed our retrospective one group experience to define the epidemiology in pediatric patients undergoing autologous hematopoietic stem cell transplantation (AH SCT) for solid tumors.

Method: We included all children treated with AH SCT for solid tumors between July 1993 and November 2009. The primary end-points for analysis were patients characteristics, overall survival, relapse rate and transplant related mortality.

Results: Fifty two patients with solid tumors, 0.85% female, median age 9.57 years were included. The main etiologies were Hodgkin Lymphoma (HL) 28.8%, neuroblastoma (NBT) 25% and Ewing sarcoma (EWS) 13.4% patients. The chemotherapy regimen most commonly administered was mephalan-busulfan (42%) and cyclofosfamide-BCNU-etoposide (26%). Sources of stem cells were bone marrow 65.4%, peripheral blood 25% and both 6.8%. Among all patients the mortality related to the procedure was 6.5%, similar to the literature. The general relapse rate was 44.4%, although it varied widely according to the type of solid tumor (HL 11.1%, NBT 40% and EWS 66%). 52.5% of the patients are alive and disease free at a median follow up of 3.4 years.
PO001

KOREAN RED GINSENG: A CANDIDATE PROTECTIVE AGENT FOR CISPLATIN NEPHROTOXICITY BUT NOT MYELOTOXICITY

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Purpose: Ginseng has many beneficial effects on different pathological and physiological conditions such as ischemia, stress and aging. Cisplatin is a widely used chemotherapeutic agent in pediatric oncology that has toxic effects on normal cells. The aim of this study is to investigate protective effect of ginseng of cisplatin nephrotoxicity and myelotoxicity.

Method: Renal tubular epithelial cells and bone marrow cells were prepared from 6–8 weeks rats. Korean Red Ginseng extract was added in these cells at 0.1, 10 and 100 µg/mL concentrations. Cisplatin (20µM) was used in the experiment at the LD50 dose for neuroblastoma Kelly cell line. Korean Red Ginseng extract was added to renal tubular epithelial and bone marrow cells for 48 hours incubations in combination with cisplatin. Cell viability was determined with trypan blue exclusion assay.

Results: Cisplatin decreased the cell viability 80% and 45% in respect to control cells renal tubular epithelial cells and myeloid cell. Ginseng at 100 µg/mL dose with cisplatin decreased the cell viability 50% and 45% in respect to control cells renal tubular epithelial cells and myeloid cell respectively.

Conclusion: Korean red ginseng at 100 µg/mL dose is found to decrease nephrotoxicity but not myelotoxicity in vitro conditions. It might be a possible nephroprotective agent against cisplatin toxicity. In vivo experimental animal models should be searched.

PO002

ANTITUMOR EFFECT OF THE DEHYDROXYMETHYLEPOXYQUINOMIC (DHEMEQ), A NOVEL NUCLEAR FACTOR-B INHIBITOR, IN PEDIATRIC OSTEOSARCOMA CELL LINES

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Purpose: Osteosarcoma (OS) is the most common primary malignant bone tumor, usually developing in children and adolescents, with a high tendency to metastasize. Metastasis is the most frequent cause of death among these patients. NF-kappaB has an important involvement in bone biology, a pivotal role in neoplastic proliferation, mitotic index, and clonogenic survival. Statistic analysis was made by one-way ANOVA and Bonferroni tests.

Method: The effects of DHEMEQ were determinate by assays of cell growth and proliferation, mitotic index, clonogenic assay, invasion and migration using different concentrations of compound on both cell lines and were performed in duplicate at 2 different moments. Statistical analysis was made by one-way ANOVA and Bonferroni tests.

Results: In both OS cell lines, DHEMEQ reduced significantly the growth and cell proliferation in dose- and time-dependent manners and demonstrated significant inhibition of mitotic index and clonogenic capacity. Interestingly, these alterations were accompanied by a significant loss of migration and invasion.

Conclusion: In this study, we showed that inhibition of NF-kappaB by DHEMEQ leads to anti-proliferation and anti-invasion effects in OS cells lines, and could be a promising candidate for molecular target therapy of OS. Further in vivo studies, especially in metastatic models of OS are necessary to confirm our results.

PO003

INHIBITION OF AURORA KINASES DECREASE PROLIFERATION AND SENSIBILIZES GlioBLASTOMA CELL LINES TO GAMMA RADIATION

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Purpose: Glioblastoma multiforme remains one of the most devastating human malignancies and despite diagnostic and therapeutic advances, there are no drugs that will significantly improve the patients' survival. Over-expression of genes Aurora A and Aurora-B have been found in different malignancies, including glioblastomas. In this study, we analyzed the effects of different concentrations of ZM447439 (ZM) (a pan-aurora kinase inhibitor) associated or not with Temozolomide (TMZ) in glioblastoma cell lines TP53 wild-type (U343p53wt) and TP53 mutated (U251p53mut).

Method: The gene expression was assessed by RQ-PCR. Functional studies of cell proliferation, mitotic index, and clonogenic survival were performed in triplicate at 3 different moments. Gamma radiation for clonogenic survival used the doses of 2, 4 and 6 Gy. Statistic analysis was made by one-way ANOVA and Bonferroni tests.

Results: Treatment with ZM e with TMZ inhibited significantly the cell line proliferation in a dose and time-dependent manner in the two cell lines, being the effects more intense in the U251p53mut. The combination of two chemotherapies did not show a synergistic effect. There was a significant decrease in cell lines mitotic index after the treatment, being more intense in U343p53wt. Again, the combination of treatments did not show synergistic effect. The clonogenic capacity was significantly reduced after treatment with ZM, sensitizing both cells to radiation. Interestingly, the U343p53wt was more sensitive for the associations between ZM+ radiation, and ZM+ TMZ treatment combined show a synergic effect in this cell line only, increasing the radiation effects.

Conclusion: These data suggest that inhibition aurora kinases may be interesting targets for future treatment of glioblastoma, and could be used as adjuvant to radiotherapy. Subsequent studies should be conducted to confirm this potential.

PO004

GEMCITABINE-DOCETAXEL FOR PEDIATRIC SARCOMA

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Purpose: We describe experience with gemcitabine-docetaxel (G+D) in patients with relapsed/refractory sarcomas.

Method: 21 patients including 14 Ewing’s (ES), 2 synovial, 1 osteosarcoma, 2 rhabdomyosarcoma and 2 undifferentiated sarcoma, were treated from April 2005 to January 2009, with gemcitabine 1000 mg/m² over 90 minutes on days 1 and 8, and docetaxel 100 mg/m² over 2–4 hours on day 8 of a 21-day cycle. Since October 2006 all newly diagnosed high-risk (pelvic and metastatic) ES patients (n=9) were treated with G+D as maintenance therapy for 3–8 cycles when minimal residual status was achieved after the completion of modified IE protocol.

Results: The patients received a total of 138 cycles of therapy (median 6 cycles; 3–12). Mild toxicities (one grade 3 skin-mucosa and 4 grade 2 myelosuppression) were all
managed in the ambulatory setting. All symptomatic patients (n = 7) responded to the regimen. 11 patients had measurable disease and by RECIST criteria, four (36%) had a complete response (CR), three (27%) had a partial response (PR), two (18%) had stable disease (SD), and two (18%) had progressive disease (PD), providing an objective response rate (CR+PR) of 63%. Ten patients (9 ES and 1 US) had undetectable disease at study entry and were treated with G/D as maintenance regimen. Overall, 3 (14%) of the 21 patients progressed on G/D. Out of the 18 patients who completed the protocol, 10 have either relapsed or progressed when G/D was stopped, median 13 months from protocol entry. For all patients, median duration of response was 19 months (range, 5–42 m). Eleven out of the 21 patients (52%) are alive, median follow-up 46 months from initial diagnosis.

Conclusion: The G+D regimen demonstrated antitumor activity against advanced pediatric (mainly Ewing) sarcomas, allowing for good quality of life. Evaluation in a large, formal phase II trial for Ewing patients is ongoing.

PP005

CDA TESTING: A POTENTIAL BIOMARKER FOR SECURING THE HANDLING OF GEMCITABINE IN PAEDIATRIC ONCOLOGY

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Purpose: Phase II studies have shown that Gemcitabine as part of combinational therapies could be efficient in treating bone sarcoma or Hodgkin disease. Gemcitabine is normally well tolerated. However, early severe toxicities have been described. Genetically driven deregulation of cytidine deaminase (CDA), the enzyme responsible for the liver detoxification of nucleosidic derivatives, has been evoked as a possible culprit for intolerance upon gemcitabine intake. Outstanding response after gemcitabine therapy in a relapsing neuroblastoma patient was hypothesized as being related to CDA deficiency (Moreau et al. PBC 2010).

Method: Screening strategy to establish CDA activities (Ciccolini et al. JCO 2010) can be used to identify cut-offs associated with a deficient status. Screening for the most frequent genetic polymorphisms (e.g., 79A>C, 433 T>C and 208G>A single nucleotide polymorphisms) was performed to establish genotype-to-phenotype relationships with CDA.

Results: 30 patients treated with gemcitabine combined with other cytotoxic drugs (oxaliplatin or taxanes) were included. Mean CDA activity was 3.7 ±2.5 U/mg (1.1–12.2). Distribution of children CDA values was similar to that of adults. No children displayed CDA values below 1 U/mg, the cut-off value associated with a maximum increased risk of developing severe toxicities with gemcitabine in adults. This result is in line with the fact that none of the 30 children displayed early severe toxicities after being administered with gemcitabine. Four out of 30 patients (13%) had a rapid-metabolizer phenotype (e.g., CDA > 6 U/mg) a condition associated with treatment failure in adults administered with gemcitabine (Dahan et al. Asco-GI 2010).

Conclusion: CDA activity can be used to identify patients at high risk of developing early and severe toxicity upon treatment with gemcitabine. Adult CDA cut-off (below 1 U/mg) can also be used in children. Establishment of pediatric normal value of CDA according to age and sex are in progress.

PP001

FIRST REPORT OF INCIDENCE OF CHILDHOOD CANCER IN SUDAN

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Purpose: The epidemiology of childhood cancer in the developed world is well documented. In contrast, incidence of childhood cancer derived from population-based cancer registries (PBCR) has been described from a very few countries in Africa with no previous reports from Sudan. We present the first report of incidence of childhood cancer from Sudan.

Method: The PBCR at Wad Medani, Sudan was established in 2005 and covers the whole of Gezira state which has a population of 3.5 million. All primary neoplasms of malignant behaviour in those aged 0 to 14 years registered during 2006–2008 were included. Incidence rates were expressed per million person years and were standardised to world standard population where appropriate.

Results: 221 children (0–14 years) with cancer were registered during 2006–2008 and the age-adjusted incidence in this age group overall was 48.9 million person years (males 54.9, females 42.9). The incidence for those aged 0–4, 5–9 and 10–14 years was 44.5, 48.1 and 55.5 respectively. The three most common cancers in males and females were leukaemias 27.3%, lymphomas 26.0%, and renal tumours 8.2%. CNS tumours formed only 6.6% of the reported childhood cancer burden. The most common cancers in those aged 0–4 years were leukaemias, lymphomas, retinoblastomas and renal tumours; 5–9 years were leukaemias, lymphomas and CNS tumours; and 10–14 years were leukaemias, lymphomas and carcinomas (mainly nasopharyngeal).

Conclusion: This first report of incidence of childhood cancer provides a baseline for cancer incidence in Sudan as well as for case ascertainment by the new registry. The report incidence of childhood cancer in Sudan is half to one-third of that elsewhere in the world (including Africa). Under-diagnosis and under-ascertainment of cases may be the reasons for this difference.

PP002

LOW BIRTHWEIGHT AND AETIOLOGY OF CHILDHOOD LIVER TUMOURS IN NORTH WEST ENGLAND

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Purpose: Low birthweight is an important indicator of adverse health outcomes. In this study we investigate the weight at birth of children diagnosed with liver tumours (LT) in North West England.

Method: Data on all children under 15 years of age with LT diagnosed 1954–2008 and resident in a geographically defined area of North West England were included. Detailed demographic variables and information abstracted from obstetric records were available. We analysed the distribution of birthweights of the cases as compared to that in the population in England and Wales. Also, we carried out similar analyses after stratifying the data by age at birth (below/above median age at diagnosis), sex, gestational age, year of birth and absence/presence of congenital anomaly.

Results: Birthweight data were available on 4952 (94%) of LT cases, of which 42 were hepatoblastoma (HB) and 7 were hepatic carcinoma (HC). 25 cases had at least one congenital anomaly. The proportion of HB cases below the 5th population birthweight percentile was 17% (P = 0.004). This excess was predominant in males whose gestational age was under 36 weeks and those who were diagnosed above the median age. The proportion of HB cases below the 5th percentile was higher than expected in those without congenital anomaly and in those born after 1940 (P = 0.02). Of the 7 HC cases, 2 (30%) had birthweight below the 10th percentile. On average, children with HC or HB weighed 6/7% less than expected, at birth.

Conclusion: We confirm the previously observed association between low birthweight and HB in our data. The association was strongest for cases without congenital anomalies (non-syndromic), those who were older at diagnosis, born before term and born after 1989. These observations are consistent with an aetiological role for factors associated with neonatal intensive care or other late gestational/early postnatal exposures. This will be explored.

PP003

SMALL-AREA ANALYSES OF BONE CANCER IN GREAT BRITAIN, 1980–2005

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FIRST REPORT OF INCIDENCE OF CHILDHOOD CANCER IN SUDAN

Purpose: The first report of incidence of childhood cancer in Sudan as well as for case ascertainment by the new registry. The report incidence of childhood cancer in Sudan is half to one-third of that elsewhere in the world (including Africa). Under-diagnosis and under-ascertainment of cases may be the reasons for this difference.
**Purpose:** To increase understanding of aetiology of primary bone cancer, principally osteosarcoma and Ewing sarcoma. We specifically aimed to analyse putative associations with deprivation and fluoride in drinking water.

**Method:** Case data on osteosarcoma and Ewing sarcoma diagnosed at age <50 years during 1980–2005 were obtained from all regional cancer registries in Great Britain and the National Registry of Childhood Tumours. Poisson regression was used to examine the relationship between incidence rates and small-area (census ward) population density, Townsend deprivation index (and its components) and fluoride in drinking water.

**Results:** The study analysed 4327 cases of thyroid cancer aged 0–14 years, the ASR increased from 0.2 per million persons per year in 1976–1980 to 4.1 per million persons per year in 2004–2005. We specifically aimed to analyse age, period and cohort effects.

**Conclusion:** Higher incidence of Ewing sarcoma was associated with living in less densely populated areas and greater levels of car ownership, both of which are characteristic of rural areas. This study contributes to the growing body of evidence linking risk of Ewing sarcoma to some aspect of agriculture and suggest further studies of environmental exposures or land use may be informative.

**PP004**


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**Purpose:** To examine temporal trends in the incidence of primary thyroid cancers diagnosed in 0–49 year olds in parts of Great Britain (GB) during the period 1976–2005. We specifically aimed to analyse age, period and cohort effects.

**Method:** Case data on thyroid cancer were obtained from four regional cancer registries in GB (Northern and Yorkshire, North West, Wales and Scotland). Age-standardised incidence rates (ASRs) and 95% confidence intervals (CIs) were calculated. The best fitting negative binomial regression model included age (P < 0.001), sex (P < 0.001) and period (P < 0.001). Non-linear period (P = 0.42) and non-linear cohort (P = 0.71) were not statistically significant. For males aged 0–14 years, the ASR increased from 0.2 per million persons per year in 1976–1980 to 4.1 per million persons per year in 2004–2005. For females, the overall ASR was 12.5 per million persons per year (95% CI: 11.9–13.1). The best fitting negative binomial regression model included age (P < 0.001), sex (P < 0.001) and period (P < 0.001). Non-linear period (P = 0.42) and non-linear cohort (P = 0.71) were not statistically significant. For males aged 0–14 years, the ASR increased from 0.2 per million persons per year in 1976–1980 to 4.1 per million persons per year in 2004–2005. For females, the overall ASR was 12.5 per million persons per year (95% CI: 11.9–13.1). The best fitting negative binomial regression model included age (P < 0.001), sex (P < 0.001) and period (P < 0.001). Non-linear period (P = 0.42) and non-linear cohort (P = 0.71) were not statistically significant. For males aged 0–14 years, the ASR increased from 0.2 per million persons per year in 1976–1980 to 4.1 per million persons per year in 2004–2005. For females, the overall ASR was 12.5 per million persons per year (95% CI: 11.9–13.1).

**Conclusion:** Increase in the incidence of thyroid cancer, which has led to a doubling of the number of cases diagnosed over a twenty year time span. The reasons for this increase are not well understood, but it is consistent with findings from other countries.

**PP005**

**SPACE-TIME CLUSTERING OF CHILDHOOD CENTRAL NERVOUS SYSTEM TUMOURS IN YORKSHIRE, UK**

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**Purpose:** We aimed to test predictions of space-time clustering occurring among childhood central nervous system (CNS) tumours which might arise as a result of environmental causal mechanisms, especially those related to infection. We specifically tested the aetiological hypothesis that a factor influencing geographical or temporal heterogeneity of childhood CNS tumour incidence was related to exposure to an infectious or similarly occurring environmental agent.

**Method:** Information was extracted on individuals aged 0–14 diagnosed with a CNS tumour between the 1st January 1974 and 31st December 2006 from the Yorkshire Specialist Register of Cancer in Children and Young People. Malignant or certain benign CNS tumours were included in the analysis occurring within Group III of the International Classification of Childhood Cancer. Ordinance Survey (OS) eight-digit grid references were allocated to each case with respect to addresses at the time of birth and time of diagnosis, locating each address to within 0.1 km. The following diagnostic groups were specified: ependymoma; astrocytoma; primitive neuroectodermal tumours (PNETs); other gliomas; total CNS tumours. We applied the K-function method for testing global space-time clustering. Tests were repeated using nearest neighbour (NN) thresholds. Kulldorff’s scan statistic identified specific space-time clusters.

**Results:** There was statistically significant evidence of global space-time clustering for PNETs only, based on time and place of diagnosis (P = 0.03 and 0.01 using the geographical distance and the NN threshold versions of the K-function method respectively). Specific space-time clusters were identified for the heterogeneous group comprising all CNS tumours based on both birth and diagnosis.

**Conclusion:** There was evidence for an environmental component to the aetiology of PNETs. The finding of specific space-time clusters for all CNS tumours combined suggests the possibility of a common aetiology.
Conclusion: Central Asia is a bi-populated, vast region in Asia continent, comprising of 5 countries, which gained independence from Soviet Union since 1991. Because of lack of primary information in the field of pediatric oncology in this region, SIOP Asia recently has given priority to this issue. A SIOP Asian subcommittee, has been established since 2007, to shed light to this field of global pediatric oncology.

Method: We searched the web (Google, Pub med, med line and Integrated National Digital Library) extensively with the following key words: Pediatric Oncology, Oncology, Malignancy, Cancer, children, child, Leukemia, tumor, Central Asia, and the names of each country.

Results: We found 32 abstracts. Most of those published in the Soviet era and shortly afterwards, were in Russian, with short abstracts in English, and some even without it. Recent articles are in fluent English, but dealing mainly with adult oncology. We found in total 8 abstracts (25%) in the field of pediatric oncology.

Kazakhstan: Eight out of 12 articles were on adults. There were two epidemiological studies on the risk of cancer (1) and thyroid disease (1) in children living in Semipalatinsk, where Nuclear tests has been carried out, and an Atom Lake created. Two other were on Retinoblastoma.

Kyrgyzstan: Six out of 8 abstracts were on adults, including food contamination with a chemo-encogen. There was an abstract on rare tumors in adolescents.

Uzbekistan: Eight out of 9 abstracts were on adult cancers associated with smoking. One abstract studied Retinoblastoma.

Turkmenistan: Two out of 3 abstracts were on Retinoblastoma.

Tajikistan: None.

Conclusion: Publications coming from this region are limited, and information scarce. So active centers and institutions should be spotted, contacts started, and Language barriers overcome. Regular meetings arranged, and agreements reached on joint projects. E-mail contacts facilitated. Students and professors exchanged. Much work should be done in this regard.

PP008
INCIDENCE RATES AND SURVIVAL TRENDS OF CANCER IN 0–29 YEAR OLDS BY ETHNIC GROUP IN YORKSHIRE, UK

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Purpose: Few studies have examined differences in the epidemiology of cancer between ethnic groups for children and young adults in the UK. We investigated incidence and survival by ethnicity (south Asian or not) across childhood (0–14) and young adult (15–29) ages using a unique specialist cancer register.

Method: Patients diagnosed from 1990–2005 in the former Yorkshire Regional Health Authority were included in the analysis. Ethnicity was assigned using name analysis programs and Hospital Episode Statistics data. Incidence rates (per 1,000,000 person-years) by ethnic group were derived using mid-year population estimates. Poisson regression was used to examine trends in incidence by ethnicity and diagnostic sub-group, adjusting for sex and age. An interaction term between year and ethnicity was added to the model and likelihood-ratio test used to determine whether incidence trends differed for south- and non-south Asians. Survival rates were assessed using Kaplan-Meier estimates and log-rank tests; Cox regression was used to assess the effect of ethnicity on survival, adjusting for age, sex, year, and deprivation.

Results: Overall cancer incidence was similar for south Asians (12.1; 95% CI 10.7–13.5, n = 275) and non-south Asians (12.6; 95% CI 12.2–13.1, n = 3259). For non-south Asians, incidence rates increased on average by 1.5% per year (95% CI 0.8–2.3); the rate of increase for south Asians was significantly higher (7.0%; 95% CI 4.2–9.9). Survival rates were significantly poorer for 15–29 vs. 0–14 year olds (HR = 1.25; 95% CI = 1.09–1.43). A significant increased risk of death was seen for south Asians compared to non-south Asians with leukaemia (HR = 1.64; 95% CI = 1.04–2.58) and lymphoma (HR = 2.26; 95% CI = 1.25–4.11).

Conclusion: The significantly higher rate of increase seen among the Asian population in Yorkshire will result in 3-times higher incidence than non-south Asians by 2020 if present trends continue. Significantly lower survival rates were seen for south Asians compared to non-south Asians with leukaemia and lymphoma, and those aged 15–29 compared to 0–14 year olds.

PP009
HEALTH DISPARITIES RELATED TO ENGAGEMENT IN FOLLOW-UP CARE FOR CHILDHOOD CANCER SURVIVORS

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Purpose: While research has identified differences in pediatric diagnosis and mortality based on gender, age, and race, the role of these factors in engagement with follow-up care after the completion of treatment is not understood. Knowing how these factors contribute to continued engagement in oncology care is important for identifying at-risk individuals who may not be receiving care to monitor for and treat relapses, secondary malignancies, and late effects of treatment. The seriousness of these potential outcomes is underscored by recommendations from the Institute of Medicine and COG guidelines to receive, at minimum, annual cancer-related follow-up care. Thus, the aim of the current study is to identify potential health disparities by examining sociodemographic predictors of engagement in follow-up care for childhood cancer survivors.

Method: The sample includes 300 patients diagnosed with cancer in 2004 and treated at The Children’s Hospital of Philadelphia. Information on sociodemographics (gender, patient age, ethnic minority status, neighborhood distress, distance from hospital, type of insurance), cancer and treatment variables (type of cancer, type of treatment, intensity of treatment, presence of relapse), and follow-up care (total number of annual visits over a 5-year period following diagnosis and after moving off treatment and whether or not patient is seen for a follow-up visit 5 years post-diagnosis and 2 years off treatment) will be gathered through the tumor registry and medical charts.

Results: Hierarchical regressions will test sociodemographic predictors of follow-up care after controlling for cancer diagnosis and treatment variables. Data analysis will be complete by the conference.

Conclusion: Results will extend knowledge on health disparities in pediatric cancer and help identify individuals at-risk for poor engagement who may benefit from intervention (e.g., better doctor-patient communication, help overcoming barriers to coming to clinic, education about long-term risks). Sustained engagement is likely to improve health, quality of life, and psychosocial outcomes.

PP010
INFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS-1 (HIV) AMONG CHILDREN WITH CANCER IN SOUTH AFRICA

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Purpose: In adults, HIV increases the risk of certain cancers known, or thought, to have an underlying infectious aetiology; the impact on the risk of cancer in children is less clear. Relative to adults, there are few published data from analytical studies on the risk of cancer in HIV infected children, primarily because both cancer and HIV infection are less common in children than in adults. Furthermore, unlike adults, the great majority of HIV infected children acquire the virus in the first months of life, while the immune system is developing and prior to exposure to many other immunological challenges. Here we report the results of an audit of HIV serostatus
among children diagnosed with cancer in four paediatric oncology centres in South Africa.

Method: Here we report results of an ongoing study at four paediatric oncology centres in South Africa in which children with suspected cancer are tested routinely for HIV. Odds ratios (OR) were estimated (with adjustment for age, sex and centre) using all children with other cancers and non-malignant conditions as a comparison group (excluding those with Kaposi’s sarcoma and lymphoma, which are known to be HIV-related).

Results: Of 882 children with cancer, 38 were HIV infected (for 12 the HIV status was unknown). HIV was associated with Kaposi’s sarcoma (all 10 cases were HIV infected; p < 0.001) and with Burkitt lymphoma (OR = 46.2, 95% Confidence Interval (CI) 16.4–130.3; 13/33). For non-Burkitt non-Hodgkin lymphoma, 2/59 were HIV infected (OR = 5.0, 95% CI 0.9–27.0). No other cancer type was significantly associated with HIV, including lymphoid leukaemias (OR = 0.4, 95% CI 0.04–2.9; 1/172).

Conclusion: Only Kaposi’s sarcoma and Burkitt lymphoma were significantly associated with HIV infection although results for non-Burkitt non-Hodgkin lymphoma were suggestive. Notably, we did not identify an association between infection with HIV and lymphoid leukaemias, for which an underlying infectious aetiology has been suggested.

PP011

COMPARISON OF METHODS TO EVALUATE NUTRITIONAL STATUS IN A POPULATION OF CHILDREN WITH CANCER IN THE AHOPCA (ASOCIACION HEMATO-ONCOLOGIA PEDIATRICA DE CENTRO AMERICA Y DEL CARIBE) CONSORTIUM

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Purpose: Many anthropometric measures are in common use to assess nutritional status, including height, weight, triceps skin-fold thickness (TSFT) and mid-upper arm circumference (MUAC), often combined with calculated indices such as BMI, weight for height (WFH) and percent ideal body weight (IBW). We considered the arm circumference (MUAC), often combined with calculated indices such as BMI, CDC WFH (WFHC), WHO WFH (WFHW), percent IBW, TSFT, MUAC and serum albumin; as well as a combination of MUAC, TSFT and albumin (MTA) were recorded. We compared the results obtained in the total population and as stratified by height class (< 25th, 25th–75th, > 75th percentile). Anthropometric measures were registered centrally in POND (Pediatric Oncology Networked Database) and analysed centrally by SOPHOLIC (Statistical Office for Pediatric Hemato-Oncology in Low-Income Countries).

Results: High percentages of malnutrition were obtained using TSFT, MUAC, albumin and MTA (58%, 51%, 55% and 82% respectively), while values of about 20% were provided by BMI, WFHC, WFHW and percent IBW. When stratified by height class, children in the 25th–75th centile range were classified as malnourished in the same proportion as the group overall. Short children were more commonly classified as malnourished according to MUAC, albumin and MTA; while tall children were more commonly classified as malnourished according to BMI, WFHW and percent IBW. No differences were observed using WFHC and TSFT.

Conclusion: Arm anthropometric measures appear to be more sensitive than measures of height and weight in identifying malnutrition. The choice of measures may be influenced by the stature of individual children.

PP012

INCIDENCE AND SURVIVAL ANALYSES IN CHILDREN WITH SOLID TUMOURS DIAGNOSED IN SWEDEN 1983–2007

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Purpose: Solid tumours constitute 40% of childhood malignancies. The Swedish Childhood Cancer Registry is population-based and includes all children with cancer reported from the six paediatric oncology centres in Sweden. The aim of the present study was to analyse incidence and survival for children with solid tumours.

Method: We used the new WHO ICC-3 for reclassification of the patients, and age standardized incidence adjusted to the world standard population according to the IARC-1998. Time trend in the incidence data was investigated by use of US NCI Joinpoint regression software, by which the annual percentage change was estimated. The probability of overall survival was estimated using the Kaplan-Meier method.

Results: There were 2487 children (< 15 years) in Sweden diagnosed with solid tumours 1983–2007. The lymphomas constituted 21.9%, nephroblastomas 14.7%, soft tissue tumours 14.5%, neuroblastomas 14.3%, germ cell tumours 10.9%, bone tumours 9.4% and other specified tumours 5.3%. The overall M/F ratio was 1.16. The annual incidence was 65.3 million children. The survival rates at 10 years follow up have improved significantly between the two time periods before/after 1995 (76 vs. 82%, p < 0.01). Of the 2487 patients, 477 died within 60 months from diagnosis. The survival rate for the 1641 patients who were alive at five years follow up was 98.1% after another 5 years, i.e. 10 years from diagnosis and they had a 94.1% estimate of long term survival 20 years after diagnosis. The five most common diagnoses among the 532 dead patients were in descending order: neuroblastomas (24.1% of the deaths), soft tissue sarcomas (18.2%), lymphomas (15.4%), bone tumours (15.2%) and renal tumours (10.9%).

Conclusion: The mean annual incidence of children with solid tumours was 65.3/ million and has been stable during the study period. Survival rate for solid tumours at 5, 10 and 20 years follow up were 80, 79 and 76%.

PP013

CHILDHOOD CANCER IN THE STATE OF SÃO PAULO, BRAZIL: AN ANALYSIS OF MORBIDITY AND FEDERAL GOVERNMENT EXPENDITURE ON TREATMENT

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Purpose: In the state of São Paulo (SP), Brazil, cancer is the fifth most frequent cause of death among children and adolescents. This study aims to describe childhood cancer morbidity and the federal government expenditure with treatment in the state of SP.

Method: A descriptive epidemiological study was conducted, using data from the network of hospital-based cancer registries (RHC-SP) in the period of 2000–2005, for children and adolescents (0–18 years). For the analysis of expenditure, information was obtained from specific governmental databases (SIH and SIA-DATASUS).

Results: 6792 cases were registered in the period (increasing from 1,032 cases in 2000 to 1,160 in 2002). Most cases (54.3%) were diagnosed in males, in the age group 0–4 years (40.2%). The most frequent cancer types were leukemias (27.8%), lymphomas (16.8%) and CNS tumors (13.4%). Eighty-five percent of the patients reside in the state of SP (85.7%). For those patients coming from other Brazilian states, the most common cancers were leukemias (21.1%), CNS tumors (14.1%) and retinoblastomas (13.1%). Individuals residing in the state capital were predominant (28.6%), but a large number of cases coming from the cities of Campinas (3.4%), Guarulhos (2.7%), Ribeirão Preto (2.1%), Piracicaba (1.3%) and São José do Rio Preto (1.3%) was noted. Chemotherapy alone (45.5%) was the therapeutic choice most commonly employed. Median time intervals between first consultation and diagnosis and between diagnosis and beginning of treatment were 2 and 4 days, respectively. Approximately 76,500 hospital admissions for cancer treatment were registered, and the expenditure increased from USD 3.8 million (2000) to 8.7 million (2005), corresponding to an increment of 127%.

Conclusion: The increasing number of new cases registered in the RHC and the augmented federal expenditure on childhood cancer care suggests that the state of SP has ensured access to cancer treatment.
NEUROBLASTOMA INCIDENCE AND SURVIVAL IN COMUNIDADES VALENCIANAS

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Purpose: To describe Neuroblastoma incidence and survival in Comunitat Valenciana (CV)


Conclusion: Incidence rates as the average annual number of cases per 106 person-years, for age-standardized rates (ASRw) the world standard population have been used. NB staging system: INSS. Estimation of observed survival (OS): By Kaplan-Meier method for 4 cohorts of cases by year of incidence (1983–1988; 1989–1994; 1995–2000; 2001–2006), and by age (0–18 months and > 18m-14y). Source of incidence data in Europe: ACCIS project. Incidence rates were compared using the standardized incidence ratio (SIR).

Results: 201 neuroblastoma were registered. Crude rate was 11.6 per 106 and ASRw 14.6. Rates according to age were: 88.4 per 106 (group 9y), 20.5 (group 1–4y), 3.8 (group 5–9y) and 0.8 per 106 (group 10–14y) respectively. INSS Stage in 147 cases: 26 stage 1, 12 stage 2A, 6 stage 2B, 30 stage 3, 64 stage 4, 10 stage 4S. An increase in non-metastatic cases as compared to metastatic cases in latter cohorts is observed.

5yOS for all cases improved from 22% (95%CI: 17–26) in 1983–1988 cohort until 68% (95%CI: 55–71) in 2001–2006 one. Survival improved from 22% (95%CI: 7–38) in cohort 1983–1988 up to 51% (95%CI: 30–72) in cohort 2001–2006 for children > 18m.

Conclusion: 1/The incidence of NB in CV is significantly higher that in Europe, especially for infants. 2/More non-metastatic cases were detected in latter cohorts. 3/ Survival improved clearly along the study period, above all in children older than 18m.
intellectual disability and neurological deficits. The aim of the study was to assess neuropsychological status of survivors of childhood brain tumors. Then the data were analyzed to search for coexisting and differential symptoms of cognitive consequences of brain tumors and learning disability.

**Method:** Psychological testing was performed in 350 childhood brain tumor survivors (various type and localization of tumor) to determine the effect of brain tumors on cognitive outcome. Age at psychological diagnosis ranged from 6 to 26 years. In each case, intellectual and educational abilities were evaluated several times (usually once a year). The patients were examined using a battery of standardized psychological and neuropsychological methods, e.g. Wechsler Intelligence Scale, Benton Visual Retention Test, L. Bender - E. Köppitz Visual Motor Test, analysis of previous educational career and medical history.

Results: in our series, we observed specific cognitive development. Low IQ, eye-motor coordination and lateralization disturbances, grapho-motor development delay, speech, memory, and attention disabilities are most commonly registered. Some of these symptoms are similar to learning disability, but also have differential features. In this cohort specific neurological conditions (e.g. cerebellar cognitive affective syndrome) also observed.

**Conclusion:** Scheme of specific neuropsychological diagnostic procedures including differential and comorbid symptoms of cognitive deficits and learning disability, as well as recommendation for specific psychological rehabilitation for childhood brain tumor survivors will be presented and discussed.

**PQ004**

NEUROCOGNITIVE EFFECTS OF CENTRAL NERVOUS SYSTEM-DIRECTED CHEMOTHERAPY IN NON-HODGKIN LYMPHOMA DISEASED CHILDREN

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**Purpose:** Because the blood-brain barrier serves as a pharmacological barrier, malignant cells can remain in the central nervous system (CNS) despite systemic chemotherapy. Consequently, CNS-directed treatment is an essential part of therapy for Non-Hodgkin lymphoma (NHL). We aimed at this analysis to determine the neurocognitive effects of CNS-directed chemotherapy in children with NHL.

**Method:** In a cross-sectional case control study 20 NHL diseased children as well as 10 healthy siblings (healthy controls) were tested for neurocognitive functions. The selection criteria in NHL diseased children were: 3 years or more after the end of NHL chemotherapy only regimen (no radiotherapy), no anaemia, no CNS or systemic diseases. Both patients and healthy controls were examined for global intelligence quotient (IQ), verbal IQ, performance IQ, attention measures, auditory tests, long and short memory, math skills and academic achievement. Written consents were taken from parents of children before examinations.

**Results:** No decline in global IQ in NHL children compared to healthy controls but there was a significant decline of attention, verbal comprehension and performance IQ. Among 20 NHL diseased children 18 had poor recent and immediate memories while remote memory was normal in 16 children. Young age at diagnosis and treatment intensity were the commonest risk factors.

**Conclusion:** In absence of cranial irradiation, childhood survivors of NHL experience long-term neurocognitive deficits after chemotherapy treatment. Global IQ is not a sufficiently sensitive measure to detect specific CNS deficits in NHL-diseased children. The deficits are mainly present in basic neurophysiological processes of attention and executive functioning.

**PQ005**

APPETITE REGULATING HORMONE CHANGES IN PATIENTS WITH CRANIOPHARYNGIOMA

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**Purpose:** Patients with craniopharyngioma (CP), an embryological tumor located in the hypothalamic and/or pituitary region, often suffer from uncontrolled eating and severe obesity. We aimed to compare peripherally secreted hormones involved in controlling food intake in lean and obese children and adolescents with CP versus controls. CP patients were recruited in KRANIOPHARYNGEOM 2000.

**Method:** Plasma insulin, glucose, total ghrelin and peptide YY (PYY) levels were assessed under fasting conditions as well as 60 minutes after liquid mixed meal in four groups: Lean (n = 12) and obese (n = 15) CP patients, and 12 lean and 15 obese otherwise healthy BMI-, gender- and age-matched controls. Homeostasis assessment of insulin resistance (HOMA-IR), as well as quantitative insulin sensitivity check index (QUICKI) were calculated.

**Results:** Obese CP subjects had significantly higher HOMA-IR, higher baseline and post-meal insulin but lower ghrelin levels, weaker post-meal changes for PYY, and lower QUICKI compared to obese controls. QUICKI data from all CP patients correlated positively with ghrelin and PYY % post-meal changes (ghrelin: r = 0.38, p = 0.023; PYY r = 0.40, p = 0.017) and negatively with standard deviation score BMI (SDS-BMI: r = -0.49, p = 0.002). Tumor growth of 87% obese and 58% of lean CP patients affected the hypothalamic area which was associated with higher SDS-BMI and weaker % post-meal ghrelin changes (p = 0.014) compared to CP patients without hypothalamic tumor involvement.

**Conclusion:** Blunted post-meal ghrelin and PYY responses in obese CP subjects are likely due to their higher degree of insulin resistance and lower insulin sensitivity compared to matched obese controls. Thus, insulin resistance in CP patients seems to affect eating behavior by affecting meal responses of gut peptides. Further studies on
pathermodynamics of eating disorders in CP patients are part of the randomized
mutational trial KRIANPHARYNGEOM 2007 (www.kri phosphoryngem.net).

**PQ006**

**HEPATITIS C VIRUS INFECTION IN CHILDHOOD CANCER SURVIVORS**

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**Purpose:** Childhood cancer survivors who had blood transfusions before 1992 are at
risk of developing HCV infection. We investigated the number of survivors who
underwent screening for HCV infection, the rate of HCV infection in childhood cancer
survivors at risk for transfusion-acquired HCV after cancer therapy, and results of
treatment for HCV hepatitis among these survivors.

**Method:** A questionnaire was sent to 9 hospitals in Japan asking how many childhood
cancer survivors underwent blood transfusions from 1980 to 1992 had been tested for
HCV-antibodies and asking for results of these tests. HCV-antibody positive survivors
identified from that questionnaire were divided into two groups according to whether
HCV-RNA findings were positive or not. We also requested data on results of
treatment for HCV infection among those who tested positive.

**Results:** Of 645 survivors, 444 underwent an HCV-antibody test (68.8%) and 93 of
these 444 (20.9%) showed positive test results. Seventy-seven of these 93 (82.8%)
underwent an HCV-RNA test, and 59 of these 77 (76.6%) showed positive findings.
Forty-seven survivors received therapy for HCV infection, 8 survivors did not, and
data were unknown for 4. In 30 of 44 survivors (68.2%) with positive HCV-RNA, their
HCV-RNA became negative after treatment with interferon or interferon with
recombinant IFN-α (Recom imp)

**Conclusion:** About 30% of survivors who were at risk for transfusion-acquired HCV
in this series did not undergo testing for HCV infection. It is necessary to establish a
program to find childhood cancer survivors who have not undergone this testing so
that HCV can be identified and treated.

**PQ007**

**FOCAL NODULAR HYPERPLASIA OF THE LIVER IN PEDIATRIC SOLID TUMOR PATIENTS: WHAT ARE THE RISK FACTORS?**

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**Purpose:** Focal nodular hyperplasia (FNH) of the liver occurs with increased
frequency in oncology patients. FNH is a rare benign lesion that may be related to the
vascular abnormality. The aim of the current study was to identify the risk factors for
vascular damage induced by completion of tumor therapy and a reaction to localized
bleeding.

**Method:** A retrospective study examined 39 patients of pediatric solid
cancers. A substantial proportion of treated patients had FNH during technetium 99m
scintigraphy (SPECT) and total body irradiation (TBI) for PBSCT. They developed grade 3 liver dysfunction during completion of tumor therapy without
veno-occlusive disease (VOD).

**Conclusion:** FNH appears to be a late complication of an iatrogenic vascular disease in
advanced neuroblastoma patients. High doses of alkylating agents and TBI for
PBSCT should be considered as risk factors for the development of FNH.

**PQ008**

**SPECIFIC BREAST-SCREENING PROGRAM FOR CHILDHOOD CANCER SURVIVORS FOLLOWING EXPOSURE TO IONIZING RADIATION**

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**Purpose:** High percentage of pediatric cancer survivors after ionization radiation (RT)
develops a second cancer that may be the leading cause of death. The aim of this study
was to evaluate the risk of developing breast cancer (BC) following exposure to chest
wall RT for pediatric cancer. We carried out an intensive screening program and
compared the sensitivity of clinical breast examination (CBE), mammography (MX),
ultrasonography (US) for screening of such women. In 2007 RM was introduced in the
screening round.

**Method:** Eightysix women, identified in an institutional database and treated with
chest wall RT+/− chemotherapy for pediatric cancer, accepted to be enrolled in the
program. The median age at the time of RT was 12.5 years. CBE, US, and MX were
performed once a year (2 rounds under 25 years old). Overall detection rate of BC
per year and sensitivity of the 3 diagnostic procedures were calculated.

**Results:** We identified 11 patients with pathologically proved BC, with a median age
at diagnosis and a median interval from RT of 33 and 18 years, respectively. The
overall incidence of BC was 2.9% per year, ten-fold higher than expected in older
women from MX screening. We found a sensitivity of 36%, 64%, and 45% for CBE,
MX, and US, respectively. Three patients had a pattern of micro calcifications detected
by MX as sole finding. After RMN was introduced, 2 cancers were detected only by
RM.

**Conclusion:** In this pediatric series we observed an increased risk of developing BC
occurring earlier compared to general population. Despite breast density in young
women, MX has shown the higher sensitivity when compared with US and CBE.
Further studies are required to evaluate whether an intensive screening for early
detection of BC can provide an effect in terms of saved years of life in such high-risk
group.

**PQ009**

**DETAILED CARDIAC MAGNETIC RESONANCE IMAGING EVALUATION OF CHILDREN UNDERGOING CARDIOTOXIC CHEMOTHERAPY: A FEASIBILITY STUDY**

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**Purpose:** Cardiotoxic chemotherapy is often a standard of care in most paediatric
cancers. A substantial proportion of treated patients will develop subclinical
symptoms of heart failure. Cardiac MRI is recognized as the standard technique in the
evaluation of systolic/diastolic biventricular function and allows an evaluation of the
patient’s cardiovascular anatomy, haemodynamics, myocardial iron overload,
perfusion and viability.

**Method:** 12 children (mean age 8.5 years) with leukaemia (n = 6), neuroblastoma
(n = 1), brain tumor (n = 1), lymphoma (n = 1), retinoblastoma (n = 2),
myelodysplasia (n = 1) were prospectively identified as candidates for chemotherapy.
All were enrolled in a pre-chemotherapy cardiac study through 1) a clinical evaluation, 2) various biomarkers (Troponin, ANF, BNP, and NT-pro-BNP); 3) EKG; 4) an echocardiogram; 5) a cardiac MRI and - when appropriate - 6) an exercise testing.

**Results:** The study was completed in all patients within the first month of diagnosis. The 5 youngest required general anesthesia. Systolic biventricular volumes, mass and function were normal in all patients, with a mean LV EF of 59.7% and RV EF of 48.3%. Diastolic function was assessed through tagging sequences obtained in various planes. Although a perfusion defect was not retrieved in any of these pre-chemotherapy assessments, mild left ventricular myocardial scarriing (4.1%) was frequently identified by gadolinium-enhanced imaging. Aortic and mtral flow were adequately measured in all patients and showed normal LV stroke volumes. No significant liver or cardiac iron overload was detected. Evaluation of the interobserver and intraobserver variability was performed for all MRI variables studied using the Bland-Altman method and confirms that the technique is reproducible.

**Conclusion:** Our preliminary study showed that a detailed cardiovascular evaluation in children undergoing a chemotherapy protocol can be achieved in a reasonable time frame. Diagnosis linked to the exact mechanisms that predict a child's cerebral neurocognitive performance is dependent on the Multidimensional Fatigue Scale (patient/parent version), the Family Impact Module (parent) and a socioeconomic questionnaire (patient). Maximum score of each questionnaire is 100, which indicates best function. Questionnaires were mailed out, participation was voluntary.

**Results:** Forty-five patients were identified, 34 eligible for the study due to upper age limits of the questionnaire. Median age of the study group was 20.5 yrs (range 12–25 yrs). So far responses from 30% of the patients/parents are available for analysis. The Quality of Life Inventory revealed an average psychosocial health summary score of 76.66 (parent) vs. 73.33 (patient). The average physical health summary score was 87.5 (parent) vs. 77.3 (patient). The Multidimensional Fatigue Scale showed an average score of 68.06 (patient) vs. 62.5 (parent). The Family Impact Module showed an average score of 82.5. The majority of the patients (75%) got a college/university degree, but are not employed on the level of their education. Only 50% are in a relationship/married or live independently.

**Conclusion:** The long-term morbidity influences the daily life of the survivors including their families. There is a high perception from the parent regarding their child's difficulties. Aftercare clinics need to address these issues and develop strategies for intervention.

**Purpose:** Essential for cure of childhood ALL is prophylactic treatment of the central nervous system (CNS). However, previous studies confirm the long-term effects of CNS treatment with radiation and/or chemotherapy on general intelligence, memory, attention, and academic abilities that become apparent after completion of ALL treatment. Studies designed to explicate the exact mechanisms that predict a child's risk for brain tissue injury during ALL treatment are needed. This prospective longitudinal study examined relationships among measures of oxidative stress and neurocognitive performance in children receiving treatment for acute lymphocytic leukemia (ALL).

**Method:** Cerebrospinal fluid (CSF) markers of oxidative stress were examined in 76 children treated with either short (4 hours), higher dose (2 g/m²) IV methotrexate (MTX) infusion during consolidation or long (24 hours), lower dose (1 g/m²) IV MTX infusion. Standardized measures of neurocognitive functioning were collected at multiple points throughout chemotherapy.

**Results:** Oxidized phosphatidylcholine (PC) significantly increased throughout the first two years of ALL treatment (Em = 0.660, p = 0.012). Working memory and receptive language skills were affected by IV MTX treatment; children who received a short, higher dose IV MTX infusion demonstrated a significant decline in performance over time. Measures of working memory two years after diagnosis were significantly correlated with CSF markers of oxidative stress throughout treatment (r = 0.404, p = 0.006). Receptive language skills and working memory one year after diagnosis significantly predicted measures of intelligence two years after diagnosis.

**Conclusion:** In this study neurocognitive decline was directly linked to measures of oxidative stress and underscores the importance of monitoring cognitive development in children treated for ALL. Working memory in particular appears impacted by IV MTX dose and/or infusion rate and appears related to the oxidative stress associated with chemotherapy.

**Purpose:** Pediatric low grade glioma (PLGG) is the most common brain tumor in this age group. As shown in many publications the overall survival is excellent, but long term morbidity quite high. Goal of this study was to investigate how these facts can influence their own and their families’ Quality of life.

**Method:** From our institutional PLGG database survivors who have been diagnosed over ten years ago. The following validated PedsQL™ questionnaires were used for the Quality of Life assessment: Quality of Life Inventory (patient/parent version), the Multidimensional Fatigue Scale (patient/parent version), the Family Impact Module (parent) and a socioeconomic questionnaire (patient). Maximum score of each questionnaire is 100, which indicates best function. Questionnaires were mailed out, participation was voluntary.

**Results:** Forty-five patients were identified, 34 eligible for the study due to upper age limits of the questionnaire. Median age of the study group was 20.5 yrs (range 12–25 yrs). So far responses from 30% of the patients/parents are available for analysis. The Quality of Life Inventory revealed an average psychosocial health summary score of 76.66 (parent) vs. 73.33 (patient). The average physical health summary score was 87.5 (parent) vs. 77.3 (patient). The Multidimensional Fatigue Scale showed an average score of 68.06 (patient) vs. 62.5 (parent). The Family Impact Module showed an average score of 82.5. The majority of the patients (75%) got a college/university degree, but are not employed on the level of their education. Only 50% are in a relationship/married or live independently.

**Conclusion:** The long-term morbidity influences the daily life of the survivors including their families. There is a high perception from the parent regarding their child's difficulties. Aftercare clinics need to address these issues and develop strategies for intervention.

**Purpose:** Endothelial dysfunction increases the risk of atherosclerosis. This study aimed to determine endothelial toxicity by calculating brachial artery reactivity (BAR) and carotid intima media thickness.

**Method:** Forty cancer patients in remission and 20 control patients were studied. Cumulative doses of anthracyclines were 100 mg/m² in 19 patients, 100–300 mg/m² in 14 and more than 300 mg/m² in 7 patients. BAR and bilateral carotid intima media thickness were assessed with USG device. Brachial artery diameters were measured at rest and 1 minute after blood pressure cuff occlusion. BAR was calculated as percent change between baseline and after cuff deflation measurements. The results were compared with Mann-Whitney U test.

**Results:** Mean ages were 13.6 ± 3.9 (4–21) and 10.9 ± 4.8 (4–19) years in 40 cancer and 20 control patients respectively. No statistically significant difference was detected between right and left carotid intima media thicknesses of the patients and the control group (p = 0.27, p = 0.07). There was no statistical difference between BAR values of all patients and the control group (p = 0.14). When the patients were allocated according to cumulative anthracycline dose more than 300 mg/m² and control patients (P = 0.003) but there was no significant difference between these groups in terms of carotid intima media thicknesses. Levels of total cholesterol, triglycerides, and blood pressures of the patients and the control groups were in normal ranges.

**Conclusion:** These results suggest that anthracyclines cause endothelial dysfunction, that is particularly evident in patients who received anthracyclines more than 300 mg/m². Brachial artery reactivity seems an earlier finding than carotid artery intima media thickness for indicating vascular endothelial dysfunction.

**Purpose:** Complement polymorphism and self-ordered search: evidence for genetic protection against cognitive late effects in childhood brain tumor survivors.

**Method:** From our institutional PLGG database survivors who have been diagnosed over ten years ago. The following validated PedsQL™ questionnaires were used for the Quality of Life assessment: Quality of Life Inventory (patient/parent version), the Multidimensional Fatigue Scale (patient/parent version), the Family Impact Module (parent) and a socioeconomic questionnaire (patient). Maximum score of each questionnaire is 100, which indicates best function. Questionnaires were mailed out, participation was voluntary.

**Results:** Forty-five patients were identified, 34 eligible for the study due to upper age limits of the questionnaire. Median age of the study group was 20.5 yrs (range 12–25 yrs). So far responses from 30% of the patients/parents are available for analysis. The Quality of Life Inventory revealed an average psychosocial health summary score of 76.66 (parent) vs. 73.33 (patient). The average physical health summary score was 87.5 (parent) vs. 77.3 (patient). The Multidimensional Fatigue Scale showed an average score of 68.06 (patient) vs. 62.5 (parent). The Family Impact Module showed an average score of 82.5. The majority of the patients (75%) got a college/university degree, but are not employed on the level of their education. Only 50% are in a relationship/married or live independently.

**Conclusion:** The long-term morbidity influences the daily life of the survivors including their families. There is a high perception from the parent regarding their child's difficulties. Aftercare clinics need to address these issues and develop strategies for intervention.

**Purpose:** Pediatric low grade glioma (PLGG) is the most common brain tumor in this age group. As shown in many publications the overall survival is excellent, but long term morbidity quite high. Goal of this study was to investigate how these facts can influence their own and their families’ Quality of life.
Results: The questionnaires of 185 CCS (72% response rate) and 1000 general population were analyzed. Median ages of CCS at diagnosis and this investigation are 8 years and 23 years, respectively. In descending order of prevalence of current physical symptoms in CCS were (1) impaired vision acuity (38.8%) (2) any allergy (26.0%) (3) irregular menstruation (24.1%) (4) dizziness (12.4%) (5) dry eye (10.5%), respectively. In comparative analysis of CCS and general population, delayed puberty (OR: 94.9, p < 0.001), suspected infertility (OR: 65.1, p < 0.001), osteoporosis (OR: 51.1, p < 0.001), hepatitis (OR: 33.9, p < 0.001), examination for fertility (OR: 28.2, p < 0.001), GH deficiency (OR: 16.7, p < 0.001), renal dysfunction (OR: 11.0, p < 0.001) were extracted as highly specific physical symptoms.

Conclusion: Although prevalence of common physical symptoms was similar in both group, comparison analysis revealed specific physical health problems for CCS. It indicates many adolescent/young adult CCS might be suffering from ongoing late effects around cancer and its treatment.

PQ015 PROSPECTIVE ANALYSIS OF ANTI-MULLERIAN HORMONE AS A MARKER OF GONADOTOXICITY IN GIRLS TREATED FOR CANCER

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Purpose: Cytotoxic treatment may accelerate oocyte depletion, leading to impaired fertility and premature menopause, but this is difficult to assess in children. Anti-Mullerian Hormone (AMH) is produced by granulosa cells of preantral and small antral follicles. The number of small antral follicles is related to the size of the preantral follicle pool, and therefore AMH represents a cycle-independent marker of ovarian reserve. Outcome studies have demonstrated that AMH levels are lower in female childhood cancer survivors, but this is the first prospective study of AMH in children before, during and after cancer treatment.

Method: 22 females (17 prepubertal), median age 4.4y (0.3–15y) diagnosed with malignancy were enrolled. AMH was measured at diagnosis, after each chemotherapy course, on completion of treatment and during follow-up. Risk of gonadotoxicity was classified as low (n = 2), medium (n = 11) or high (n = 9) based on chemotherapy agent, cumulative dose, and radiotherapy involving the ovaries.

Results: Median pre-treatment AMH was 1.27 (0.11–3.75) ng/ml. AMH then decreased progressively over the first four courses of chemotherapy (to 0.93, 0.39, 0.13 and 0.07 ng/ml respectively, P < 0.0001). At completion of treatment AMH in the medium and high gonadotoxic risk groups was 0.36 (< 0.01–2.25) ng/ml and < 0.01 (< 0.01–0.26) ng/ml respectively (P < 0.001). The medium risk group showed progressive AMH recovery to 1.6 (0.35–3.66) ng/ml within 1 year and 2.03 (0.45–2.72) ng/ml between 1 and 3.6 years after treatment completion. By contrast, the high risk group showed no AMH recovery up to 2.7 years following treatment (median AMH < 0.01 ng/ml throughout, P < 0.05 versus medium risk group).

Conclusion: AMH falls rapidly during cancer treatment in both prepubertal and pubertal girls, and may fail to recover up to 3 years following gonadotoxic therapy. This may be indicative of future reproductive impairment and could improve the provision of information for patients and their families. Long-term follow-up is required.

PQ016 OVERWIGHT INCIDENCE IN ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVORS COMPARED TO GENERAL POPULATION

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Purpose: To investigate physical health status and late effects in adolescent/young adult survivors of childhood cancer.

Method: We conducted a cross-sectional survey with self-rating questionnaires on the current or past health problems for childhood cancer survivors (CCS). General population (matched with age, gender, living area and job to CCS) as a control group was recruited by web-based research using the same questionnaire. Prevalence of current health problems consisted of 72 subjective items, and O square-tests in comparative analysis using self-rating questionnaires were evaluated.

Results: The questionnaires of 185 CCS (72% response rate) and 1000 general population were analyzed. Median ages of CCS at diagnosis and this investigation are 8 years and 23 years, respectively. In descending order of prevalence of current physical symptoms in CCS were (1) impaired vision acuity (41.1%) (2) irregular menstruation (30.3%) (3) any allergy (30.3%) (4) dry eye (18.4%) (5) migraine (16.8%), and physical symptoms in general population were (1) impaired vision acuity (38.8%) (2) any allergy (26.0%) (3) irregular menstruation (24.1%) (4) dizziness (12.4%) (5) dry eye (10.5%), respectively. In comparative analysis of CCS and general population, delayed puberty (OR: 94.9, p < 0.001), suspected infertility (OR: 65.1, p < 0.001), osteoporosis (OR: 51.1, p < 0.001), hepatitis (OR: 33.9, p < 0.001), examination for fertility (OR: 28.2, p < 0.001), GH deficiency (OR: 16.7, p < 0.001), renal dysfunction (OR: 11.0, p < 0.001) were extracted as highly specific physical symptoms.

Conclusion: Although prevalence of common physical symptoms was similar in both group, comparison analysis revealed specific physical health problems for CCS. It indicates many adolescent/young adult CCS might be suffering from ongoing late effects around cancer and its treatment.
**PQ017**

**MYOCARDIAL STRAIN FOR DETECTION OF TREATMENT-RELATED CARDIAC TOXICITY IN ADULT SURVIVORS OF PEDIATRIC CANCER**

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**Purpose:** Strain is a novel echocardiographic measure of regional tissue deformation recently identified in the general (non-cancer) population as more important than ejection fraction (EF) in predicting both cardiac rehospitalization and mortality. Abnormal strain may identify adult survivors of childhood cancer with reduced cardiac function, manifested as reduced exercise capacity, before detectable decline in EF occurs.

**Method:** Adult survivors previously treated with anthracyclines (n = 82, median dose 144 mg/m2, range 48.5–574 mg/m2) and/or cardiac RT (n = 26, median dose 5030 cGy, range 3400–8790 cGy) had 3D echocardiogram with 2D speckle tracking for strain analysis (GE Vivid 7) and evaluation of exercise capacity (six minute walk). Rates of abnormal global strain (> -17%), longitudinal strain (any segment > -13%) and abnormal EF (< 50%) were calculated. Associations with poor exercise capacity (> 15 meters below expected 6-minute walk distance for sex, age and height) were identified using logistic regression.

**Results:** Among 95 survivors (current median age 39.2, range 24.1–55.7; median 37.3 years from diagnosis), 65 (68%) had reduced exercise capacity, 20 (20%) had 3D EF < 50%; 51 (54%) had abnormal global strain and 73 (77%) had abnormal longitudinal strain. As expected, 90% of survivors with EF < 50% also had abnormal strain values (global and longitudinal). However, even among survivors with EF > 50%, 44% had abnormal global strain and 73% abnormal longitudinal strain. In a multivariable model, EF < 50% was not associated with reduced exercise capacity (OR 0.5, 95% CI 0.2–1.9). In contrast, survivors with abnormal 2-chamber longitudinal strain were six times more likely to have reduced exercise capacity (OR 5.9, 95% CI 1.9–18.7).

**Conclusion:** Abnormal strain is prevalent among survivors exposed to cardiotoxic therapy, and in contrast to EF, significantly predicts reduction in exercise capacity. Longitudinal studies will be needed to determine if this regional measure of myocardial function may be useful for early detection of toxicity.

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**PQ018**

**GSTP1 ILE105VAL POLYMORPHISM AND DOXORUBICIN INDUCED TOXICITY IN CHILDREN WITH SOLID TUMORS**

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**Purpose:** Doxorubicin is an anthracycline antibiotic with antineoplastic activity. It is used against a wide spectrum of human cancers but it can induce a dose-dependent cardiotoxicity. Glutathion S-transferase P (GSTP) plays a role in detoxification process of some chemotherapy agents including anthracyclines. GSTP1 Ile105Val substitution lies within the substrate-binding site and it was reported to be associated with altered catalytic activity of the enzyme. The aim of our study was to evaluate the correlation between GSTP1 105 polymorphism and doxorubicin induced cardiotoxicity and hematotoxicity in children with solid tumors in Croatian population.

**Method:** Our study was performed on 46 children with solid tumors treated in Children’s Hospital Zagreb. All patients received doxorubicin chemotherapy. Toxicity was assessed according to the NCRI Common toxicity criteria (version 2.0). The study was approved by the Ethics Committee of the Children’s Hospital Zagreb. GSTP1 polymorphism was analyzed using predeveloped real-time PCR Taqman® SNP genotyping assay.

**Results:** Higher occurrence of cardiotoxicity and hematotoxicity grade 3 were noticed in carriers of GSTP1 minor allele -313G (AG and GG genotypes).

**Conclusion:** This finding supports the thesis that GSTP1 105 SNP alters the catalytic efficacy of GSTP1 and thus can cause severe toxicities to the patient. These results are a part of prospective pharmacogenetic study of correlation of polymorphisms in genes regulating chemotherapeutic metabolism and chemotherapy used for treatment of children with solid tumours in Croatian population. We hope that the results of this project will be used for improvement of antiumour therapy in affected children.
The second neoplasms were Osteosarcoma (5), ALL(3), AML(2), and in 1 each pt. including PNET, Soft tissue sarcoma, Lymphoblastic Lymphoma, Rhabdomyosarcoma, Glioma, colon carcinoma. The mortality was present in 75% of these pt. 6 pt. died of chemotherapy toxicity, 6 pt. with tumor activity, 1 abandon treatment, I alive with tumor activity, I currently under treatment and I alive without treatment and in follow up.

Conclusion: The incidence of SMN is 0.36%. Osteosarcoma and Acute Leukemia (ALL + AML) were the most common (51%). The main related factors associated with SMN were etoposide, cyclophosphamide, doxorubicin, and radiotherapy. The survival was 18.7%. The preventable strategies should include always the knowledge of those factors that might cause SMN, without compromising the survival.

**Conclusion:**

**Purpose:**

- To examine the prevalence of health behavior practices among childhood cancer survivors.
- To identify factors associated with adherence to long-term follow-up care by pediatric cancer survivors treated at UT MD Anderson Cancer Center.

**Method:**

- A 40-year review
- Out of 588 newly diagnosed children less than 18 years-old registered at UTMDACC from 1996 to 2000, a retrospective chart review identified 268 pediatric cancer survivors that were residing in the US and had successfully completed cancer therapy. Demographic (age, race, social history), clinical (diagnosis date, treatments, last follow-up date, etc.), and logistic information (location, health insurance type, status) were collected and analyzed. Descriptive univariate analysis including chi-square and means, and multivariate logistic regression analysis were utilized to examine associations between the information collected in the chart review, and five- and seven-year follow-up status.

**Results:**

- Adherence and active attendance to follow-up five and seven year’s post-diagnosis was 64% and 52% respectively. Descriptive analysis indicated survivors that were African-American, diagnosed with CNS tumors or other (non-sarcoma) solid tumors, underwent only surgery as cancer therapy, or were without private health insurance were associated with being lost to follow-up five-years post-diagnosis (p-values < .05). Furthermore, survivors that were older aged (> 18 years) or diagnosed with other solid tumors (non-sarcoma/CNS tumors) were associated with being lost to follow-up seven years post diagnosis (p-values < .05). Using logistic regression, the five year post-diagnosis multivariate model revealed that those who underwent surgery alone (OR = 2.60, 95%CI = 1.36–4.97), and survivors without private health insurance (OR = 2.58, 95%CI = 1.41–4.74); and the seven-year model identified those older aged (OR = 2.30, 95%CI = 1.27–4.16), surgery alone (OR = 1.92, 95%CI = 1.00–3.69), and survivors without private insurance (OR = 3.09, 95%CI = 1.71–5.60) were more likely to be lost to follow-up.

**Conclusion:**

- The findings in this study show that clinical and socioeconomic factors are associated with diminished adherence to recommended follow-up care, and underscore the importance for developing an effective approach for sustaining follow-up for childhood cancer survivors.

**EVALUATION OF BONE MINERAL DENSITY IN CHILDREN WITH ACUTE LYMBOPLASTIC LEUKEMIA**

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**Purpose:** This study was performed to determine the degree of reduced bone mineral density (BMD) in children with acute lymphoblastic leukemia (ALL) after completion of treatment.

**Method:** Dual-energy-x-ray-absorptiometry (DEXA) was performed in 103 cases of ALL survivors of ALL. BMD measured in spine (L2-L4) and neck of femur. Z Score < -2.5 defined osteoporosis and Z(-1 -2.5) osteopenia.

**Results:** Total patients 103, mean age at study 13.5(5–27) years, males 54(52.4%), females 49(47.6%). ALL L1: 86%, L2: 12%, L3: 3%, PRED B: 88.3%, T-cell: 11.7%, 52% received only chemotherapy and 48% chemo and cranial radiotherapy. The mean interval between end of treatment and time of undergoing BMD was 4.2 had history of fracture. The results of BMD were as follows: In spine normal BMD Z = -1 in 35%, osteoporosis Z(-1 -2.5) in 4%, osteopenia Z(-2.5 -2) in 20%. BMD of femur: normal 51%, osteopenia 34.3%, osteoporosis 14.7%.

**Conclusion:** Most of our patients in this study had reduced BMD. Thus the use of DEXA to evaluate BMD in children with ALL is recommended.

**HEALTH BEHAVIORS AND PREFERENCES OF CHILDHOOD CANCER SURVIVORS**

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**Purpose:** The goal of this study was to identify factors associated with adherence to long-term follow-up care by pediatric cancer survivors treated at UT MD Anderson Cancer Center.

**Method:** Out of 588 newly diagnosed children less than 18 years-old registered at UTMDACC from 1996 to 2000, a retrospective chart review identified 268 pediatric cancer survivors that were residing in the US and had successfully completed cancer therapy. Demographic (age, race, social history), clinical (diagnosis date, treatments, last follow-up date, etc.), and logistic information (location, health insurance type, status) were collected and analyzed. Descriptive univariate analysis including chi-square and means, and multivariate logistic regression analysis were utilized to examine associations between the information collected in the chart review, and five- and seven-year follow-up status.

**Results:** Adherence and active attendance to follow-up five and seven year’s post-diagnosis was 64% and 52% respectively. Descriptive analysis indicated survivors that were African-American, diagnosed with CNS tumors or other (non-sarcoma) solid tumors, underwent only surgery as cancer therapy, or were without private health insurance were associated with being lost to follow-up five-years post-diagnosis (p-values < .05). Furthermore, survivors that were older aged (> 18 years) or diagnosed with other solid tumors (non-sarcoma/CNS tumors) were associated with being lost to follow-up seven years post diagnosis (p-values < .05). Using logistic regression, the five year post-diagnosis multivariate model revealed that those who underwent surgery alone (OR = 2.60, 95%CI = 1.36–4.97), and survivors without private health insurance (OR = 2.58, 95%CI = 1.41–4.74); and the seven-year model identified those older aged (OR = 2.30, 95%CI = 1.27–4.16), surgery alone (OR = 1.92, 95%CI = 1.00–3.69), and survivors without private insurance (OR = 3.09, 95%CI = 1.71–5.60) were more likely to be lost to follow-up.

**Conclusion:** The findings in this study show that clinical and socioeconomic factors are associated with diminished adherence to recommended follow-up care, and underscore the importance for developing an effective approach for sustaining follow-up for childhood cancer survivors.
North America, of patients under 20 years of age diagnosed with primary cancer (PM) from January 1970 till December 2009. Results: Of a total of 2,207 PM patients, 41 (1.8%) were identified with SMN. Among 41 SMN patients, male to female ratio was 1:1.4; median age at PM diagnosis was 9.9 years (range 0.2–19.7). The five commonest PM diagnoses in SMN patients were lymphomas (Hodgkin and non-Hodgkin -29%), central nervous system tumors (CNS-24%), leukemias (ALL – 12%), sarcomas (all types-10%), and neuroblastomas (7%). Radiation therapy (XRT) was administered to 27 (66%) patients. The five commonest SMN diagnoses were carcinomas (41%), CNS (17%), sarcomas (17%), leukemias (7%), and melanomas (5%). Median time to diagnosis from PM to SMN was 10.5 years (range 0.5–27.9). Fifteen (36%) SMN patients are known to be deceased. Two SMN patients developed TMN-one carcinoma of the breast and the other carcinoma of the urinary bladder, 3.1 and 4.7 years respectively, following the diagnosis of SMN.

Conclusion: To our knowledge, this is the first report of TMN as a late sequela of primary cancers in childhood. The reported gradual but progressive increase in SMN calls for a review of the definition of cure as it relates to childhood cancers. Further research into interactions among genetic, radiotherapeutic, and chemotherapeutic factors, all known to induce carcinogenesis, could result in treatment strategies designed to mitigate the onset of SMN and TMN.

DENTAL STATUS AND ORAL HYGIENE OF CHILDREN-SURVIVORS OF MALIGNANT BRAIN TUMORS

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Method: Oral cavity status was assessed in 54 children, 17 girls and 37 boys, aged from 6 to 18 years, who were treated with chemotherapy and whole brain irradiation of malignant brain tumor. Median age at treatment was 5 years, at examination 13 years. There were 9 patients with milk dentition, 25 with mixed and 20 with permanent teeth. Caries incidence (percentage of patients with caries), caries intensity (dmft/DMFT score), oral hygiene based on dental plaque index (OHI-p), and treatment required were evaluated.

Results: Dental caries were observed in 100% of patients. Intensity of dental caries for milk dentition (dmft) was 15.3, for milk teeth in mixed dentition - 6.88 and for permanent teeth (DMFT)-5.28 and in the group with permanent dentition only- 18.3. OHI was satisfactory in the whole group (OHI – 1.95), but for milk teeth OHI was 2.31. The necessity for conservative treatment for milk teeth was 70.4%, in mixed dentition 52.2% for milk and 99% for permanent teeth and 94.5% for permanent dentition. Mean number of teeth with caries was 13.9 out of 20 examined, mean number of teeth for extraction was 4.1. Most teeth with caries which required conservative and surgical treatment were observed in children with milk dentition. Non caries associated dental impairment presenting as white or rusty stains were observed in 68,5% of children. They were localized on the cheek or lip surface, near the cervical region and usually occupying more than one surface of the tooth. Root agenesis and other abnormalities were also observed.

Conclusion: Survivors of childhood brain tumors are at great risk of dental problems including dental caries and non curios teeth impairments. Follow-up of such patients should include regular dental examinations.

LATE MORTALITY OF 5 YEARS SURVIVORS OF CHILDHOOD CANCER.

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Purpose: To assess the late mortality of survivors of childhood solid tumour treated from 1942 to 1986, to compare this mortality with that expected in the general population and to determine its variations over time.

Method: The cohort included 3086 patients who had survived at least 5 years, representing 68159 person-years of observation. Median duration of follow-up was 28 years and median age was 35 years (range: 6 to 65 years) at the end of follow-up. Death rates were compared with the French general population.

Results: There have been 526 (17%) late deaths. Overall mortality was 15.9% [14.5–17.5] and 42.3% [35.3–50.1%] 30 and 50 years from diagnosis. Overall standardized mortality rate (SMR) was 8.2 [7.5–9.0] and decreasing with time, but absolute excess rate increased with follow-up, from 6.6 [5.7–7.6] deaths in excess each year for 1000 patients 5 to 15 years after 1st cancer, to 24.0 [11.9–48.4] 45 years afterwards. The highest SMR was found for survivors with brain tumours (18.7), retinoblastoma (14.0) and Hodgkin’s lymphoma (11.0). Primary cancer was the main cause of deaths during the first years while deaths were largely due to other medical reasons, of which treatment-related causes, after 30 years. The multivariate model indicated that female gender, first diagnosis (brain tumour, Hodgkin’s lymphomas, soft tissue sarcomas other than rhabdomyosarcoma, osteosarcoma, retinoblastoma and other subtypes of cancer), young age at diagnosis were risk factors for late mortality. Radiotherapy was also associated with a risk of late mortality. Despite the fact that interaction between chemotherapy and radiation therapy was not significant, the SMR for combined modality therapy was higher than the product of SMRs for each modality.

Conclusion: With the updated plan of follow-up, this cohort will be a very important resource for assessment of very late mortality of survivors of childhood cancers.

SUBTLE LONG-TERM NEUROPSYCHOLOGICAL DEFICIT DUE TO CHEMO AND RADIOTHERAPY IN CHILDHOOD LEUKEMIA

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Purpose: The increasing survival rate of pediatric oncology patients introduced the study of neurocognitive sequelae by neuropsychological examinations and imaging (focal damage in both white and grey matter, related to brain maturation stages). Recent studies reveal subtle changes in both gray and white matter related to chemoradiotherapy. Our objective was to try to find clues about the relation of mild brain damage and subsequent neuropsychological deficit.

Method: 118 children from 2003 to 2007 were assessed: 24% leukemia, 11% leukemia RT. Mean age: 7, range 0–19 years. Clinical variables: pathology, RT, age at diagnosis, time since diagnosis and sex.

A comprehensive neuropsychological protocol was performed, including 54 cognitive measures, psychopathology (Achenbach) and attention (Conners CPT-II), Statistical analyses (univariate, discriminant analysis, Logistic regression and Categorical Principal Components Analysis) were carried out by using SPSS 17.0 package.

Results: LLA: focal deficit in VIQ, receptive language, working memory and attention related to: early age at diagnosis, more time elapsed and female. LLA:RT: the same deficit areas as LLA with worse scores. These deficits can determine long-term academic, social and work functioning.

Conclusion: Older age at diagnosis is a good protection against neurocognitive deficit in CNS pathologies, not in leukemia patients.

PARENT-DIRECTED INTERVENTION FOR CHILDREN WITH CANCER-RELATED NEUROCOGNITIVE LATE EFFECTS

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**Purpose:** Children treated for cancer experience neurocognitive sequelae. Studies to treat such sequelae have shown mostly small effects that are not sustained. Alternative or complimentary treatments remain necessary. We proposed an intervention directed at parents for the purpose of improving “pro-learning” parenting behaviors and to improve the child’s cognitive outcomes. We hypothesized that parents who received the parent intervention program (PIP) will show increased knowledge of ways to facilitate their child’s learning and greater frequency of “pro-learning” behaviors, and decreased parenting stress, compared to parents in the usual care control (UCC) group. We also aimed to collect preliminary data on the child’s outcomes.

**Method:** Forty-four survivors with cognitive deficits and their parents were randomized to the PIP or UCC arm. PIP Parents participated in 8 training sessions over a 3 month period (Phase 1), and then received phone support over the next 3 months (Phase 2). Parents completed assessments at three timepoints, and children completed testing at baseline and at 6 months.

**Results:** Repeated measures ANOVA found a significant interaction between Parent Knowledge and study arm (F = 14.48; p = .001) with increased knowledge in the intervention group at 3 months, which was sustained at 6 months. This effect was also noted for Parent Efficacy (F = 5.43; p = .009), and for Parent’s “Pro-Learning” Behaviors (F = 4.27; p = .033). Parent stress also improved in PIP relative to UCC (F = 3.90; p = .034). Data analyses for child outcomes were recently initiated and will be completed within the next 3 months.

**Conclusion:** The PIP intervention is effective in improving parents’ knowledge, efficacy, and “pro-learning” behaviors on behalf of their children, and also appears helpful in decreasing parent stress. The effects observed at Time 2 appear to be sustained at Time 3.

**PQ028**

**LOW DEPRESSIVE SYMPTOM AND MENTAL DISTRESS SCORES IN ADULT LONG-TERM SURVIVORS OF CHILDHOOD ACUTE LYMPHOBlastic LEUKAEMIA**

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**Purpose:** Long-term survivors of childhood leukaemia are thought to be at risk of psychological difficulties. We examined the prevalence of depressive symptoms and mental well-being in adult long-term survivors of childhood acute lymphoblastic leukaemia (ALL) at a mean of 20 years after the cessation of therapy.

**Method:** This study included all young adult survivors of ALL treated at Oulu University Hospital in 1971–1994 who were at least 18 years old within 6 months of the invitation. From the 87 survivors that fulfilled the inclusion criteria 74 (85%) agreed to participate in the study. Depressive symptoms were assessed with Beck Depression Inventory (BDI-21) and mental distress with General Health Questionnaire (GHQ-12) among the survivors and 146 healthy controls. Of the 74 survivors (26 male), 46 had been treated with cranial irradiation and chemotherapy while 28 had solely been treated with chemotherapy. The mean follow-up time since diagnosis was 20 years (range 10–32 years). Ten patients had been successfully treated for a relapse and one patient had undergone bone marrow transplantation (BMT) in the first remission. Treatment-related late effects were found by expert rating in 70% and severe late effects in as many as 36.5% of the survivors.

**Results:** BDI scores indicated moderate or severe depression significantly less frequently in the ALL survivors compared to the controls (1.4% vs. 8.9%, p = 0.039). BDI scores indicated no depression in 80.8% of the ALL survivors and 73.3% of the control group. The female ALL survivors obtained lower BDI scores than did the female controls (p = 0.005). No difference was found in GHQ-12 scores between the survivors and the controls.

**Conclusion:** Survivors of childhood ALL report fewer depressive symptoms and equal mental well-being compared to healthy controls. Our findings support the idea that childhood leukaemia survivors’ subjective experience of well-being is possibly affected by reproductive adaptive style.
PR001

THE RELATIONSHIP BETWEEN LEVELS OF SERUM PROINFLAMMATORY CYTOKIN, C-REACTION PROTEIN AND PROCALCITONIN AND BACTERIAL SEPSIS IN FEBRILE NEUTROPENIC CHILDREN WITH MALIGNANCIES

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Purpose: The primary objective of our study was to compare the diagnostic relevance of C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6) and interleukin-8 (IL-8) in various types of febrile neutropenia (FN) such as clinically documented infections (CDI), sepsis, fever of unknown origin (FUO) and microbiologically documented infections (MDI).

Method: We determined serum CRP, PCT, IL-6 and IL-8 in 54 nonfebrile neutropenic patients from 30 pediatric cancer patients whose age ranged from 15 to 191 months old. Diagnostic relevance of the markers were analysed.

Results: Twenty four (44.4%) episodes were CDI, 17 (31.5%) episodes were FUO, 10 (18.5%) episodes were sepsis and 3 (5.5%) episodes were MDI. The levels of PCT, IL-6 and IL-8 were higher in sepsis group than the other types of FN. But the differences were not statistically significant (p > 0.05). Due to the variability of cut-off levels, the possibility of sepsis/bacteraemia was found to be very high (p < 0.05). The cut off levels of CRP and IL-6 were not important for diagnosis of sepsis. But if the level of PCT was > 10 ng/ml or the level of IL-8 was > 200 ng/ml, the possibility of sepsis/bacteraemia was high, but the specificity was low. Negative predictive value of the markers was higher than their positive predictive value.

Conclusion: The levels of PCT, IL-6 and IL-8 are more reliable than CRP level for prediction of sepsis. The negative predictive value of these markers is more reliable for excluding the diagnosis of sepsis.

PR002

CURCUMIN PROTECTS HUMAN OROPHARYNGEAL CELLS AGAINST UPPER RESPIRATORY TRACT BACTERIA IN VITRO - POTENTIAL ROLE FOR PATIENTS WITH CANCER THERAPY INDUCED MUCOSITIS?

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Purpose: Curcumin exerts its anti-inflammatory activity via inhibition of NFkB. NFkB is a main mediator of the mucosal inflammatory response to cytotoxic therapy. Oropharyngeal epithelia and residing bacteria closely interact in inflammation and infection. This in vitro model investigated the effects of curcumin on bacterial survival, adherence and invasion of upper respiratory tract epithelia and studied its anti-inflammatory effect. We aimed to establish a model which could offer insights into the host-pathogen interaction and the possible topical use of curcumin in cancer therapy induced mucositis.

Method: Moraxella catarrhalis (Mcat) and the oropharyngeal epithelial cell line Detroit 562 were used. Time-kill curves assessed the inhibition of bacterial growth. Adherence assays and gentamicin protection assays, respectively, determined the effect of curcumin-preincubation of cells on bacterial adherence and invasion. The synergistic role of secretory IgA (sIgA) on adherence was investigated. Curcumin mediated inhibition of pro-inflammatory activation by Mcat was determined by measuring IL-8, IL-6, GM-CSF, MCP-1, TNFα, VEGF, IFNy, and FGF-2 concentrations in the supernatants using ELISA and LumineX10 technology.

Results: Curcumin was bactericidal at concentrations > 50 μM. Pre-incubation of Detroit cells for 60 minutes demonstrated that curcumin concentrations > 100 μM inhibited bacterial adherence. Together with sIgA, curcumin inhibited adherence at concentrations > 50 μM. Both 100 and 200 μM curcumin significantly inhibited cell invasion by Mcat. Curcumin inhibited Mcat induced pro-inflammatory activation by strongly suppressing the release of IL-8, IL-6, GM-CSF, MCP-1, TNFα, and VEGF in an exposure time and concentration dependent manner. A 60 minute exposure with 200 μM curcumin resulted in complete suppression of all six mediators. There was no inhibitory effect on IFNy and FGF-2.

Conclusion: Curcumin was highly relevant concentrations for topical use - effectively protects human oropharyngeal epithelial cells against the facultative pathogen Mcat by inhibiting bacterial growth, adherence and invasion and by inhibiting pro-inflammatory cell activation in vitro.

PR003

THE ROLL OF PRIMARY CARE IN THE EARLY DETECTION OF CHILDHOOD CANCER. CAN WE DO MORE?

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Purpose: Early detection and treatment of childhood malignancy remains a problem in South Africa. The delay in referral has mainly been attributed to the care givers. However there is often a delay in referral or misinterpretation of clinical signs at the primary care level. The aim of this study is to evaluate the basic knowledge of the danger signs of childhood cancer, the knowledge of the referral pathway and to test any hindrances in this pathway.

Method: All health care facilities within the referral area of the Steve Biko Academic Paediatric Oncology Unit were identified. 20 centres were contacted. The health care professional on duty was questioned according to a standard questionnaire. The question tested knowledge of the danger signs of childhood cancer, the identification and management of basic oncology emergencies and the correct route of referral for a child with suspected malignancy.

Results: The smaller clinics were more difficult to contact. Doctors as expected had a slightly better knowledge with regard to the danger signs and had a clearer understanding of the referral pathway. The referral system was complicated by inability of doctors to make telephonic contact or access to the receiving physician. The referral pathway often meant that children would have to be sent from a primary to secondary and finally to the oncology centre.

Conclusion: Service delivery load, lack of basic knowledge of danger signs and understanding the referral system are all factors that may lead to the delay in patients receiving adequate medical care. These problems can be addressed by simple outreach and education programs. A review of the referral pathway will also help children with suspected malignancy and oncology emergencies to be seen and managed earlier.

PR004

MAINTENANCE OF IMMUNOLOGICAL SAFETY AT IMMUNOCOMPROMIZED CHILDREN, RECEIVING ACCOMPANYING HAEMOTRANSFUSION THERAPY

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Purpose: Increasingly there are reports about posttransfusion graft-versus-host diseases at immunocompromised patients after transfusion of haemocomponents. The purpose was to working out biomonitoring of efficiency of blood components X-ray irradiation for precautions of posttransfusion graft-versus-host diseases at children with acute leukemia, receiving accompanying haemotransfusion therapy.

Method: Whole blood of 25 donors was used as experimental model of transfusion medium. Each sample was analyzed before and after the X-ray irradiation, the delayed effects was studied in 4, 24 and 72 hours. The X-ray irradiation of donor peripheral blood samples was spent on «RadGis» installation (Giardini, Italy) at total dose 25 Gy in 30 minutes.
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Evaluation of viability, immunophenotype and peripheral blood lymphocytes estimation was spent using the multiparameter analysis with stage-by-stage gating on flow laser cytometer fluorometer «Facs Canto II» (Becton Dickinson, USA) with use of viability dye 7-AAD and monoclonal antibodies.

Results: The level of viability cells significantly decreased in donor blood samples right after the X-ray irradiation, continuing to decrease in 4, 24 and 72 hours. Absolute quantity of B-lymphocytes significantly decreased in 4 hours after the X-irradiation which gave evidence of their high sensitivity to X-rays exposure. In 24 hours after the X-irradiation there was a significant decrease in absolute quantity of leukocytes, lymphocytes and T-cells, including their subpopulations (such direct participants of posttransfusion graft-versus-host reaction as T-helpers, T-cytotoxic cells, O-NK-cells). The absolute quantity of NK-cells did not differ essentially in exposed and control donor blood samples (p > 0.05). It referred about their relative radioresistance.

Conclusion: The maximum cellular destruction of T- and B-lymphocytes occurs in 24 hours after irradiation at total dose in 25 Gy. Percentage decrease of viability cells after the X-ray irradiation in the investigated samples can be used as a marker of efficiency of the ray immunocompetent cells inactivation in blood components.

PR005 SEDATION AND ANALGESIA PRACTICES FOR LUMBAR PUNCTURE AND BONE MARROW ASPIRATION IN PAEDIATRIC ONCOLOGY PATIENTS IN INDIA

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Purpose: Repeated lumbar punctures(LP) and bone marrow aspirations(BMA) are part of childhood cancer management. Adequate sedation and analgesia for these procedures in a safe environment is desirable. We evaluate current practice related to this in India.

Method: Clinicians attending the 2nd Annual India Pediatric Oncology Initiative meeting at New Delhi in February 2010 were invited to complete a questionnaire. Questionnaires were also sent to the remaining major paediatric oncology centres not represented at the meeting.

Results: Responses were obtained from 25 centres which manage 15 to 1100 (median 110) new children with cancer per year. Median number of LP and BMA were 10 and 5 per week respectively. LP: In 12% of institutes no local or systemic sedation/analgesia was used. Topical local anaesthesia(LA), injectable LA and conscious systemic sedation/analgesia was used in majority(75±100%) of procedures in 24%, 12% and 36% of institutes respectively. General anaesthesia(GA) was not used. In 64% of institutes additional physical restraint was needed for more than half of the children undergoing the procedure. BMA: Topical LA, injectable LA and conscious systemic sedation/analgesia was used in majority(75±100%) of procedures in 16%, 88% and 52% of institutes respectively. GA was not used. In 48% of institutes additional physical restraint was needed for more than half of the children undergoing the procedure. For both procedures, monitoring after conscious systemic sedation/analgesia was mainly by observation of vital parameters. Pulse oximetry was used in around 50% of centres. Essential supportive equipment (oxygen, suction, bag and mask, endotracheal tube) was available in most/all centres providing conscious systemic sedation/analgesia.

Conclusion: There is varied use of sedation and analgesia for LP and BMA in management of children with cancer in India. Further research is needed to identify the reasons for this. Evidence-based guidelines tailored to local circumstances could address some of these issues.

PR006 ANTIEMETIC MEDICATION FOR PREVENTION AND TREATMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING IN CHILDHOOD: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose: Nausea and vomiting continue to trouble children undergoing treatment for malignancies, despite advances in antiemetic therapies. Optimal paediatric dosing and scheduling of antiemetics remains uncertain. This results in inconsistencies and variation in prescribing, often underpinned by personal preference and experience as opposed to high quality evidence. This systematic review examined pharmaceutical approaches to prevent or reduce anticipatory, acute and delayed nausea and vomiting in children and young people with cancer.

Method: This study is a Cochrane Childhood Cancer Review [DOI: 10.1002/14651858.CD000776]. RCTs comparing pharmaceutical antiemetics and cannabinoids with active or placebo controls in children and young people (< 18 years old) undergoing chemotherapy were included. Searches included CENTRAL, Medline, EMBASE, DARE, PsychINFO and LILACS and trial registries and major conference abstracts. Two researchers independently screened titles and abstracts, resolving disagreements by consensus. Data extraction was checked independently. Further data and clarification of methods were sought from authors. Data were entered on RevMan5. Crossover trials were analysed using paired data where possible. Synthesis was undertaken using generic inverse-variance models.

Results: 844 articles were initially identified, 68 examined in detail and 28 finally included. These studies examined a wide range of different pharmaceutical antiemetics, using different doses and comparators, and reporting adverse events (25 studies), total control of acute emesis (22 studies) or nausea (13 studies). No study reported quality of life. Meta-analysis compared complete control of vomiting with steroid added to 5HT3 antagonists (RR 2.0; 95% CI 1.4 to 3.0, 2 studies), and granisetron 20 microg/kg compared with 40 microg/kg (RR 0.93; 95% CI 0.80 to 1.1, 3 studies). No other meta-analyses were possible.

Conclusion: Our knowledge of the effectiveness of antiemetics to prevent chemotherapy-induced nausea and vomiting in childhood is incomplete and imprecise. Those in our care may continue to receive sub-optimal management until assessment of symptoms, dosing and scheduling of antiemetics improves.

PR007 WHAT PARENTS FACE AS THEIR CHILD IS DYING AND THE ROLE OF CAREGIVERS.

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Purpose: To explore how parents of a terminally ill child deal with two extraordinarily hard realities: 1. Their child is going to die; 2. Their child is still living and needs their support. This clinically driven abstract explores how different parents negotiate psychologically these two realities including the function of anticipatory grief. It considers caregivers‘ roles in the process.

Method: An adaptation of the Dual Process Model of Grief (DPMG) is the theoretical framework used to propose what happens. Parent narratives will illustrate different paths taken. How parents can experience and yet modulate anticipatory grief and different relevant caregiver approaches will be considered.

Results: Parent narratives illustrate how many parents appear able to move flexibly back and forth between the two realities and experience and express feelings appropriate to each reality at different moments. Thus they can be with their child and prepare themselves somewhat for the death of their child. However a few parents deny until the end that their child is going to die allowing no opportunity for anticipatory grief. And a few parents are so grief stricken that they are hard pressed to be with their child as death nears. They appear overwhelmed by anticipatory grief. Individual and situational mediating variables appear involved. Caregivers‘ roles in the process are described.

Conclusion: Most but not all parents do engage in this back and forth process and do experience some but not overwhelming anticipatory grief. Suggestions for caregivers will be given. Research suggests some anticipatory grief helps bereavement later (Rando T. 2000). Sensitive prospective longitudinal research with parents whose child is terminally ill that would continue through bereavement would gather valuable information about whether difficulty moving back and forth between the two realities prior to death indeed predicts complicated bereavement and give valuable information to caregivers about how to help the process.

PR008 FOODBORNE BACTEREMIC ILLNESSES IN FEBRILE NEUTROPENIC CHILDREN

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Purpose: To study the occurrence of bacteremic illnesses that are suspected of food- or water-borne in origin in febrile neutropenic children in a tropical country.

Method: This is a retrospective hospital chart review of all children with cancer or hematological disorders undergoing cytotoxic chemotherapy or hematopoietic stem cell transplantation in the Parkwy Children’s Haematology and Cancer Centre. Those who have documented episodes of bacteremia between March 2007 and January 2010 were included. Cases in which the infection was suspected of food- or water-borne in nature are described.

Results: A total of 21 bacteremic illnesses from 16 children were reviewed. Three (14%) were highly suspected of food-borne in origin. A 17-year-old boy with osteosarcoma had septicemic shock from Sphingomonas paucimobilis after consuming nasi lemak (rice soaked in coconut cream and wrapped in pandan leaf) from a street hawk. A 2-year-old girl with acute lymphoblastic leukemia developed septicemic shock from Chryseobacterium meningosepticum after a sushi meal. Another 2-year-old girl with acute lymphoblastic leukemia presented with Lactobacillus bacteremia that was probably acquired from probiotic-containing beverage. All the infections were cleared with appropriate antibiotics.

Conclusion: Foodborne pathogens are an important source of bacteremic illnesses in febrile neutropenic children in the tropical region. Compared with other pathogens, this source of infection can be readily prevented by strict adherence to food hygiene and dietary restrictions.

PR009

PRESCRIPTIVE TREATMENT FOR MALARIA IS NOT JUSTIFIED IN CHILDREN RECEIVING CANCER CHEMOTHERAPY: PROSPECTIVE STUDY OF 100 EPISODES OF FEBRILE NEUTROPHINIA FROM INDIA

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Purpose: Predominant etiologies of febrile neutropenia (FN) include infections with bacteria, fungi and viruses. Infection with malarial parasite is a possibility in regions endemic for malaria. Presumptive administration of antimalarial for fever is unjustified. Pediatric oncologists practicing in malaria endemic regions can effectively exploit diagnostic tools for malaria for a rational decision.

Method: This is a retrospective hospital chart review of all children with cancer or hematological disorders undergoing cytotoxic chemotherapy or hematopoietic stem cell transplantation in the Parkwy Children’s Haematology and Cancer Centre. Those who have documented episodes of bacteremia between March 2007 and January 2010 were included. Cases in which the infection was suspected of food- or water-borne in nature are described.

Results: A total of 21 bacteremic illnesses from 16 children were reviewed. Three (14%) were highly suspected of food-borne in origin. A 17-year-old boy with osteosarcoma had septicemic shock from Sphingomonas paucimobilis after consuming nasi lemak (rice soaked in coconut cream and wrapped in pandan leaf) from a street hawk. A 2-year-old girl with acute lymphoblastic leukemia developed septicemic shock from Chryseobacterium meningosepticum after a sushi meal. Another 2-year-old girl with acute lymphoblastic leukemia presented with Lactobacillus bacteremia that was probably acquired from probiotic-containing beverage. All the infections were cleared with appropriate antibiotics.

Conclusion: Foodborne pathogens are an important source of bacteremic illnesses in febrile neutropenic children in the tropical region. Compared with other pathogens, this source of infection can be readily prevented by strict adherence to food hygiene and dietary restrictions.

PR011

PAI-1 AS A BIOMARKER OF HEPATIC VENO-OCCULUSIVE DISEASE (VOD) IN WILMS TUMOR (WT) PATIENTS

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Purpose: Hepatic VOD is one of the most severe complication encountered in the treatment of patients with Wilms tumor (WT) with an incidence ranging from 1.2 to 8% in different series. The diagnosis of VOD relies on the same criteria used for patients undergoing bone marrow transplantation. No specific diagnostic biochemical markers of VOD have been identified so far.

Method: In addition to the usual liver function tests we studied an possible alteration in immunocompetent cells, PT, aPTT, fibrinogen, antithrombin activity, D-dimer, plasmagen activator inhibitor 1 (PAI-1) antigen and activity, WT treatment was given according to SIOP 2001 protocol and was based on different combinations of actinomycin-D, vincristine and doxorubicin, according to post surgical stage and histology. McDonald criteria were used for the VOD diagnosis (presence of 2 of the following: jaundice, hepatomegaly and/or right upper quadrant pain, 5% weight gain with/without ascites).

Results: VOD was diagnosed in 5 of 35 patients (14%) All patients had hepatomegaly, weight gain, severe thrombocytopenia, increase of transaminases, and inversion of portal flow. Jaundice was present in 2 patients. Prolonged PT and increased D-dimer levels were observed in all cases, whereas altered aPTT and antithrombin values were present in 4 patients and reduced fibrinogen in 2 patient. An increase of PAI-1 activity (63.7 to 175, normal value < 25 ng/ml) and PAI-1 antigen (43 to 130, normal values < 10 U/L) was evident in all 4 patients treated. The diagnosis of VOD was histologically confirmed in 2 cases.

Conclusion: We have shown that VOD feeding is an effective and acceptable form of nutritional support, whether used as a prophylactic measure or as treatment for malnutrition. PEGs also have the advantages of being an alternative route for oral medications, and allows convenient nutritional support at home.

PR010

IMPACT OF GASTROSTOMY TUBE FEEDING AS SUPPORTIVE CARE IN PAEDIATRIC ONCOLOGY

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Purpose: To study the occurrence of bacteremic illnesses that are suspected of food- or water-borne in origin in febrile neutropenic children in a tropical country.
PR012
SIBLINGS PERCEPTIONS ABOUT PARTICIPATION IN RESEARCH REGARDING THE LOSS OF A BROTHER OR SISTER TO CANCER

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6Dana-Farber Cancer Institute, Pediatric Hematology Oncology Clinic between 1 November 2009 – 2010 PANDEMIC

Purpose: The scarcity of data about bereaved siblings’ may reflect fears about doing research in this population. The aim of this report is to describe bereaved siblings’ perceptions about the experience of taking part in a questionnaire study regarding the loss of a brother or sister to cancer.

Method: Between 2008 and 2009 we surveyed siblings who lost a brother or sister to cancer using a postal questionnaire (174 from Sweden and 59 from two U.S. pediatric cancer centres; response rates of 72% and 42% respectively). Bereaved siblings were 16 years or older and either belonged to families who had lost a child to cancer between 1990 and 2004 and participated in a prior end-of-life study (U.S.) or to any family who had lost a child to cancer between 2000 and 2007 (Sweden). Seven (Sweden) and six (U.S.) questions investigated siblings’ perceptions about participating in the study.

Results: Ninety-eight percent (171 of 174) of the Swedish siblings and 100% (59 of 59) of the American siblings thought it was valuable to conduct such a survey. Most siblings, 82% (142 of 174) of the Swedish and 92% (54 of 59) of the American cohorts, reported it to be a positive experience participating in the study. Twelve percent (21 of 174) of the Swedish siblings and 34% (20 of 59) of the American siblings reported the survey to be a negative experience. Still, 43 of 59 (73%) siblings from the American cohort found their participation to be emotionally beneficial.

Conclusion: The vast majority of bereaved siblings found the study related to the loss of a brother or sister to cancer to be valuable. Even though some reported being negatively affected by their participation, many found the experience to be emotionally beneficial. These findings may encourage further involvement of bereaved siblings in research.

PR013
NOVEL INFLUENZA A (H1N1) INFECTION IN A PEDIATRIC HEMATOLOGY ONCOLOGY CLINIC IN ISTANBUL DURING 2009–2010 PANDEMIC

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Purpose: The novel H1N1 influenza A virus was recognized as a pandemic infection by the World Health Organization in 2009. The infection started in Mexico and North America in April 2009, subsequently spread throughout the world leading to a large number of cases in Turkey. The consequences of H1N1 influenza A virus infection on immunosuppressed patients are not known. To better understand the characteristics of this infection in hematologic patients, we reviewed our experience with H1N1 influenza outbreak at Cerrahpasa Medical Faculty Hospital (CMFH), Pediatric Hematology Oncology Clinic between 1 November 2009–14 January 2010. 

Method: From November 2009 all respiratory samples at CMFH were tested for influenza A by multiplex polimerase chain reaction (PCR) (Seegene RV12 ACE Detection (Seegene, Germany). Patients’ symptoms, signs and medical information were recorded prospectively.

Results: Between November 2009 and January 2010, a total of 156 children from pediatric emergency department, pediatric out- and inpatient clinics in CMFH were tested for H1N1 influenza A, 60 (38.4%) were found to be positive. These included 10 (16.7%) of 56 children with hematologiconcological conditions. Three patients had acute lymphoblastic leukemia, 2 medulloblastoma, 1 acute myeloblastic leukemia, 1 osteosarcoma, 1 soft tissue sarcoma, 1 hepatoblastoma and 1 had hereditary spheroctysis. Fever (100%) and cough (90%) were the most common symptoms. Of 8 patients who were radiographically assessed, 3 (30%) had lower airway disease. Four were inpatients, others were hospitalized. One patient required mechanical ventilation, however he had concomitant invasive fungal infection and this patient died. Eight patients were treated by oseltamivir, all tolerated the drug well. Conclusion: Pandemic H1N1 Influenza caused mild symptoms in children with cancer and/or hematological conditions and was not fatal. This may be associated with decreased cytokine production in neutropenic patients and that this type of H1N1 virus causes less severe infection and mortality.

PR014
VIDEOTELEPHONY: AN INNOVATIVE MODE OF PALLIATIVE CARE SERVICE DELIVERY IN REGIONAL AND REMOTE AREAS.

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Purpose: To identify the role, feasibility and acceptability of in-home telehealth, utilizing web based videoconferencing (VC).

Method: The Queensland Children’s Cancer Centre (QCCC), Royal Children’s Hospital Brisbane (RCHB), is one of the largest tertiary centres in Oceania, receiving referrals from QLD, NSW, NT, PNG and the Pacific Rim. The needs of health professionals and families caring for dying children have been previously identified resulting in handbooks for health workers and families, 24-hour on-call service and incorporation of telemedicine into multidisciplinary patient care. A randomised trial investigating in-home, Internet and personal computer based VC was initiated, but recruitment was challenging. Subsequently, a feasibility and acceptability study of in-home based VC was undertaken.

Results: Demographics identify that the majority of patients live outside the Brisbane Metropolitan Area and receive multidisciplinary, multi-site and coordinated care from a range of professionals. Following the success of the Health Professionals Guide, an updated second Edition has recently been published. Eleven families participated in the feasibility and acceptability study of in-home VC. Twenty-five calls were made by the QCCC nurse with 11/25 including the Paediatric Oncologist. All links provided carer support and 22/25 resulted in changes to symptom management. During the trial period, updated hardware and software was incorporated and all costs of the trial were met by the Study.

Conclusion: Research during palliative care is challenging, with respect to subject recruitment, ethical issues and acceptability. Most patients wish to be cared for in their home environs which can be burdensome for families and local health careers. The QCCC. RCHB has developed multiple strategies to facilitate care, including; an on-call service for health care professionals and families, published guides, teleconferencing and recently in-home videotelephony. These strategies are acceptable to families and health professionals and have broader application across all care parameters and geographical locations.

PR015
LIPOSOMAL AMPHOTERICIN B (L-AMB) TWICE WEEKLY AS ANTIFUNGAL PROPHYLAXIS IN PEDIATRIC CANCER PATIENTS

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Purpose: Invasive fungal infections (IFI) still represent a major cause of morbidity and mortality in pediatric cancer patients. Unfortunately, there are only few data on antifungal prophylaxis in children.

Method: Prospective observational study in children receiving prophylactic L-AMB (2.5 mg/kg twice weekly). Efficacy was compared with a historical control group with comparable age and comparable underlying diagnoses not receiving systemic antifungal prophylaxis.

Results: Overall, 33 high-risk patients (16 boys; mean age: 7 years) receiving 135 episodes of antifungal prophylaxis (EAP) were analyzed. Diagnoses included high-risk ALL and ALL-relapse (n = 9 and 8 respectively), AML/ALL-relapse (n = 10
and 2, respectively), and high-risk NHL (n = 5). Mean duration of neutropenia (< 500/µl) and EAP was 13 and 28 days, respectively. No proven/probable IIFI occurred in patients receiving L-Amb, and only 1 patient was diagnosed with possible IIFI (pulmonary infiltrate). In 47/135 EAPs, febrile neutropenia occurred leading to hospitalization and empiric antibiotic or antifungal therapy. In comparison, 1 proven, 1 probable, and 6 possible IIFIs were seen in 43 control patients not receiving systemic antifungal prophylaxis (P = 0.03 versus patients receiving prophylaxis). Antifungal prophylaxis did not affect the incidence of febrile neutropenia. Adverse events: L-Amb was discontinued in 4 patients because of acute allergic reactions (CTC grade 2 and 3 twice each). No elevation of creatinine > grade 2 occurred, whereas elevation of AST and ALT > grade 2 were noticed in 11 and 23 EAPs, respectively. In 62 episodes of hypokalemia, intravenous substitution of potassium was required in 11 cases; one of these patients had to be hospitalized. Conclusion: Systemic antifungal prophylaxis with L-Amb seems to be safe and might reduce the risk of IIFI. However, prospective comparative trials in pediatric patients are warranted.

PR016

PROPHYLACTIC TAURUROLIDINE USE IN CENTRAL VENOUS CATHETERS OF PEDIATRIC CANCER PATIENTS: A PROSPECTIVE RANDOMIZED STUDY FROM SINGLE CENTER

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Purpose: We aimed to investigate the effectiveness of prophylactic use of taururolidine in preventing catheter-associated bloodstream infections (CABSIs) in pediatric cancer patients with central venous access device (CVAD).

Method: A study was undertaken at our unit with pediatric oncology patients between September 2008 and February 2010. Patients were enrolled either into taururolidine (3 ml, taururolidine 1.35% + Sodium Citrate 4%; Taurolidinck33). TauerPharm GmbH) or, heparin group (3 ml, heparin lock with 100 IU/ml sterile normal saline 0.9%), CABSIs and related complications were recorded.

Results: 49 and 48 patients were enrolled into taururolidine and heparin group respectively. Microorganisms were cultured in 29 catheters in taururolidine group and in 21 in heparin group (p = 0.61) in taururolidine and heparin group respectively. Single Gram (+) agents were detected in 19 catheters, single Gram (-) agents in 3 and multiple Gr (+) agents in 3 catheters in taururolidine group. In heparin group single Gram (+) agents were cultured in 13 catheters, single Gram (-) agents in 3 and multiple Gr (+) agents in 2 catheters. Recurrent infections due to candida species were detected in three patients in heparin group, in two of them concurrent fungemia was present and in one of them the device was removed. In the taururolidine group, in 4 catheters candida species were cultured, Candida tropicalis was detected, in one patient’s port, which was cleared with taururolidine lock in one week, however, the other patient’s catheter was extracted because of fungemia.

Conclusion: According to the results of our study, the prophylactic use of taururolidine does not reduce the number of CABSIs or catheter colonization in pediatric cancer patients. The effectiveness of the taururolidine against Candida species deserves future investigations for more unambiguous deductions.

PR017

EFFECT OF PATIENT RURALALITY, DISTANCE FROM TREATMENT CENTER AND THE USE OF OUTSIDE HOSPITALS AND HOME HEALTH CARE ON CENTRAL LINE INFECTION AND REMOVAL RATES IN PEDIATRIC CANCER PATIENTS

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Purpose: To evaluate the impact of location of patients’ residence and their use of home health care or outside hospital services on central line infection and removal rates in pediatric cancer patients.

Method: We performed a single institution, retrospective cohort study using a database of all central lines placed in pediatric cancer patients from 2000 to 2010. Commute time was estimated using an online mapping program. Rurality was classified using the Rural-Urban Commuting Area (RUCA) coding system. A survey was administered to a subset of patients. Data were analyzed with Fisher’s exact test.

Results: Of 845 lines in the database, 669 and 176 were in patients with “urban” and “rural” residence, respectively. There was no difference in early removal rate based on rural classification (18% both groups, p = 0.87) or travel time (< 1 hour 17.4% (n = 517) versus > 1 hour 17.4% (n = 526), (p = 0.87). 7.8% of early removals were due to infection with no association with rurality or travel time. In survey responders (143 patients, 173 lines), early removal was reported for 19/99 (19%) in patients who reported use of outside hospital care versus 9/74 (12.2%) in those who did not (p = 0.2). 8.1% versus 2.7% were due to infection (p = 0.2) and 30% versus 21.5% of patients reported at least one positive culture (p = 0.3), respectively.

In patients receiving home health care (n = 133), 37 (27.8%) had at least one positive culture, 18 (13.5%) were removed early with 6 (4.5%) removals due to infection. No patients denying home health care (n = 10) had positive cultures (p = 0.06) or early removal (p = 0.36).

Conclusion: “Rural” residence, greater travel time, and utilization of outside hospitals and home health care were associated the infection-related central line removal rate. The trend towards increased line infections in patients receiving home health care is limited by sample size and should be further explored.

PR018

EFFECTS OF ORAL GLUTAMINE SUPPLEMENTATION ON CHILDREN WITH MALIGNANCIES

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Purpose: In this study, we aimed to evaluate the effect of glutamine administration on chemotherapy toxicity in children with hematologic malignancies and solid tumors.

Method: The study was conducted on 38 children with different types of malignancies, aged 3 months–16 years (6.5 ± 4.13) receiving different chemotherapy protocols. Patients also were used as their own controls. Patients received one course of chemotherapy with glutamine and an identical course without. Alternate patients were allocated to have the glutamine with course 1 or with course 2. Patients received glutamine suspension (1 g/m2/dose four times daily) to swallow and swallow on days of chemotherapy administration and 7 additional days. Wong-Baker Faces Pain Scale was administered to all children 1, 5 and 10 days after chemotherapy started. Hematologic parameters and biochemical parameters as well as the occurrence of stomatitis, diarrhea, febrile neutropenia and the need for antibiotic therapy were investigated on the 1, 5 and 10 days after chemotherapy. Data were analyzed with courses with glutamine against courses without glutamine using Student’s t-test, Mann–Whitney U-test and chi-square test. The p values less than 0.05 were accepted as statistically significant.

Results: The comparisons of the parameters measured on the first day of the courses with and without glutamine supplementation revealed no statistical significance. Although there were no statistically differences in the incidence, severity or duration of gastrointestinal toxicity; glutamine supplementation significantly reduced both the development and severity of oral mucositis. There was a significant difference in the face scale score between two groups (p < 0.05). Glutamine supplements significantly reduced the incidence and severity of neutropenia (p < 0.05).

Conclusion: We conclude that oral glutamine supplementation in children with malignancies is feasible and possibly associated with better tolerance to treatment.
950 SIOP ABSTRACTS

Serum samples were examined for total protein, albumin, prealbumin, Se and Zn levels. Relation of these data with each other and clinicopathologic characteristics were investigated.

Results: Of 82 children (32% lymphomas, 13% neuroblastomas, 11% brain tumors; in 34% abdominal location), mean age was 8.2 years (males: females 51:31); 1/3 had rural origins, 70% had low socioeconomic status (SES); 60% had localized disease. Percentages of cases with Z-scores < -2 were: WPA, 2%; HFA, 4.9%; WFH 3.7%; BMI, 6.1%; MUAC, 8.6%; TSFT, 4.9%. Patients with disseminated disease had lower mean Z-scores in all anthropometric parameters but WFH. In patients with low SES mean TSFT Z-scores, in rural origin cases and abdominal tumors mean MUAC and TSFT Z-scores were significantly lower. Mean Z-scores for WFA, HFA, MUAC, TSFT at initial diagnosis and in follow-up were not different. Mean Z-scores for WFH and BMI decreased in the follow-up. In 7.3% of cases initial serum albumin levels, in 54.6% cases initial serum prealbumin levels were low (Rural origins, abdominal primaries, and disseminated disease were related with much lower levels). At initial diagnoses all cases had normal serum Z scores, 51% had low Zn levels. Lymphoma cases had significantly lower mean Zn levels which increased in the follow-up.

Conclusion: For children with cancers, MUAC and TSFT are indispensable for evaluating nutritional status, body weight measurements are misleading. Low serum prealbumin levels indicate ‘occult malnutrition’. Lower SES, rural origin, abdominal primary tumors and disseminated disease are nutritional risk factors. Close monitoring of arm anthropometry and prealbumin levels and planned nutritional support are vital.

PR020

FAMILY CHOICE AT THE END OF LIFE IN CHILDREN WITH CANCER

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Purpose: Analyze the characteristics at the end of life of children diagnosed in our Pediatric Cancer Unit from February 2005 to February 2010 and compare with the cohort from January 1991 to January 2005 to assess changes in the site of death.

Method: Retrospective study of children treated in our unit who die in the last five years. Age at diagnosis, gender, type of tumour, site, age and cause of death, palliative care and time, were analyzed. The statistical analysis was performed by SPSS18.0.

Results: 56 children died (55% boys). Mean age at diagnosis was 7.2 years (S.D 4.5). Most frequent diagnoses were brain tumours 44.6%, ALL 12.5%, bone tumours 10.7%, neuroblastoma 5.4%, rhabdomyosarcoma 3.6%, ANLL 1.8%, lymphoma 1.8%, hemophagocytic lymphohistocytoses 1.8%, others 17.6%. Mean age of death was 10.7 years (S.D 5.8). Cause of death was progression 87.5%, relapse 1.8%, hemophagocytic lymphohistiocytoses 1.8%, others 8.9%. Most of them died at the Pediatric Oncology Unit (46.4%), 34% at home (with hospital support and primary pediatricians), 12.5% at the Intensive Care Unit and 7.1% in other hospitals. Palliative treatment was started in 96.4% with a median of 18 days (1–180 days). Comparing with previous group, we observed an increase of children who died at home (30% vs 13.5%; p = 0.012). Also, hospital support at home has risen during the last five years (2.1% vs 5.4%).

Conclusion: We observed a change in the parent election of the site of death for their children in the last years, increasing the patients who die at home. This fact could be associated with the increasing of children who die in the last years, increasing the patients who die at home. This fact could be rm this observation.

PR021

COMPARISON OF MICROBIOLOGY SURVEILLANCE STOOL CULTURES AND RECTAL SWAB CULTURES IN PAEDIATRIC ONCOLOGY PATIENTS

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Purpose: To compare surveillance rectal swabs and stool cultures in detection of antibiotic-resistant bacteria in paediatric oncology patients. The aim of routine surveillance of gastrointestinal flora is to detect carriage of antibiotic-resistant microorganisms which may cause endogenous septicemia due to gut translocation. Such knowledge may be used to select the most appropriate empiric antibiotics for patients presenting with febrile neutropenia.

Method: We have questioned our practice to check surveillance cultures from rectal swabs only, as a recent study on paediatric ICU patients suggested better detection of resistant organisms from stool cultures. We conducted a prospective study among paediatric oncology patients and cultured stools and rectal swabs collected on the same day or within 14 days.

Results: We cultured 106 paired samples from 46 patients between July and October 2009. Antibiotic-resistant Gram-negative bacteria were isolated from 24 samples (11.3%) including 13 stool samples and 11 rectal swabs. The same resistant organism was isolated from stool and rectal swab in 7 (6.6%) pairs. In 5 (47.8%) pairs resistant Gram-negative organisms were isolated only from stool and not rectal swab (including ciprofloxacin resistant E.coli 3 cases, gentamicin resistant Enterobacter 1 case and cephaparolin resistant Enterobacter 1 case). In 3 (28%) pairs resistance Gram-negative organisms were isolated only from rectal swabs (including Pseudomonas – 2 cases and aminoglycoside resistant E.coli - 1 case). In 1 case different resistant bacteria were followed up in stool and rectal swab. We did not isolate MSSA, MRSA or VRE from any of the samples collected.

Conclusion: This study suggests a benefit from stool samples as compared to rectal swabs in identifying carriage of resistant organisms. Further work using more paired samples is required to confirm this observation.

PR022

END-OF-LIFE EXPERIENCE OF CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT FOR CANCER: PARENT AND PROVIDER PERSPECTIVES AND PATTERNS OF CARE

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Purpose: Because the end-of-life (EOL) experience of children who underwent stem cell transplant (SCT), intensive therapy delivered with curative intent, has not been described, we aimed to evaluate parent and physician perspectives and patterns of EOL care for children after SCT.

Method: Retrospective, cross-sectional survey of 141 parents of children who died of cancer, and primarily received care at one of two tertiary care pediatric institutions (response rate 64%). Children for whom SCT was the last cancer therapy (n = 31) were compared with those for whom it was not (non-SCT, n = 110).

Results: The median (IQR) interval between last cancer treatment and death was 65 (30–127) days (SCT group) and 25 (8–59) days (non-SCT group) (p < 0.001). SCT parents and physicians recognized no realistic chance for cure (RCC) later than their non-SCT peers (parents: median (IQR) 4 (1–822) days before death vs 84 (29–237), p < 0.001, physicians: 16 (2–30) days vs 84 (29–166), p < 0.001). SCT children were more likely to be intubated at EOL (p < 0.001), with less opportunity for location of death (LOD) planning (p < 0.001) or hospice involvement (p < 0.001). They were more likely to suffer highly from their last cancer therapy (p = 0.019), and suffered from more physical symptoms (mean (SD) 3.5 (2.0) vs 2.4 (1.9), p = 0.009) and psychological symptoms (mean 2.2 (1.0) vs 1.5 (1.2), p = 0.005). The 13 SCT children whose parent and physician recognized no RCC > 7 days before death were less likely to be intubated at EOL (p = 0.05) or suffer from breathing difficulties (p = 0.02), and were more likely to have LOD planned (p = 0.02). If the parent’s primary goal was to reduce suffering, their goal was more likely to be achieved if they, along with the physician, recognized no realistic chance for cure at least 7 days before death (p = 0.03).

Conclusion: SCT is associated with significant suffering and less opportunity to prepare for EOL.
Purpose: The Central American Association of Pediatric Hemato-oncology (AHOPCA) was created in 1998 with the participation of specialist from five Central American nations (Guatemala, Honduras, El Salvador, Nicaragua and Costa Rica) aiming to promote inter-country cooperative efforts for research and treatment of childhood cancer in the area. After 13 years AHOPCA has extended to Panama and Dominican Republic and currently has 12 collaborative treatment protocols. In collaboration with the Pediatric Oncology Group of Ontario (POGO) the AHOPCA centers conducted a survey to evaluate current practices of cytotoxic chemotherapy handling aiming to identify main problems and design guidelines based on POGO’s Safety Chemotherapy Handling guidelines.

Method: Data was collected through a checklist assessing aspects related to prescription, preparation, administration and disposal of chemotherapy at AHOPCA centers.

Results: A mean of 860 doses of chemotherapy/month are prepared at AHOPCA centers. A standard chemotherapy form is used in 6/7 (85%) participating institutions. Double control process is performed in 6/7 centers by oncologist, pharmacists, and trained nurses. In every institution chemotherapy is prepared under laminar flow hood. Basic protection equipment is available for preparation in every center. Parents are given verbal and written instructions on oral chemotherapy handling but no protection material is provided due to limited resources. Preparations are labeled according to patients name, drug, dose, route, dilution, and date of preparation but no biohazard/cytotoxic label is affixed. During chemotherapy administration 5/7 institutions compiled with basic protection equipment. Only 6/7 institutions have a protocol to handle chemotherapy spills. A mechanism for incident/error reporting exists in 6/7 centers. Written instructions to handle chemotherapy extrusions are lacking in all institutions.

Conclusion: After 13 years of successful partnership with groups such as POGO, the AHOPCA group has identified the need to improve and standardize the administration of chemotherapy in pediatric oncology.

PR025

MUCOSITIS PREVENTION: EFFICACY OF SUPERSATURATED CALCIUM AND PHOSPHATE SOLUTION IN HIGH RISK PAEDIATRIC ONCOLOGY PATIENTS

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Purpose: Mucositis remains a major morbidity with intensive chemotherapy regimens. Prophylactic supersaturated calcium and phosphate mouthwash solution (Caphosol) taken prior to chemotherapy administration, may prevent or lessen mucositis severity. Present evidence in paediatric practice is very limited. In order to assess the possible benefit of this solution in high risk patients for mucositis, 50 patients were identified and Caphosol prescribed. Preliminary audit data is reported, upon which power calculations for future definitive randomized controlled trials could be based.

Method: Audit department approval was obtained (3222). Inpatients prescribed Caphosol were those receiving anthracyclines, methotrexate, cytarabine containing regimens and transplant patients. Presence and grade of mucositis (WHO scale) for each cycle of chemotherapy, with or without Caphosol, and in a historical group receiving similar chemotherapy, was determined.

Results: Twelve patients received Caphosol; 10/12 (84%) tolerated the mouthwash, 2 (16%) found the taste unpalatable. The 12 patients received 45 cycles of chemotherapy; 27 with Caphosol (60%). Sixteen cycles of chemotherapy were complicated by mucositis, 7 in those taking Caphosol (25.9%), 9 in those not (50%). Poor compliance with Caphosol was noted in 2 individuals in cycles where mucositis occurred; other cycles with good compliance were not associated with mucositis in these patients. Historical controls (7 patients with Ewing’s) were evaluated: mucositis was noted in 14/42 cycles (33.3%).

Conclusion: Compliance was difficult in the 1st cycle of chemotherapy as patients had not experienced mucositis. Once this had occurred, compliance improved significantly, and the prophylactic aspect of Caphosol was appreciated. In a targeted, high risk population, compliance with a preventative treatment of supersaturated calcium and phosphate mouthwash may reduce the incidence of mucositis. A randomized controlled trial is needed to fully determine efficacy. Based on this data, a sample size of 103 chemotherapy cycles per arm would provide a 95% chance of demonstrating a difference (α = 0.05).

PR026

COLLABORATIVE INTERNATIONAL TRIAL OF AMPHOTERICIN B LIPID COMPLEX FOR TREATMENT OF INVASIVE FUNGAL INFECTION IN PEDIATRIC HEMATOLOGY AND ONCOLOGY PATIENTS

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Purpose: A retrospective cross-sectional mail survey was conducted among 124 parents of the 62 children who deceased between November 2004 and November 2008 while supported by the KITES-team. Parents were informed about the study aim and design and were only included when they provided written informed consent to participate.

Results: Sixty-four of the 124 contacted parents consented to participate, of which 47 (73.4%) completed and returned the questionnaire. Most parents found that different professional caregivers were sufficiently involved in the palliative care. Eighty percent of parents reported that their child died at home, 93.3% that their child died at the planned place, and 91.1% was satisfied with the actual place of death. All parents indicated that care was available to them 7 days per week and 24 hours per day and 80.0% thought the KITES-team was involved on time. The great majority of parents (respectively 93.1% and 85.7%) perceived quality of care delivered by home nurses and general practitioners as good or very good. For 89.7% and 87.2% of parents, the home nurse and the general practitioner usually or always paid attention to their needs. Ninety-six percent of parents would use the KITES-team again, and 90.7% were satisfied with the general course of their child’s end-of-life period.

Conclusion: Support as delivered by the KITES-team is related to high levels of satisfaction amongst bereaved parents, and represents a feasible model for appropriate pediatric palliative home care.
A comparative study of single dose oral ondansetron and granisetron in prevention of chemotherapy induced nausea and vomiting in children with acute lymphoblastic leukemia

Purpose: We performed our study to evaluate safety and efficacy of different amphotericin B (AmB) preparations for treatment of invasive fungal infection (IFI) in pediatric hematology and oncology patients.

Method: It was a retrospective multi-center trial conducted in seven Russian and Ukrainian hospitals. 224 children with aplastic anemia (7), leukemia (181), lymphoma (26), hemophagocytic lymphohistiocytosis (1) and solid tumors (9) were included in our study. IFI demanding AmB administration during development of the neutropenia; the diagnosis of IFI was produced according to EORTC-MSG criteria. It was proven in 5 patients, probable - in 30 cases and possible in 144. All patients were separated into two groups. AmB lipid complex (ampholip) (ABLC) dosed at 1-5 mg/kg/d was used for treatment of IFI in 112 children, conventional deoxycholate AmB (cAmB) dosed at 0.5–1.5 mg/kg/d was used for another 112 children.

Results: The efficacy of therapy was evaluated as a rate of fever and infectious lesions resolution. Complete response was achieved in 93 cases (83%) in 8.8 days of ABLC group and in 84 cases (75%) in 6.2 days of cAmB group. The difference was insignificant (p = 0.075). Nephrotoxicity (increase of serum creatine and urea levels) was revealed in 25 cases (22%) among the patients of ABLC group and in 66 cases (59%) among cAmB group (p = 0.0). Electrolyte disorders were revealed in 28 patients (25%) of ABLC group and in 71 (63%) of cAmB group (p = 0). ABLC was used with nephrotoxicity in background in 25 cases, in 23 (92%) of them it was effective, and we observed a normalization of creatine serum level to the day 10 of ABLC course.

Conclusion: ABLC (ampholip) demonstrated a reduced incidence of nephrotoxicity and electrolyte disorders and the same efficiency in comparison to cAmB.

PR027

IDENTIFICATION OF EDUCATIONAL AND INFRASTRUCTURAL BARRIERS TO PROMPT ANTIBIOTIC DELIVERY IN FEBRILE NEUTROPENIA: A QUALITY CONTROL PROJECT

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Purpose: Prompt antibiotic administration in 60 minutes is considered standard of care in febrile neutropenia (FN), but anecdotal evidence suggests this benchmark is often missed. Few studies have examined the prevalence of or reasons for antibiotic delay. We describe the median time to antibiotic administration, as well as barriers and predictors of delays in order to suggest future interventions.

Method: Using LEAN techniques, adapted from automotive industry methods designed to identify system inefficiencies, a trained moderator conducted group interviews with representatives from all groups involved in the emergency care of neutropenic children. Consensus on barriers to prompt antibiotics was sought. Independently, a random sample of 50 episodes of FN presenting to the ER between December 2008 and November 2009 were subject to chart review. Triage time, initial MD assessment, reporting of lab results and antibiotic administration were recorded. Patient, family and ER variables were examined as possible predictors of delayed administration.

Results: The LEAN process identified important areas of delay and several misunderstandings between hospital departments, leading to interventions including the development of an ER pre-printed order sheet for FN. The chart review showed a median time of 216 minutes from triage to antibiotic administration (interquartile range [IQR] = 151–274). The time of greatest delay occurred between the lab reporting bloodwork results and antibiotic administration. Only season significantly predicted time to antibiotics, with longer times seen in the fall (Median = 263 minutes, IQR 218–294; P = 0.04).

Conclusion: This study has shown that time to antibiotic administration in children with FN greatly exceeds our one hour benchmark. The chart review and the LEAN process suggested targets for both educational and infrastructural interventions, including a pre-printed order sheet and targeted nursing education. Extra resources may be justified during the fall. Our methodology represents a model in improving process efficiency and developing “best-practice” benchmarks at pediatric oncology institutions.

PR028

PAIN MANAGEMENT AND OPIOID USE IN PAEDIATRIC ONCOLOGY IN INDIA: A QUALITATIVE APPROACH

Afiful Islam

Bangladesh: A qualitative approach

Purpose: To compare the efficacy of orally administered ondansetron and granisetron to prevent chemotherapy induced nausea and vomiting.

Method: A prospective, randomized, double blind, single center study was conducted on a total number of 60 children with ALL receiving high dose methotrexate (2gm/m2) and who had not received antemetic in last 24 hours. To conceal allocation, ondansetron and granisetron were supplied with a code number (1–60) and the drugs were randomized along with the code number. The patients and investigators were not aware of which drug they received until the end of the analysis. Thirty children received ondansetron (4mg) and 30 children received granisetron (1mg) orally half an hour before starting chemotherapy. The patients were followed up from day 1 to day 5 of chemotherapy. The number episodes of nausea and emesis were recorded every 24 hours and specific scoring according to modified MANE scale was done.

Results: There was no significant difference between the two treatments in terms of complete control of acute nausea and vomiting in the first 24 hours after chemotherapy. Twenty seven patients (90%) in the granisetron group versus 21 patients (70%) in ondansetron treated group achieved complete control of CINV. The minimum score of vomiting for ondansetron treated patients was 1.07 ± 2.17 observed on day 4, whereas that of granisetron treated patients was 0.07 ± 0.37, the difference was statistically significant (P < 0.05). In terms of the requirement of additional doses, the difference between the two groups was statistically significant (p = 0.012) on day 2. In this study 3% patients had anticipatory nausea, and subsequent vomiting. Common adverse event such as headache were observed in both the treated groups.

Conclusion: Single dose of oral granisetron is able to prevent acute as well as delayed nausea and vomiting caused by a moderately high emetogenic chemotherapy.

PR029

PARENTERAL NUTRITION IS NOT SUPERIOR TO REPLACEMENT FLUID THERAPY FOR THE SUPPORTIVE TREATMENT OF CHEMOTHERAPY INDUCED ORAL MUCOSITIS IN CHILDREN

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Purpose: Many pediatric oncology centers apply parenteral nutrition (PN) in children with severe oral mucositis after chemotherapy. However no convincing data exist to support this treatment strategy. The aim of our study was to elucidate a possible advantage of PN versus intravenous replacement fluid therapy (FT).

Method: In a prospective randomized study 30 children with mucositis WHO grade IV were assigned to receive either PN or intravenous replacement fluid. Weight, total body water, fat free mass (measured by impedance analysis) and peripheral white blood cells were assessed daily. For aspects of quality of life and economics, the advantages of PN versus FT were assessed.

Results: Children with PN gained body weight significantly compared to baseline (p < 0.001, day 10 versus day 1) and to FT (p < 0.005) due to an augmentation of fat mass while total body water and fat free mass significantly decreased (p = 0.066 and 0.02 respectively). In children with FT, body weight remained stable while total body water and fat free mass significantly increased (p = 0.034 and 0.03), thereby loosing fat mass. We observed no differences in recovery of peripheral white blood cells (WBC) (p = 0.865), incidence of infections (p = 0.136), hospitalization time (p = 0.817), days on intravenous antibiotics (p = 0.53), days on opioid analgesics (p = 0.345) and delay of the next scheduled chemotherapy cycle (p = 0.627).

Conclusion: Although children with PN gained weight in form of fat mass, this did not translate into a clinical benefit for the patients such as earlier recovery of WBC counts, shorter hospitalization time, a decreased use of analgesics or less delay of the next scheduled chemotherapy cycle. Our findings therefore do not support the hypothesis that PN is superior to FT.
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Purpose: Palliative care in India is poorly developed, and opioids consumption for pain relief is very low. Qualitative inquiry was utilized to identify obstacles to opioids use and optimal pain management in Paediatric Oncology.

Method: The project was part of a collaboration between Indian and Canadian Institutions, and was carried out by a Paediatric Haematology/Oncology fellow during an elective rotation. Semi-structured interviews were conducted with oncologists working in a dedicated paediatric oncology setting. A mixed sampling strategy was used, including maximum variation, confirming and disconfirming cases, and snowball. Where available, palliative care specialists were interviewed. Interviews were audio-recorded, transcribed verbatim and analyzed using a thematic analysis methodology. Key informants were identified in the hosting Institutions.

Results: Twenty-three interviews were carried out, representing 17 Institutions (8 private, 9 governmental or charitable) from 6 cities in 3 states. Main problems reported were: 1. poor access to opioids; 2. insufficient human resources (very low nurse and physician/patient ratio, shortage of beds); 3. inadequate education of health-care providers on pain management; 4. nurses’ organization (lack of specialized oncology-trained nurses and of a dedicated paediatric oncology nursing team); 5. cultural issues (morphine associated to death, fear of addiction or side effects, belief that pain is unavoidable associated to cancer and cannot be relieved, poor awareness of signs of pain in children). Children from rural areas, governmental hospitals, and lower socio-economic classes appeared to be disadvantaged. A significant inequality gap was highlighted between few private Institutions, where state-of-the-art treatment was provided, and the average Institutions.

Conclusion: The study illuminates the complexity of pain management in paediatric oncology in India, in which poor availability of opioids and financial constraints play a dominant role, but lack of education among health-care providers and parents emerged as an important contributing factor. Urgent interventions are needed, and some are currently being planned.

PR031

INFLUENZA A (H1N1) INFECTION IN CHILDREN WITH CANCER

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Purpose: In 2009, a new subtype of influenza virus, the H1N1 caused a world pandemic. Patients with comorbidities as immunosuppression may develop serious clinical presentation with respiratory failure.

Method: Between July and October 2009, we had 1,727 consultations in the pediatric oncology department. All patients/pt) with flulike symptoms received oseltamivir after nasopharyngeal swab for respiratory virus was collected.

Results: 25 cases of flu syndrome were diagnosed in 24 pt, 11/13 female/male ratio, median age 5 years old (range 2–15y). 18/25 (72%) had acute lymphoid leukemia (ALL), 2/25 acute myeloid leukemia (AML), non-Hodgkin lymphoma, rhabdomyosarcoma, lissocytosis and primitive neuroectodermic tumor in one each case. 5/25 (20%) were H1N1 positive, all had leukemia. 3/5 pt had no neutropenia and showed good clinical outcome after 5 days of oseltamivir. 2/5 pt had pancytopenia and interstitial bilateral pneumonia at diagnosis. These two pt received oseltamivir for 14 days and wide range antibiotics therapy, including to atypical germs and Pneumocistis carinii. A 14 years old girl with AML on pancytopenia and interstitial bilateral pneumonia at diagnosis. These two pt had good clinical outcome after 5 days of oseltamivir. 2/5 pt had neutropenia and showed good clinical outcome after 5 days of oseltamivir. 2/5 pt had pulmonary failure in the 5 day of hospitalization needing high ventilator parameter. She died after 19 days of hospitalization with multiple organ failure. A 3-years-old girl with ALL at induction phase of treatment (Granulocytes: 150/mm3) needed high ventilator parameter in the third day of hospitalization and lasted for 30 days. She was released from hospital after 2 months in intensive care unit with lung fibrosis. None of these two pt presented positive hemoculture during hospitalization.

Conclusion: This influenza virus, H1N1, in children with cancer presented worse evolution when associated with neutropenia. Lung involvement showed difficult management and was the main complication factor.

PR032

EFFICACY OF PHOSPHATE BINDER SEVELAMER IN CHILDREN WITH HYPERPHOSPHATEMIA DUE TO TUMOR LYsis SYNDROME

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Purpose: Hyperphosphatemia is a known complication of tumor lysis syndrome (TLS). Sevelamer hydrochloride, a phosphate binder, has not been extensively used in children. We looked at the efficacy of Sevelamer in pediatric oncology patients with hyperphosphatemia due to TLS.

Method: Charts of all newly diagnosed children with malignancy developing hyperphosphatemia (age-related values) in the days following induction chemotherapy were reviewed from Oct 2007 to December 2009. All received hyperhydration, Allopurinol and Sevelamer. Efficacy was assessed by decrease in phosphate level, calcium-phosphate product and TLS score as per Cairo Bipho definition.

Results: Twenty patients younger than 16 years of age were included in the study. Four children requiring dialysis were further excluded from analysis. The remaining 16 patients had T-cell ALL/NHL (n = 4), pre-B ALL (n = 4), Burkitt lymphoma (n = 3), biphenoypathic leukemia without TLS in 7. Two received Rasburicase. Sevelamer dose was given according to weight, most often 400 mg twice to thrice daily. No significant toxicity occurred. Mean phosphatemia decreased from 7.8 ± 2.6 mg/dL (95% CI 6.4–9.2) to 6.0 ± 1.6 (95% CI 5.2–6.8) in 24 hours (p = 0.02), 5.7 ± 2.1 mg/dL (95% CI 4.3–6.9) in 48 hours, 4.8 ± 2.1 mg/dL (95% CI 4.0–5.5) at 72 hours and 3.9 ± 1.0 mg/dL (95% CI 1.9–5.8) at 96 hours. Hyperphosphatemia subsided within 24 (n = 3), 48 (n = 5), 72 (n = 3) or 96 hours (n = 5) in all patients. Mean calcium-phosphate product decreased from 60.5 ± 15.1 mg/dL (95% CI 54.1–69.9) to 50.6 ± 10.7 (95% CI 43.2–51.2; p = 0.002) in 24 hours, 44.9 ± 18.0 in 48 hours and 41.8 ± 14.5 in 72 hours. TLS score was corrected in 96 hours in all patients.

Conclusion: Sevelamer is efficacious and safe in children with malignancy-associated hyperphosphatemia.

PR033

INTERLEUKIN 6 AND PROCALCITONIN ARE GOOD EARLY MARKERS OF SEPSIS IN CHILDREN WITH FEBRILE NEUTROPEINIA

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Purpose: Children with febrile neutropenia (FN) are at high risk of contracting life-threatening infections. Blood culture, the gold standard for sepsis, is often negative. Thus other specific markers of sepsis i.e. interleukin 6 (IL6) and procalcitonin (PCT) are needed to predict the risk of sepsis in these patients.

Method: This study assesses the serum concentrations of IL6 and PCT along with blood culture obtained from 62 consecutive episodes of FN (Test Group) at admission. Cut-off values were deduced using ROC curves. These values were further tested for prediction of sepsis in the next 67 consecutive febrile neutropenic episodes (Validation Group). IL6 and PCT were analysed by chemiluminescent immunoassay assay (Immutide, DPC, Germany); Bact/ALERT microbial detection system was used for blood culture.

Results: There were 15 episodes of culture-proven sepsis in test group and 10 in validation group. In the test group, the mean IL6 and PCT levels were significantly higher in bacteremic (BE) and non-bacteremic (NBE) episodes (IL6: 457 ± 419 pg/ml and 185 ± 419 pg/ml respectively; PCT: 25 ± 35 pg/ml vs. 18 ± 32 pg/ml respectively; P = 0.03). Similarly mean PCT values in BE and NBE were 16 ± 16 pg/ml and 5 ± 16 pg/ml (P = 0.046) respectively. In this group, at a cutoff value of 3.3 ng/ml PCT was 80% se and 85% sp for predicting risk of sepsis. Conclusion: PCT and IL6 levels at onset of febrile neutropenia are good markers to predict the risk of sepsis. Their utility in making therapeutic decisions needs to be studied further.
ZINC NUTRITIONAL STATUS IN INDIAN CHILDREN WITH CANCER

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Purpose: To study the peripheral zinc nutritional status in Indian children with cancer, correlate it with the overall nutritional status and assess impact on morbidity and course of therapy

Method: 56 children with cancer were studied for nutritional; status parameters including weight for age, height for age, body mass index (BMI), serum albumin, serum creatinine and dietary intake in recent past. Serum zinc levels were estimated at diagnosis, at 3 weeks and when possible at 1 year (normal: 63.8–110μg/dl; subnormal: < 63.8μg/dl; low normal 63.8–70μg/dl) Impact parameters included, infectious complications and mortality during the first 3 months of treatment.

Results: Study population characteristics included median age of 5.2 yr (2.5 mth–16yr), male:female ratio of 3:1, with 2/3 of patients having ALL and the rest solid tumors. Clinical grading showed 16% to have grade III/IV malnutrition and over 50% with grade III/II malnutrition, and BMI < 10th centile was noted in 57.1% Mean serum zinc levels at diagnosis and 3 weeks were 90.3±28 μg/dl and 83.2±22 μg/dl respectively (p = ns). All samples studied at 1 year showed normal zinc levels. Children with ALL and those under 3 years of age tended to have lower zinc levels. Overall 12/56 had subnormal/low normal levels while 7/17 under 3 yrs age had a compromised zinc status, two of whom had symptomatic deficiency with zinc responsive perioral/acral dermatitis. Zinc levels did not correlate well with degree of malnutrition or adverse early outcome. However, those patients with lower levels did have significant infections with diarrhea in particular.

Conclusion: This study highlights the occurrence of zinc deficient state in Indian children with cancer. Given its association with impaired humoral and cellular immunity, larger studies are required to assess the need for and benefits of zinc supplementation early during cancer chemotherapy.

INCIDENCE AND CLINICAL IMPACT OF EXTENDED SPECTRUM β-LACTAMASE(ESBL) PRODUCTION AND CEPHALOSPORINE RESISTANCE IN BLOODSTREAM INFECTIONS IN PEDIATRIC CANCER PATIENTS

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Purpose: This study was conducted to define risk factors and outcomes associated with ESBL-producing organisms bloodstream infections in children,and to study the effects of restricted inpatient treatment with cephalosporines -most commonly linked to emergence to these organisms.-

Method: We conducted a retrospective case-control study using data from the Children’s Cancer Hospital of Egypt(CCHE) from January 1, 2008, to December 31, 2008. Eligible patients were identified from the hospital database of microbiology laboratory records. Clinical characteristics and outcome of patients infected by ESBL-producing isolates and frequency-matched controls infected by non-ESBL organisms were analyzed. Antibiotics used during this period, and their pattern of resistance were also reviewed.

Results: One hundred forty subjects were included in the study. Fifty five patients were infected with ESBL-producing organisms (30 females, 25 males), while eighty five patients were caused by non-ESBL producing isolates (40 females, and 45 males); leukemias (49 patients were ALL, 36 patients had ANLL),and NHL (constituting 22 patients) were mostly affected. Risk factors associated with infection by ESBL producing isolates were mainly recent antibiotic exposure -within 30 days before the episode-(47.2% in ESBL vs 32.9% in non-ESBL). Other potential factors included application of central venous lines,admission to ICU, comorbid conditions, and prolonged hospitalisation. All ESBL-producing, non-ESBL producing isolates were susceptible to carbapenem, and to a lesser extent to piperacillin-tazobactam antibiotics. Increasing resistance to cephalosporines was observed. Although a substantially higher proportion of children with ESBL-producing isolates died (in-hospital mortality: 12.7% vs7.1%), this difference was not statistically significant.

Conclusion: Receipt of extended spectrum cephalosporines in the 30 days prior to infection was significantly associated with having an ESBL-isolates infection in hospitalized children. Curtailed use of cephalosporins among high-risk groups may reduce the occurrence of ESBL-EK infections. Future studies on identifying high-risk children and investigating the impact of curtailed third-generation cephalosporin use to limit additional emergence of ESBL-isolate infections should be undertaken.

IMMUNOGLOBULIN LEVELS OF CHILDREN AND CORRELATION WITH PERIPHERAL BLOOD LYMPHOCYTE PROFILE IN THE INDIAN SUBCONTINENT

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Purpose: In children innate and adaptive immunity are often altered in children with malignancies, affecting patient management and outcome. Peripheral blood lymphocyte subsets and serum immunoglobulin levels vary in different populations. Purity of such data from the Indian subcontinent necessitated this study to determine immunoglobulin levels of children and correlate them with the peripheral blood lymphocyte and profile, disease status, and patient characteristics.

Method: Samples were taken from cord blood and children up to 5 years of age reporting to a tertiary center for health visits, without major illness or bacterial infection in the past. Complete blood counts, serum immunoglobulin levels (by turbidimetry) and lymphocyte subsets (by flow cytometry) were studied.

Results: 403 samples were analyzable -53 cord blood, and 350 children aged 1 month to 5 yrs, stratified into 4 age-groups. There was a marginal female preponderance. Neutrophil counts remained stable throughout all age groups. Lymphocytes gradually decreased from cord blood till 5 yrs age. IgG levels were high at birth and decreased in the first six months followed by a rise thereafter. IgM remained low in infancy and peaked at 13–36 months. IgA levels were very low at birth but gradually increased with age. CD4 counts were high in cord blood, which sustained till 3 years age and then declined. CD8 counts remained steady till 5 years age. CD19 was mostly constant in all ages. CD56 increased after the age of 2 years. Normal ranges for each parameter in each sub-group were established.

Conclusion: While the trends in our data correlated well with published literature, notable differences were seen in range of absolute values. Most marked were higher IgM levels seen in 1–3 year age group and higher NK cells through all age groups in our study. Our results provide the largest database of its kind from our country.

EFFECT OF MORPHINE ON FEAR, DISTRESS AND PAIN IN NEEDLE PROCEDURES IN CHILDREN WITH CANCER

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Purpose: Children with cancer often mention needle procedures as the most frightening, distressing and sometimes painful aspect of the disease and treatment. The aim was to investigate whether children experience less fear, distress, and/or pain according to parents, nurses, and children > 7 years of age when they receive oral morphine vs. placebo before a needle is inserted in a subcutaneously implanted intravenous port and if there is a difference in procedure time.

Method: Fifty children 1–18 years of age who were being treated in a pediatric oncology and hematology setting were included consecutively when undergoing routine needle insertion into an intravenous port. All children were subjected to one needle insertion and received EMLA in this randomized, triple-blind, placebo controlled study in which orally administered morphine (n = 26) 0.25 mg/kg body weight was compared with placebo (n = 24). Parents, nurses and children > 7 years reported the patients’ fear, distress, and pain on 0–100 mm Visual Analogue Scales. In addition behavioral observation with CHEOPS for pain and PBCL for procedure related distress was performed.

Results: No differences between the morphine and the placebo group were found with respect to age, weight, height, physical status, sex, weeks from diagnosis, or weeks...
from latest needle insertion. According to parents, nurses, and children oral morphine in a dose of 0.25 mg/kg body weight did not reduce the primary outcome measure fear; neither did it reduce distress nor pain in the morphine group compared to placebo. No differences in behavioral observations with CHEOPS and PBCL or procedure time for morphine vs. placebo were found.

**Conclusion:** Surprisingly, oral morphine in this dose does not add any value in reducing fear, distress or pain combined with topical anaesthesia in pediatric oncology patients undergoing subcutaneous port needle insertion, and it probably would not add any value for other similar procedures, e.g. venous cannulation.

**PR038**

**END OF LIFE CARE FOR CHILDREN WITH CANCER IN ENGLAND**

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**Purpose:** To describe patterns of hospital contact for children who were diagnosed with cancer and died during 1999–2006 in England. This is the largest population-based study of place of death involving childhood cancer registrations and hospital data. The Department of Health in England is committed to improving palliative care services for children with cancer, but the availability and quality of palliative care services varies widely and the information base is poor.

**Method:** The National Registry of Childhood Tumours (NRCT) has been linked to hospital records and death certificate (DC) data for children who were diagnosed with cancer and died during 1999–2006. These children have been categorised by age, sex, type of cancer, ethnicity, specialist treatment centre, clinical trial status, duration of last admission and survival.

**Results:** The NRCT contained records of 1,947 children who were diagnosed with cancer and died during 1999–2006, of whom 96% could be linked to hospital records. Hospital deaths (86% agreement) and ethnicity (88% agreement) were validated between data sources. According to the DC, 47% of children died in hospital, 44% at home, 8% in a hospice and 1% elsewhere. In the small proportion of children who were treated in non-specialist centres 79% of deaths took place in hospital. The duration of last hospital admission varied considerably by place of death, cancer type and between specialist treatment centres. Clinical trial participation did not affect place of death.

**Conclusion:** The linkage between NRCT and hospital records is excellent. Validation of place of death and ethnicity showed a good concurrence. Further investigation is required to understand variations by place of death and between specialist treatment centres.

**PR039**

**ETHICAL ISSUES AT THE BESIDE IN PEDIATRIC END OF LIFE CARE: THE STAFF NURSES PERSPECTIVE**

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**Purpose:** Ethical issues at the bedside in Pediatric Oncology End of Life Care: The Staff Nurses Perspective

**Method:** Pediatric oncology end of life care is perhaps one of the most challenging, and sometimes the most rewarding, endeavor any healthcare provider may find him or herself involved in. The goal of enabling the elusively “good death” of a child or young adult can prove frustratingly difficult for all involved, regardless of role or experience. This presentation will focus on the experience of the Staff Nurse and attempt to explain why we often leave the bedside with the feeling that we could have done better, that we have failed in our primary objective: to minimize the suffering of a dying child.

**Results:** To that end we will examine how health care is provided in the United States as opposed to in other industrialized nations, including the American conception of patients as “consumers” of health care services as opposed to the traditional medical “paternalistic” model still prevalent throughout most of the world. We will consider the basic philosophical theories of medical ethics as they relate to our attempts to providing holistic, family-centered care in a multi-ethnic, and dare I say, litigious society.

**Conclusion:** Consideration will be given to several contemporary theories, including the concept that the wellbeing of the surviving parents is just as, and perhaps more, important than the comfort of the child. Special emphasis will be given to the issue of communication between health care providers during this period of crisis. Our goal will be to provide the Staff Nurse with an ethical and cultural framework within which to reference contemporary issues in pediatric end of life care.

**PR040**

**COMPARISON OF ISOLATES AND ANTIBIOTIC SENSITIVITY PATTERN IN PAEDIATRIC AND ADULT CANCER PATIENTS; IS IT DIFFERENT?**

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**Purpose:** Infection is common cause of mortality and morbidity in cancer patients. Organisms are becoming resistant to antibiotics; age appears to be one of the factors responsible. So, we analysed common organisms and their antibiotic sensitivity pattern in correlation with age.

**Method:** This is a single institutional, retrospective analysis of all culture positive adult and pediatric cancer patients from January 2008 to December 2008. For statistical analysis Z test for the proportions was used and p values were obtained.

**Results:** There were 929 isolates in adult and 487 in children. Gram positive organisms were 293 (32%) and 205 (42%) while gram negatives were 636 (68%) and 262 (54%) in adults and children respectively. The commonest source in adult (34%) and in children (44%) was peripheral- blood. Most common organisms in adults were Pseudomonas– aeruginosa (16%) while in children it was Staphylococcus-aureus (17%). Extended-spectrum-B-lactamase producing organisms were found in 13% and 7% in adults and children respectively. Statistically significant difference in antibiotic sensitivity pattern was observed in adult versus pediatric groups. In pediatric group higher sensitivity was seen for Cefoparazone-sulbactum, Cefipime, Cefazidime, Ceftriaxone, Pipracillin-Tazobactum, Ticarcillin-Sulbactum, Amikacin, Gentamicin, Tobramycin, Vancomycin, Clindamycin and Levofloxacin. Sensitivity-pattern was same in both groups for Imipenem, Meropenem, Teicoplanin, Colistim, Polymixin and Cefotaxime. No resistance was found for Linezolid while Ertapenem was not used in paediatric patients.

**Conclusion:** The isolates in both children and adults were predominantly gram negatives, though children had proportionately higher gram positive organisms. High dose ceftriaxone use, cotrimoxazole prophylaxis, and more use of central lines in children especially in hematological malignancies could partly explain this observation. Children harbor less antibiotic resistance than adults; Uncontrolled, cumulative exposure to antibiotics in our community with increasing age, age related immune factors and variable bacterial flora in different wards might explain the higher antibiotic resistance in adults.

**PR041**

**CHRONIC DISSEMINATED CANDIDIASIS IN PATIENTS WITH ACUTE LEUKEMIA IN INDIA - INCIDENCE, RISK FACTORS AND PROGNOSIS**

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**Purpose:** Chronic disseminated candidiasis is an increasingly recognized complication of treatment with chemotherapeutic agents, especially in acute leukemia. Method: We reviewed retrospectively all patients with leukemia (948) with invasive fungal infections (IFI) over past 5 years to ascertain the cases with chronic disseminated candidiasis. Modified EORTC/MSG criteria for IFI were applied for diagnosing IFI.

**Results:** A total of 154 patient with IFI(16.2%) were analyzed,118 ALL, and 36 AML. Cumulative incidence of CDC was 13/154(7.8%) of IFI and 1.3% of all leukemia. Solitary hepatic and splenic involvement was seen in 3 and 4 patients respectively and both in 6 patients. Commonest presentation was fever without any localizing features (9/13,69.2%), in 4/13 it was detected on asymptomatic screening. There were concomitant renal (5/13), and Cutaneous lesions (2/13), with no cases of concurrent endocarditis/endothromitis. Hypodense multiple (> 3) lesion in 10/13(76.9%) and
target lesions in (9/13.69%) were detectable on abdominal ultrasound. These included 4 proven, 4 probable and 5 cases of possible fungal infections. The proven cases included 3 cases of Candida albicans and one case of Candida tropicalis., Transaminitis (7/13), and elevated serum bilirubin (4/13) were remarkable. First line antifungals included amphotericin B (7/13; survival = 4), liposomal amphotericin B (4/7; survival = 3), voriconazole (2/13; survival = 1), and second line caspofungin (4/13; survival = 3). Combination antifungals were employed in 4/13 patients, with no added benefit. The median duration of therapy was 84 days. Following therapy, radiologically the lesions calcified and underwent fibrosis in 4/13 (30.7%) and persisted as sterile abscesses with reduced size in 3/13 (23.1%), and completely disappeared in 2/13 (15.4%). Four patients died; two due to unrelated septic events, and two due to leukemia.

Conclusion: CDC criteria for IFI in acute leukemia which causes morbidity without mortality. All patients post steroid based therapy are susceptible to IFI. High index of suspicion in patients with fever with transaminitis and early abdominal imaging clinches the diagnosis.

PR043

FUNGAL INFECTIONS IN PEDIATRIC CANCER PATIENTS, CAIRO, EGYPT

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Purpose: Fungal infections are a common cause of morbidity and mortality among pediatric cancer patients. The purpose of this study was to determine the frequency of fungal infections among oncologic pediatric patients, and related mortality.

Method: During the period from June 2007 till December 2008, four hundred and twenty seven pediatric patients with hematologic malignancies presented at the National Cancer Institute, Cairo University and the Children Cancer Hospital. One hundred and two patients were diagnosed with Acute Myeloid Leukemia(AML), while 325 patients with Acute Lymphoblastic Leukemia (ALL). One hundred and twelve (26.2%) cases developed invasive fungal infection. Only 3 cases diagnosed with solid tumors were encountered to have fungal infection during this period (total number of solid tumors was not estimated). Methods for diagnosis were Computerized Tomography (CT), blood cultures, galactomannan antigen detection test and tissue pathology. Antifungal therapy was administered after 72 hours of persistent fever, or immediately for patients with previous history of systemic fungal infection. Antifungal agents included conventional amphotericin B, liposomal amphotericin B and voriconazole.

Results: Out of 427 cases diagnosed as acute leukemias, 112 (26.2%) cases developed fungal infections (17.5% of ALL patients and 54% of AML patients). Only 3 patients with solid tumors were encountered to have fungal infections. Aspergillus was the causative pathogen in 97/115 (84.3%) of cases, yeast infections (Candida spp.) in 15/13% cases, histoplasmosis in 21/7% cases. Cryptococcus infection in one case (0.9%). CT was the diagnostic tool used in 75.5% of cases. During the chemotherapy induction phase, 76 patients (66.1%) developed fungal infections, while the rest during different phases of treatment. The main clinical manifestation was persistent fever. Fungal infection related mortality was 31/115 (26.9%).

Conclusion: Pediatric patients with hematological malignancies are at high risk of fungal infections, especially AML patients. Prophylactic antifungal therapy should be considered for AML pediatric patients during treatment.

PR044

INFECTION CONTROL PRACTICES DURING INDUCTION CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS OF A SURVEY FROM THE DANA-FARBER CANCER INSTITUTE ALL CONSORTIUM

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Purpose: Purpose of Study: Contemporary multiagent chemotherapy induction regimens have achieved complete remission rates above 95% for children with ALL. A major limitation of this success is treatment-related toxicity, especially infectious complications during induction. We report the results of a survey of the site principal investigators of the Dana Farber ALL Consortium aimed at identifying infection control practices, as an initial step for investigating interventions to improve the rate and outcome of infectious complications.

Method: Methods: Principal investigators were asked to complete a twenty-two question survey. The survey addressed discharge practice, central venous line (CVL) management, antibacterial, antifungal and antiviral medication use during induction chemotherapy.

Results: Summary: All principal investigators completed the survey. Concordance was observed in the use of antibacterial and antifungal medications. No institutions advocate antibacterial prophylaxis during induction chemotherapy and 7 do not recommend antifungal prophylaxis. Criteria for use of antibiotics and antifungals for the empiric therapy of febrile neutropenia were consistent with the Infectious Disease Society of America guidelines. In contrast, we found variability in the discharge criteria and in the management of central venous lines (CVL). Five institutions recommend discharge after recovery of the acute phagocytic count (APC) while 5 base their decision on clinical parameters. The re-hospitalization rate for children discharged prior to recovery of APC is above 50%. In regards to choice of and timing of CVL placement, 4 institutions advise permanent CVL insertion at diagnosis, 3 at recovery of APC, and 3 base the decision on the presence or absence of fever. CVL removal due to infectious complications occurs very rarely.

Conclusion: Differences in approaches toward infection control practices should be analyzed in relation to rate and outcome of infectious complications during induction chemotherapy. Standardization of infection control policies and its impact on reduction of infections should be further investigated in the multi-center setting.

PR045

RISK FACTORS, OUTCOME PREDICTORS AND RESPONSE TO ANTIFUNGALS IN LEUKEMIC CHILDREN WITH INVASIVE FUNGAL INFECTIONS: A LARGE EXPERIENCE FROM INDIA

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Purpose: Cerebral aspergillosis (CA) is the most feared and life threatening opportunistic infection in immunocompromised children with leukemia. We reviewed, retrospectively, all patients with invasive fungal infections (IFI) over past 5 years to ascertain the risk factors, presentation and outcomes of CA.

Results: A total of 154 patient with IFI were analyzed; 118 ALL, and 36 AML. The cumulative incidence of CA was 9/154 (5.8%); 8 ALL and 1 AML. The common clinical presentations included seizes 39/77(8%), fever 79/77(78%), altered sensorium 59/55(6%) and focal neurological deficit 49/ (44.4%). Radiologically, they involved parieto-occipital lobe (7, 7.7%), followed by frontal (3, 33.3%) and temporal lobes (2, 22.2%). The best modality for delineation of lesions was MRI. Cerebral infaction was found in 69% (66.7%) of these cases. There was associated invasive fungal infection of paranasal sinuses (49, 44.4%), and lungs (39, 33.3%). First line antifungals included amphotericin B (39; survival = 2), liposomal amphotericin B (29; survival = 0), voriconazole (69; survival = 3), and caspofungin (19; survival = 1). Seven patients also underwent surgery. Median survival was only 72 days and five patients died. Among the four survivors, focal neurological deficits and porencephalic cysts were remarkable in two children. The risk factors for CA included: ALL [Hazard ratio (HR) = 15.8, p = 0.001], steroid based therapy phase (HR = 4.16, p = 0.02), and concurrent sinis-IFI (HR = 2.42, p = 0.04). The risk factors for mortality included disease not in remission (HR = 22.2, p = 0.001), abscess size > 1.5cm (HR = 12.2, p = 0.001), incomplete surgery (HR = 9.9, p = 0.001), and > 36cits of lesions (HR = 3.16, p = 0.2).

Conclusion: CA, despite aggressive pharmacological and surgical management, is associated with a high mortality rate. The survivors, too, have long term morbidity with focal neurological deficits. A high index of suspicion and prompt initiation of voriconazole based antifungal regime with early surgery hold the key to good outcome.
**Purpose:** Invasive fungal infections (IFIs) cause morbidity and mortality in leukemia.

**Method:** We analyzed records of 948 children ≤12y of age with acute leukemia from Jan 2005 to Dec 2009. Modified EORTC/MSG criteria were applied for diagnosing IFI.

**Results:** IFIs were observed in 154/948 (16.2%) patients; 118/646 (18.3%) ALL, and 36/302 (11.9%) AML. They comprised 18 (11.7%) proven, 67 (43.5%) probable, and 69 (44.8%) possible IFI. The infected sites included lungs (18.76%), intestine (21.2%), and brain (9.58%). The risk factors for IFI included severe malnutrition [Hazard ratio (HR) = 1.030, 95% CI = 1.004-1.060, p = 0.029], baseline serum albumin < 2.7 mg/dl (HR = 1.038, 95% CI = 1.24-2.51, p = 0.046), > 7 days of hospitalization in last 30 days (HR = 3.2, 95% CI = 2.44-5.26, p = 0.02), induction therapy (HR = 2.248, 95% CI = 1.96-4.03, p = 0.008), and steroids usage > 7days (HR = 1.91, 95% CI = 1.46-2.33, p = 0.016). Response to antifungals varied from 57.1% to amphotericin B and 63% to liposomal-amphotericin B, to 31% for voriconazole and 70% for caspofungin. Overall, the response for combination antifungals was not better than single agents except for voriconazole which fared worst when used as monotherapy. IFI related cumulative mortality was 38.24%, 24(20.3%) ALL, and 14(38.8%) AML. The risk factors predicting IFI-related mortality included: AML (HR = 14.82, 95% CI = 4.61-88.22, p = 0.001), > 7 days of hospitalization in past one month (HR = 2.06, 95% CI = 1.99-3.4, p = 0.03), induction therapy (HR = 1.94, 95% CI = 1.38-5.38, p = 0.04), uncontrolled disease (HR = 8.8, 95% CI = 6.32-16.42, p = 0.01), prolonged- profound neutropenia (HR = 4.28, 95% CI = 2.46-8.39, p = 0.01), proven IFI (in contrast to probable/possible IFI, HR = 4.65, 95% CI = 1.46-5.89, p = 0.008), and use of azoles [itraconazole (HR = 3.34, 95% CI = 3.1-4.24, p = 0.001), voriconazole (HR = 2.18, 95% CI = 1.90-2.87, p = 0.02)]. Caspofungin as first line antifungal was the predictor for good survival (HR = 0.41, 95% CI = 0.11-0.59, p = 0.01).

**Conclusion:** IFI significantly contribute to mortality/morbidity in acute leukemia. The important risk factors for IFI include malnutrition, prolonged hospital stay, and induction therapy, and for mortality include AML, prolonged-profound neutropenia, and uncontrolled disease. Conventional antifungal produce good response consistent with literature and caspofungin had the best outcome. Combination therapy appears no better than single-agent-therapy.

**PR046**

**MOOD AND ADAPTATION DISORDERS DURING THE PERIOD OF INTENSIVE TREATMENT OF ADOLESCENT CANCER PATIENTS**

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**Purpose:** Cancer diagnosis and subsequent aggressive treatment may be traumatic for children. Medical health providers should distinguish normal distress reactions to anxiety, mood or adaptation disorders. The purpose of the study was to assess the incidence of mood and adaptation disorders during intensive treatment of adolescent cancer patients.

**Method:** This study covered history of 101 consecutive adolescent cancer patients diagnosed between Jan, 2007 – March, 2010 in pediatric onco-hematology ward. The mean age was 14.9 yrs. Planned psychosocial support program was designated to all patients. The frequency of mood and adaptation disorders occurrence was rated with use of clinical interview.

**Results:** Mood and adaptation disorders were revealed in 39.6% of adolescent patients. The mean time of observed disorder symptoms was 74.8 days. The most frequently diagnosed disorders were: regressive behavior – 15.8% pts and adjustment disorder- 11.9% pts. Moreover, 4 pts showed manic symptoms that were caused due to medical conditions. Mood disorders symptoms were disclosed in other 6 boys with proved CNS lesions. Additionally, two adolescent boys revealed intensification of behavior disorders that occurred prior to the cancer diagnosis. In the study only 19.8% of patients received antidepressant treatment. Remaining patients with behavior disorders received only hydroxyzine, that was added to individuals on the different level of frequency.

**Conclusion:** 1. Symptoms of mood and adaptation disorders were diagnosed in high percentage of adolescent cancer patients. 2. Usage restraints in antidepressant medicines can be caused by unclear rules of their application during chemotheraphy as well as difficulties related to proper disorder diagnosis. 3. It is advised to formulate procedures that will designate the way of dealing with adolescent patients who disclose mood and adaptation disorders.
Conclusion: Survivors of pediatric brain tumors are at increased risk for suicidal ideation compared to the general population. Disease specific variables and psychological symptoms and treatment were independently associated with risk for suicidal ideation among this sample of survivors. Study results highlight the need for close psychosocial follow-up care for pediatric brain tumor survivors.

A national health database was used to identify all potential participants for the ACSIS study. Of those who were eligible (12-18 years of age; cognitive and language ability to understand and answer the questionnaire) and invited to participate, 48% did.

Results: Data collection has just been completed. Preliminary results on the standardised measures of psychological well-being, and their comparison with the Youth2007 control group data, will be presented.

Conclusion: This study is unique in terms of being a nationwide New Zealand study and having comparison (control group) data from a large, normative sample. The findings of this research will make a significant contribution to our understanding of the well-being and needs of this population and provide a sound basis for the development of service initiatives from diagnosis to late effects monitoring.

**PS003**

**PEDIATRIC CANCER AND CHILDREN’S PEER RELATIONSHIPS**

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**Purpose:** Having friends is central to children’s psychosocial adjustment, and experiences with childhood cancer treatment may interfere with peer relations. Yet, there is mixed evidence on whether survivors of childhood cancer show difficulties with peers. Some studies suggest that survivors have poorer social competence than healthy peers while others find survivors to be no different than peers on measures of loneliness, social acceptance and reciprocated friendships. Contradictory findings may be due to overreliance on teacher and parent reports of peer quality, which focus on general dimensions of peer functioning (e.g., acceptance) and fail to capture subtle component processes of intimate friendships. Adults also have somewhat limited opportunities to observe and evaluate peer interactions. Studies also have included participants with varying types of cancers and ages, which may make interpretation of results difficult. The current study used observational methods to assess the quality of peer relationships in fifty-one 7–12 year old Acute Lymphoblastic Leukemia survivors as compared to healthy children.

**Method:** Children were audiotaped as they engaged in free play with their best friend. Interactions were coded to assess their ability to maintain engagement with one another, as well as the affective dimension of their play.

**Results:** MANOVA analyses indicated that dyads that included a survivor of childhood cancer were less likely to be highly engaged with their best friend (F(1, 44) = 4.73, p = .04, partial-c2 = .09) and more likely to experience disengagement (F(1, 44) = 4.49, p = .04, partial-c2 = .09). Significant group differences were found in the amount of fantasy play (F (1,48) = 5.88, p < .02) with dyads that included a survivor showing less non-stereotyped fantasy play (M = 54) than dyads that did not include a survivor (M = 3.09). There were no differences in positive or negative affect.

**Conclusion:** Friendships of childhood cancer survivors may be compromised in specific areas. Higher disengagement and lower engagement were observed, which may interfere with relationship closeness and be associated with loneliness.

**PS004**

**PSYCHOLOGICAL WELL-BEING OF ADOLESCENT SURVIVORS OF CHILDHOOD CANCER IN NEW ZEALAND: A NATIONWIDE STUDY**

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**Purpose:** There is no published research on the psycho-social well-being of adolescent survivors of childhood cancer in New Zealand. The nation-wide Adolescent Childhood cancer Survivors Impact Study (ACISIS) was designed to gather information on the psycho-social well-being of this population. This information will provide an understanding of the well-being and needs of this population which in turn will be used to guide the development and implementation of assessment protocols and interventions.

**Method:** The ACSIS study used an internet-based branching questionnaire to gather data. Youth2007 is a research study that gathered a range of information on the health and well-being of a normative sample of New Zealand adolescents aged 12 - 18 years. Data was collected from 9,100 adolescents around the country. The Youth2007 participants provide the control group for the ACSIS study. The ACSIS questionnaire was adapted from the Youth2007 questionnaire in collaboration with the Youth2007 research team. Participants in both studies were anonymous. Psychological well-being was assessed using the standardised measures RADS-2 SF; MASC-10; SDQ, and WHO-5.

**Conclusion:** We concluded that the animal-assisted therapy complements the conventional oncology treatment; this therapy exerts a positive influence in the psychosocial well-being of our patients and it is a positive factor in order to address the feelings, fears and other psychosocial symptoms that are related to the disease.

**PS005**

**ANIMAL-ASSISTED THERAPY AS AN APPROACH TO PSYCHOSOCIAL SYMPTOMS IN ONCOPEDIATRIC PATIENTS**

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**Purpose:** The benefits of therapy assisted with animals have been documented since the 1960 decade, finding that “animals can act as therapeutic tools given that an intense relationship between the human and the animal is a psychological stimulation that favors the healing process of the patients”. According to this, the Fundación Cardiointfantil IC hospital has introduced, in the integral care of the child with cancer, complementary and alternative medicine (CAM) therapies as the animal-assisted therapy and the art therapy. Thus, based on an integrative oncology and implementing a biopsychosocial approach to the patient and their family, we look after with the animal-assisted therapy to improve the patient’s quality of life and strengthen the relationship of the patient with the health team.

**Method:** An observational-qualitative study of case type 2 with previous and posterior evaluations to the intervention was used; based also in the observation and psychological methods. The universe was constituted by 15 patients among 3 and 15 years old and their families, attended in this service during the month of December of 2009.

**Results:** The results show that there was no clinical complication after finishing therapy in any patient. The therapy generates positive emotional states in all evaluated cases, diminishing stress and anxiety generated by being hospitalized; it canalized the social interaction by encouraging positive reactions in children and their families as well as facilitated the physician-patient relationship and helped to the physical relaxation of the child.

**Conclusion:** We concluded that the animal-assisted therapy complements the conventional oncology treatment; this therapy exerts a positive influence in the psychosocial well-being of our patients and it is a positive factor in order to address the feelings, fears and other psychosocial symptoms that are related to the disease.

**PS006**

**A ONE-YEAR PROGRAM EMPOWERING YOUNG ADULT SURVIVORS TO OFFER CRITICAL SUPPORT TO THEIR PEERS FIGHTING CANCER**

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**Purpose:** The results achieved in impacting current AYA patients’ behaviour in treatment compliance and helpfulness measures by inviting them to interactive programs of a cancer survivor group were significant on the wards of three hospitals. A comprehensive nation-wide plan was needed to aid the formation of local focus groups and facilitate the networking of adolescent cancer survivors with current cancer patients across the country, especially the less supported regions of Romania.

**Method:** Forty young people ages 14 - 24 were recruited to design a nation-wide information and peer-based support program specifically targeting AYA cancer patients. 24 survivors of paediatric cancer made up four focus groups of six participants. Four siblings, four current patients and eight patient support volunteers contributed with feedback on content. The program involved the creation of information messages, short films and communication posters and AYA cancer survivors hosting discussions in 11 rural hospitals.

**Results:** 500 cancer patients and their families benefited from the messages of hope and encouragement shared by the cancer survivors nation-wide. Information that is especially relevant for the AYA demographic is now available in all pediatric
PS007

EMOTIONAL DIFFICULTIES EXPERIENCED BY CHILDHOOD CANCER PATIENTS’ SIBLINGS

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Purpose: Childhood cancer has substantial emotional impact on siblings as they must adapt to tremendous changes in their lives. The current paper attempts to study effects with the aim of ensuring improved coping.

Method: CPAA’s Patient Care department assists childhood cancer patients and family members at hospitals and at our centre. This paper is part of a larger study aimed at achieving deeper understanding of the cancer experience and its effect on family members at hospitals and at our centre. This paper is part of a larger study aimed at ensuring improved coping.

Results: The study showed significant differences between the component of difficulty in feeling between siblings and patients. Compared to the control group (46.0), patients showed significantly higher levels of alexithymia (60.6). Surprisingly, siblings showed even higher levels (69.5). The consequences of alexithymia can be seen in poor adjustment. Siblings of children with cancer have higher levels of empathy compared with healthy brothers and sisters.

Conclusion: The findings reinforce our observation that more needs to be done in terms of communicating openly with children, discuss feelings and externally oriented thinking. The subjects were chosen from families of middle to lower economic strata undergoing therapy at various hospitals in Mumbai.

PS008

YOUNG CHILDREN WITH CANCER AND THEIR PARENTS REPORT DECREASED HEALTH RELATED QUALITY OF LIFE SHORTLY AFTER END OF SUCCESFULL TREATMENT

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Purpose: Health related quality of life (HRQOL) has been assessed during several moments in and out of treatment in children with cancer, but there is limited knowledge about HRQOL shortly after finishing therapy. Aim of the current study was to determine HRQOL of children with cancer shortly after end of successful treatment, compared to healthy and chronically ill peers.

Method: HRQOL was measured with several age-specific questionnaires: ITQOL (generic, proxy-report, report, 0 to 4 years), CHQ PF 50 (generic, proxy-report, 5 to 7 years), Kidscreen (generic, self-report, 8 to 18 years) and Disabkilds (chronic generic, self-report, 8 to 18 years).

Results: 191 children with cancer (mean age 9.25, SD 5.06, 47.1% female) participated. 0 to 4 and 5 to 7 year olds were rated significantly lower than the norm on almost all scales. HRQOL of 8 to 11 and 12 to 18 year olds was only decreased for physical well-being. Moreover, 12 to 18 year olds had significant better HRQOL scores than the norm on several emotional, social and school scales. Compared to chronically ill peers, 8 to 18 years olds demonstrated no differences, except for 12 to 18 year olds who had significantly more physical limitations. Additionally, we found that parents of children aged 0 to 7 years also reported a significantly reduced HRQOL.

Conclusion: Young children with cancer have decreased HRQOL shortly after end of treatment. Older children and adolescents however, show hardly any differences with the norm, or even score better. In addition, parental HRQOL of young children is reduced. Our study results imply monitoring HRQOL in clinical paediatric oncology practice.

PS009

SHOULD PREADOLESCENT CHILDREN BE PRESENT DURING CONSULTATIONS: QUALITATIVE INTERVIEW STUDY WITH PARENTS IN THE MONTHS AFTER THEIR CHILD’S DIAGNOSIS WITH CANCER

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Purpose: To examine parents’ views regarding their child’s presence during consultations.

Method: Qualitative interview study which used maximum variation sampling to recruit 66 parents (39 mothers, 27 fathers) of 42 children aged 1-12 years (median 4 years). Children were receiving treatment for acute lymphoblastic leukaemia at 6 UK paediatric oncology tertiary centres. The constant comparative method of analysis was used.

Results: Parents acknowledged the benefits of communicating openly with children, but only 5 of the 53 parents who spoke on this issue thought their child’s presence in consultations was automatically desirable. Parents described how their child’s presence restricted their own communication with doctors, made it difficult for them to concentrate on what was said and interfered with their efforts to help their child feel safe and hopeful. The child’s presence was particularly difficult for parents when ‘significant’ issues, such as the prognosis, adverse test results and medical procedures, were discussed. Parents felt these discussions were a potential threat to their child, particularly when they had not first discussed the information with doctors separately from their child, whereas separate discussions enabled parents to absorb the information themselves and to sanction its communication to their child. Some parents experienced difficulties in accessing separate consultations with doctors.

Conclusion: The difficulties we identify are unlikely to be satisfactorily resolved by either systematically excluding children from consultations or the reverse. However, these difficulties could potentially be addressed by extending, beyond the diagnosis period, the practice of sequencing ‘significant’ information so that it is first communicated to parents in separate consultations, and by periodically discussing with parents what information would be in their child’s interests to hear. To ensure ongoing parental access to separate consultations, consideration should be given to ways of facilitating these, including shifting the onus for initiating separate consultations from parents to doctors.

PS010

THE IMPACT OF MEDICAL AND PSYCHOSOCIAL FACTORS ON THE QUALITY OF LIFE IN CHILDREN WITH CANCER AND THEIR FAMILIES

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960 SIOP ABSTRACTS

Purpose: To improve pediatric QOL (quality of life), a better understanding and comprehension of the current QOL that a child experiences under different medical conditions is necessary. This is done through examining the child’s diagnosis, disease stage and determining how different social and family factors play into a child’s QOL with respect to his/her medical condition.

Method: This study was conducted at Meyer Children’s Hospital at Rambam Medical Center in Haifa, Israel with 50 patients from the oncology department. The sample included both genders from ages 5 to 18. Several questionnaires regarding QOL were administered to the patient, parents, and siblings. The questionnaire was taken from The Children’s Quality of Life Questionnaire developed by Kreitler and Kreitler.

Results: The comparison of the child’s and parent’s QOL yielded significant results (with a p value of <.05) in the scales of family, school, negative thoughts, cognition, health, self-esteem, body image, efficacy and motivation. The parents consistently recorded a higher mean value than the child in these scales. Comparing the child and parent proxy (how the parent thinks the child views his/her own QOL), three scales produced significant data (negative thought, cognition and motivation). The siblings consistently reported a higher mean value for these scales. In comparing the different diagnoses, the children with leukemia/lymphoma recorded significantly lower mean values in the two scales: body image and self-esteem.

Conclusion: The child demonstrates a lower QOL than the parent. The parent believed the child to be more motivated and have less negative thoughts than the child actually felt. The parents underestimated the child’s magnitude of suffering. The sibling reported a better quality of life within the family, school and having fun. Lastly, children with leukemia/lymphomas presented a lower self-esteem and body image than those children with solid tumors.

PS011

A PROSPECTIVE MIXED METHODS STUDY TO DETERMINE THE COSTS INCURRED BY FAMILIES OF CHILDREN NEWLY DIAGNOSED WITH CANCER IN ONTARIO

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Purpose: Pediatric cancer may place significant economic burden on families. The study purposes were to: (a) identify costs incurred by families of children newly diagnosed with cancer, (b) identify the determinants of cost, and (c) explore the impact of costs on families.

Method: A prospective concurrent mixed methods design was utilized to study parents of children newly diagnosed with cancer from two paediatric hospitals. Parents recorded resources consumed and direct (out-of-pocket expenses) and indirect (productivity losses) costs incurred during one week per month for three consecutive months following diagnosis and listed additional costs incurred since diagnosis. Parents also discussed the impact of these costs in individual interviews. Descriptive statistics and multiple regression were used to describe families’ costs (expressed in 2007 Canadian dollars) and to determine influential cost factors. Qualitative content analysis was used to analyze the impact data.

Results: Ninety-nine parents (28 fathers and 71 mothers) completed the study. The mean total three month expenditure was $28,475 (SD $12,670; range $2013 to $79,249) per family. No statistically significant factors influenced families’ direct costs, however, indirect costs were influenced by language spoken at home. Parents described their costs and the coping and management strategies used to lessen the financial impact including managing their expenses and seeking ways to increase their cash flow.

Conclusion: Families are confronted with unavoidable, unexpected, and potentially catastrophic costs following their child’s diagnosis. Study implications are geared towards optimally supporting families manage their new financial reality and rendering other childhood cancer costs visible.

PS012

DEVELOPMENT OF AN ONLINE PSYCHO-EDUCATIONAL GROUP INTERVENTION FOR CHILDREN WITH CANCER

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Purpose: Considering the adverse effects of pediatric oncology treatments, the uncertainty about the further course of the disease and other psychosocial implications of childhood cancer, there is a need for disease-specific interventions for survivors of childhood cancer. Development of an online intervention would expand the accessibility for especially adolescents. Objectives are: to study whether the development of an online group program (www.opkoeronline.nl) is feasible and effective and how satisfied participants and trainers are with the program.

Method: Children treated for cancer, between 12–18 years and having finished treatment were eligible. The course (6 sessions) utilizes the principles of cognitive behavioral therapy. A face-to-face course was translated into an online intervention. Children completed questionnaires about disease related skills and psychosocial functioning before and 0–4 weeks after the course. They were asked about the sign-in procedure, the course, the home-work program and the chat-box utilities. Every session evaluation of the content and utility took place. Psychologists who provide the course were interviewed.

Results: Until now three courses took place with 9 participants. They were from different pediatric oncology centres. All participants participated during all sessions and were positive about the course. The psychologists were also positive. Several adaptations were made to the course based on the reactions. Next courses are scheduled. Preliminary results show positive changes on the psychosocial outcome questionnaires.

Conclusion: E-mental health technologies are developed over the past years, with most e-health interventions focusing on adults, and to a lesser extend for children. First results are promising for this online chatcourse for children with cancer. This course will give many young childhood cancer survivors the opportunity to profit from this preventive chat-group intervention at home on an individual basis.

PS013

THE VALUE OF INFORMATION IN GAINING TRUST - EXPERIENCES FROM A CHILDREN®S CANCER HOSPITAL IN EGYPT

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Purpose: More than 65 percent of children diagnosed with cancer in Egypt die every year, a situation that could be explained in part as an effect of avoidable or manageable health-care related factors. This study determined if improved information sharing between health-care providers and caregivers of the children increased caregivers’ trust in health-care professionals and medical treatment provided.

Method: Questionnaires were distributed to 304 caregivers of children admitted for their first and third chemotherapy treatments between 10 February and 10 September 2008 at the largest children’s cancer hospital in Africa and the Middle East. Data are presented in terms of relative risk (RR) and 95 percent confidence interval (CI).

Results: One third of caregivers reported not being informed by medical staff about their child’s disease (103/304 – 34%), about treatment (98/304 – 32.7%) and the health-care staff (relative risk 9.0; 95% CI 4.5–17.7) than caregivers who got no information. Caregivers receiving information were more likely to report
that the situation was manageable (11/14–79%) than those who did not receive information (relative risk 11.0; CI 6.6–17.8). These caregivers felt they had better communication with the doctors (11/12–92%) than those who did not receive information (relative risk 10.3; 95% CI 5.4–19.6).

Conclusion: Parents of cancer-sick children in this setting in the Arab World reported that receiving moderate amounts of information creates a moderate degree of trust of health-care and of doctors. Trust reported in our study group seems to have positive effects on the caregiver’s perception of their present situation and a positive effect on their communication with their child’s doctors.

PS014

THE RELATIONSHIP BETWEEN POSTTRAUMATIC STRESS SYMPTOMS AND POSTTRAUMATIC GROWTH IN YOUNG ADOLESCENT SURVIVORS AND PARENTS

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Purpose: To examine the psychological late effects of childhood cancer experiences in survivors and parents: (1) Relationship between posttraumatic stress symptoms (PTSS) and posttraumatic growth (PTG) in survivors and parents; (2) Relationship between PTSS/PTG and time after diagnosis, appraisal of treatment intensity and life-threat. Method: Participants were 52 cancer survivors (116 years, 24 males, 28 females), and 227 survivors’ (6 years) parents (126 mothers, 101 fathers) at 7 hospitals. Response rate was 40.8%. Self-reported questionnaire is consisted of the UCLA PTSD index : PTSD (Pynoos, et al., 1998)PTG inventory-Japanese version: PTGI-J(Taku, et al., 2007), and subjective appraisal of the intensity of cancer treatment scale and the life threatening scale (Stuber, et al., 2004). Results: The mean of PTDS and PTG total scores were male survivors (ptsdiM = 7.8, SD = 9.1; ptgim = 58.4, SD = 22.2), female survivors (ptsdiM = 9.4, SD = 10.3; ptgim = 58.0, SD = 20.8), fathers (ptsdiM = 10.0, SD = 10.6; ptgim = 53.8, SD = 21.1), and mothers (ptsdiM = 10.5, SD = 9.7; ptgim = 62.4, SD = 19.6). ANOVA found no significant difference for PTSD and PTG total scores among survivors and parents, but found for PTG only between fathers and mothers (M = F). PTSS was found in both survivors (male = 25%, female50%) and parents (fathers44%, mothers47%). The frequency of PTSS was in same order in all groups; 1. Re-experiencing. 2. Increased arousal and 3. Avoidance. Two survivors and three parents exceeded the clinical cutoff on the PTSD. Significant correlations were found between PTSS and father’s/mother’s appraisal of treatment intensity (p < .05), father’s appraisal of life-threat (p < .01) and PTG (p < .01). Survivors (116 years male/female) appraisal of treatment intensity and PTG significantly related. Conclusion: Not all survivors and parents have PTSD after treatment, but some showed the score suggested a clinical range of PTSD. A study on prediction factor is expected. The relationship between PTSS and parents’ perception of treatment intensity indicates that treatment may cause of a post traumatic experience. PTG may relate with perception of overcoming treatment in survivors and PTSS in fathers. No relationship between time after diagnosis. It tells the decreasing process of PTSD in childhood cancer experience may be different from that of general PTSD.

PS016

PROMOTING HEALTHY TRANSITIONS FOR CHILDREN COMING OFF ACTIVE CANCER TREATMENT

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Purpose: Pediatric cancer patients are at higher risk for obesity, diminished exercise capacity, hypertension and metabolic syndrome features related to cardiovascular disease (CVD) as adults than healthy children in the general population. Rates of overweight/obesity for childhood cancer survivors (CCS) are found to be over 40% five years after cancer treatment, with 21.2% classified as obese. While treatment intensity and cranial radiation have not been found to be important predictors of BMI or blood pressure change, and in line with others, we argue that parental perceptions of eating and exercise behaviors may play an important role in the development and amelioration of the risk factors associated with these medical late effects (see Childhood Cancer Survivor Studies). Given this background, we are testing the feasibility of a prevention program addressing overweight/obesity in CCS by adapting an empirically supported parent-education intervention (NOURISH) for parents of children 5-12 years old who have ended treatment and are transitioning to survivorship (NOURISH-T).

Method: To inform the development of NOURISH-T, focus groups have been conducted with pediatric oncology health care providers (HCPs; N = 11) and parents of CCS (ongoing).

Results: Data collected during the focus groups on HCP and parental concerns regarding changes in eating behaviors, physical activity and parental behavior changes have been incorporated into NOURISH-T. Concerns discussed during these groups included food becoming a form of reward for enduring difficult procedures, the encouragement of unhealthy food consumption to increase caloric intake during treatment, concerns over sedentary lifestyles during treatment and difficulty of giving up these unhealthy habits once treatment was over. Other concerns included parental overprotectiveness and parenting styles as related to eating and exercise behaviors.

Conclusion: We are evaluating the feasibility and acceptability of NOURISH-T by parents of CCS and will present these findings and their implications for a planned randomized control trial.
PS017
SUN EXPOSURE IN CANCER SURVIVORS ON AND OFF THE BEACH: RESULTS FROM PROJECT REACH

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Purpose: Although skin cancers are among the most common second cancers, many survivors do not practice recommended sun protection to reduce their risk. A mailed survey of sun exposures, protective behaviors, and perceived vulnerability was conducted to examine factors associated with sun exposure in this at-risk group.

Method: Participants were 203 survivors (61% females, median age 31, 77% diagnosed < age 30) enrolled on Project REACH, a cohort study of locally-treated cancer survivors. Survivors were classified into groups reflecting extent of adherence to recommended sun protection practices. Separate classifications were produced for adherence during sunbathing (SB) vs. incidental sun exposure (IE).

Results: 26% of participants had low adherence to protection recommendations during SB, and 29% had low adherence during IE. No relationship (p = .13) was found between adherence to sun protection for SB and IE. Survivors treated with radiation did not differ on overall sun exposure, SB or IE adherence, or perceived vulnerability to sun exposure, despite the fact that these survivors generally felt more susceptible to skin cancers (p = .001). Higher levels of personal vulnerability were significantly related to adherence in the IE (p < .005) but not SB context (p = .49).

Conclusion: Despite known risks of skin cancer, a large proportion of survivors have significant sun exposure and do not practice adequate sun protection. Although previous studies have focused on SB, factors associated with sun exposure and protection differ between SB and IE contexts, and assessment of SB exposure alone fails to capture high levels of IE. Survivors treated with radiation may recognize their increased risk of skin cancer, but not the role of sun protection in modifying that risk. The implications for survivor education, including results from a pilot study to increase sun protection using appearance-based health messages, will be presented.

PS018
CHILDHOOD CANCER AND ITS IMPACT ON THE FAMILY: AN ASIAN EXPERIENCE

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Purpose: There is lack of information available in Singapore on the impact of childhood cancer on family as a whole. We set out to assess medical and non-medical costs as well as its psycho-social impact in our local context.

Method: All patients diagnosed and treated at Department of Pediatrics, KK Women’s and Children’s Hospital and National University Hospital, Singapore are eligible. Families were given 2 self-administered questionnaires: “about your child and family” and Impact–On–Family scale. Total score is obtained by summation of all scores with high score correlating to high impact. Statistical analysis performed using SPSS v7.0.

Results: Seventy-nine parents were enrolled during study period (10/08 - 2/09). There were 48 (61%) males and 51 (72%) of respondents were mothers. 51% were children < 5 years, 25% between 5–10 years and 24% > 10 years age. Chinese were majority at 54%, followed by foreign patients at 33%, and Malay/Indian making remainder at 13%. Those with hematologic malignancies make up 44 (56%) whilst those with solid tumors make up 38%. Findings by domain: I, financial burden — reported higher than U.S. and Italian studies; II, familial/social burden - none of Malay/Indian care-givers reported high disruption (p = 0.05); III, psychological burden - all Malay/Indian care-givers reported ‘low-moderate’ and large proportion of Chinese reported ‘high’ score (p = 0.003); IV, mastery- Chinese reported highest levels of mastering within ethnic subgroups (p = 0.001). Cronbach’s alpha, internal reliability was 0.64.

Conclusion: Overall, the burden of childhood cancer in Singapore is comparable to other countries. However, we see a higher impact in Financial Burden and Social/ Familial Impact domains. Factors associated with high impact are: ethnicity; employment status; and leave status. Use of Impact on Family Scale needs further research to see whether all domains are applicable to our local culture.

PS019
QUALITY OF LIFE IN MOTION: A COMBINED PHYSICAL EXERCISE AND PSYCHOSOCIAL INTERVENTION PROGRAM FOR CHILDHOOD CANCER PATIENTS

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Purpose: Physical fitness has shown to be reduced during and after childhood cancer with physical inactivity being one of the most prominent causes. Psychosocial factors can affect the amount of physical activity. Physical inactivity ultimately leads to obesity, fatigue, a poor skeletal and/or mental health, and ultimately a compromised health-related quality of life (HRQOL). Aim of the study is to evaluate the short- and long-term effectiveness of a combined physical exercise and psychosocial intervention program, implemented during or shortly after treatment, in improving the physical fitness of childhood cancer patients (CCP). Secondary outcomes include fatigue, body composition, daily physical activity levels, depression, HRQOL, self-perception and behaviour.

Method: In this multi-centre randomized clinical trial all CCP (8–18 years) on treatment with chemo- and/or radiotherapy or no longer than 12 months off treatment, are eligible. Patients requiring bone marrow transplantation and/or growth hormone treatment, those depending on a wheelchair or unable to “ride a bike”, and those with mental retardation are excluded. In total, 100 consenting patients will be randomized to either the intervention or the control group after stratification according to type of malignancy, age group and moment of inclusion into the study. The 12-week intervention consists of a combined physical exercise (2x/week; cardiorespiratory and muscle strength training) and psychosocial support program followed by a 1 day booster session. The psychosocial support program (6 child and 2 parent sessions) includes psycho-education and cognitive-behavioural therapy. The control group will receive care as usual. All participants will undergo physical performance tests and complete questionnaires prior to randomization, after 12–14 weeks and at 12 month follow-up. At 6–9 months from baseline only the questionnaires will be completed.

Results: The study started recently; until now the first 15 patients have been included. Conclusion: Feasibility and the first results of this combined program seem promising. Grant: Dutch Cancer Society
Purpose: This study examined utility of self-report psychological screening in survivors of pediatric brain tumors, a population not well studied in previous psychological screening research.

Method: Participants were survivors followed in a neuro-oncology outcomes clinic who participated in Project REACH, a cohort study of locally-treated cancer survivors. 44 adolescents (age 12–18) completed the Beck Youth Inventory (BYI) and 52 young adults (age 19–30) completed the Brief Symptom Inventory-18 (BSI-18). Parents completed either the Child or Adult Behavior Checklist (CBCL/ABCL), depending on survivor age. Previously established cut-off scores were used to identify cases of significant distress.

Results: 84% of participants completed measures in <30 minutes, and 90% reported no distress associated with participation. In the young adults, 8.5% reported clinically significant distress and 34% reported moderate distress. Adolescent survivor and parent ratings had significant correlations ranging from .41-.44. (p < .01). Among adolescents, 38% reported clinically significant distress. Association of adolescent ratings of depression with parent ratings were strong (.51, p < .01), but adolescent report of anxiety was not associated with any parent ratings. Overall case agreement between survivor and parent ratings was only moderate, and cases identified as distressed by one reporter were not consistently captured by the other.

Conclusion: Many pediatric brain tumor survivors are capable of completing self-report psychological measures in a clinical setting without associated distress or burden. While survivors and parents demonstrate general agreement in ratings, each group provides unique information not available from the other. Assessing adolescent self-report may be of particular importance given that parent report does not provide a cohesive picture of important issues such as anxiety.

PS021

IS SURVIVOR IDENTITY ASSOCIATED WITH PHYSICAL AND BEHAVIORAL HEALTH?: RESULTS FROM PROJECT REACH

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Purpose: Health implications associated with cancer survivor identity are not well understood. This study examined the association of “Survivor” and “Victim” self-identification with health outcomes and health behaviors in a group of adults treated for childhood cancers.

Method: Participants were 200 survivors (52% female, median age 27) enrolled on Project REACH, a cohort study of locally-treated cancer patients. Participants responded to questions regarding the overall impact of cancer on their sense of identity and extent of identification with the terms “Cancer Survivor” and “Cancer Victim.” Responses to these two questions were dichotomized to capture strong identification with each.

Results: Survivor identification was endorsed by 68% of the sample, while only 8.5% reported Victim identification. Victim identification was associated with poor physical (p = .034) and emotional functioning (p = .008), as well as problematic health behaviors including binge drinking (p = .031). In contrast, those strongly identifying as survivors did not differ on physical or emotional functioning or health behaviors compared to those who did not. 38% of participants reported cancer strongly affected their identity, while 33% reported it had little or no effect. Participants who reported cancer had a strong impact on their identity were more likely to report poor emotional health outcomes (p = .037).

Conclusion: Surviving cancer does not guarantee adoption of a “Cancer Survivor” identity, and many childhood cancer survivors report little effect of cancer on their identity. Victim identity is uncommon, but associated with poor health outcomes and behaviors. Survivor identity is not linked with better health outcomes or health behaviors — a finding with important implications for post-treatment education and clinical care. The role of physical and emotional health outcomes in identity development and the implications for research and clinical care are explored.

PS022

SEXUAL FUNCTION IN CHILDHOOD CANCER SURVIVORS: RESULTS FROM PROJECT REACH

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Purpose: Sexual functioning in childhood cancer survivors is not well understood. We examined the report of sexual dysfunction in childhood cancer survivors and its relationship with physical and emotional functioning.

Method: Participants were 167 childhood cancer survivors (Mean age 30 yrs; Mean age at dx 10 yrs; 56% female), enrolled in Project REACH, a longitudinal research study. Measures included the MOS Sexual Functioning scale which assesses problems with desire and elements of the sexual response cycle including arousal and orgasm, and the SF-12. Participants who endorsed 2 or more of the 5-item MOS Sexual Functioning scale were classified as having significant sexual dysfunction.

Results: Forty percent of participants (N = 66) reported significant sexual dysfunction with prevalence being significantly higher among females (45%) vs males (21%), (p < .001). Type of cancer, age at diagnosis and previous radiation treatment were not related to sexual functioning. Sexual dysfunction was significantly correlated with poor emotional functioning (p < .001), but contrary to expectations, it was not related to current pain or overall physical functioning.

Conclusion: Results highlight the unexpectedly high prevalence of significant sexual dysfunction, as evidenced by reported problems in more than one area of sexual function, especially in female survivors. These findings call for a better understanding of the particular relationship between sexual dysfunction and emotional well-being in this relatively young population. Of note, the predictors of sexual dysfunction previously reported in adult cancer patients (e.g., diagnosis, physical function, radiation therapy) were not associated with sexual problems in this sample of childhood cancer survivors. These findings strongly underscore the need for clinicians to thoroughly assess sexual function in long-term childhood cancer survivors even when these survivors are young and in the absence of other physical health problems.
Purpose: In the last two decades, there has been great interest in understanding the psychosocial sequelae and identifying areas of intervention with childhood cancer survivors. Several studies found that parents and children face different kinds of effects that co-exist: post-traumatic stress, psychosocial sequelae, deficits and maladjustment on one hand and post-traumatic growth, resilience on the other. The objective of the study was to explore parents and children personal meanings about the experience, to analyze the relationship between age at diagnosis, communication style and coping style in the family with type of trace in the adolescent as well as presence or absence of memories.

Method: Cross-sectional and descriptive study, based on qualitative interviews made during regular visits at the follow-up clinic. Inclusion criteria: Acute Lymphoblastic Leukemia patients; treated by the same team, at least 5 years since diagnosis and 2 years or more since end of treatment. Exclusion criteria: concurrent or previous disease.

Results: Thirty-five survivors and their parents were interviewed in a six month period. Sample was divided in four groups regarding age at diagnosis. Inductive thematic analysis was made and interviews were coded considering some categories: trauma/elaboration/memories, before/after, talk/no talk about illness, post-traumatic growth, coping strategies, references to threat or death. Six typologies were constructed. Post traumatic growth appears in cases of older children, with own memories and perception of threat. Traumatic symptoms appear in survivors that were younger at diagnosis or whose parents neither elaborated the experience nor found new meanings in their life.

Conclusion: Parents’ role is crucial influencing meaning making as well as the way children elaborate the experience. Age at diagnosis seems to be a very important variable regarding effects and post traumatic growth. The cut off for having own memories and meanings seems to be puberty and adolescence. Further research of these typologies is needed.

PS025
MUSIC-BASED INTERVENTION REPORTING GUIDELINES TO IMPROVE RESEARCH AND CLINICAL PRACTICE IN PEDIATRIC ONCOLOGY
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Purpose: Despite widespread use of complementary and alternative medicine (CAM) by children with cancer and parents (46–84%), there are limited data to determine efficacy and in turn guide application of interventions like music therapy. In addition, inconsistent quality of existing research reports particularly in the area of intervention reporting inhibit interpretation, replication, and translation of research into practice. The purpose of this study was to conduct a critical analysis of how music-based interventions are described in published research literature. Outcomes from the review led to subsequent reporting guideline recommendations for music-based intervention studies.

Method: This review examined pediatric music-based intervention studies with randomized and non-randomized designs. Twenty-two studies that met specific inclusion criteria were reviewed for content in 11 areas that were based on CONSORT and TREND guidelines and expanded to include information specific to music-based intervention studies.

Results: This review revealed significant gaps in intervention reporting. Problems were particularly pronounced in eight of the eleven areas evaluated, indicating the need for reporting guidelines to improve music-based intervention reporting and advance clinical practice.

Conclusion: Results from this review, along with broader-based reviews of behavioral intervention reporting, were used to formulate reporting guidelines for music-based intervention studies. Recommendations pertain to reporting seven different components of music-based interventions including intervention theory, intervention content, intervention delivery schedule, interventionist, treatment fidelity, setting, and unit of delivery. These recommendations are intended to support CONSORT and TREND statements for transparent reporting of interventions while taking into account the variety, complexity, and uniqueness of music-based interventions.

PS026
PRISMA STUDY: THE EFFICACY OF NEUROFEEDBACK TO IMPROVE SPEED, MEMORY AND ATTENTION IN PEDIATRIC BRAIN TUMOR SURVIVORS: A RANDOMIZED CONTROLLED TRIAL
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Purpose: The aim of this study is to investigate the efficacy of neurofeedback (NFB) to improve attention, memory and processing speed in children treated for a Brain Tumor (BT). In the United States of America every year approximately 2,200 children under 20 years of age are diagnosed with a BT. Nowadays the 5-year relative survival rate of these children is 65%. Neurotoxicity caused by treatment for a BT is a major cause of neurocognitive decline in Pediatric Brain tumor Survivors (PBS).

Method: NFB is a training to optimize brain activity, through the principle of operant conditioning. Several studies have shown that NFB has the capacity to improve the brain systems mediating selective attention and response inhibition in children with Attention Deficit/Hyperactive Disorder (AD/HD). PBS exhibit symptoms comparable to those of children with AD/HD. However, NFB has not been used as an intervention in PBS yet. The effectiveness of NFB in PBS will be investigated in a multicenter randomized controlled trial. The intervention group of 35 patients will receive 30 sessions of NFB. The control group will also consist of 35 patients, will receive 30 session of placebo neurofeedback. Placebo neurofeedback is partly based on muscular tension of the patient and partly on a random signal generator.

Results: Neuropsychological tests and psychosocial questionnaires will be used to evaluate pre- and post-NFB intervention functioning, as well as a 6-month follow-up. Questionnaires will be administered online. To control for test-retest effect, a group of 35 healthy siblings will be included in the study. They will not receive any intervention.

Conclusion: Relevance: If NFB proves to be effective for PBS this will be a great improvement for their (neuro-) psychological functioning and quality of life.
Examining the relation of the parent variables well-being, illness and worse QoL than young adults without a history of cancer. The aim of the present study is to confirm that survivors with a benefit because of childhood cancer even achieved fewer developmental milestones and experience worse QoL than survivors without a benefit.

Method: Survivors aged 18–30 completed the Course of Life Questionnaire (developmental milestones) and the RAND-36 (QoL). Survivors with a benefit because of childhood cancer (N = 53, 40.4% brain tumours, age at diagnosis 7.3 years) were compared to survivors without a benefit (N = 313, 5.4% brain tumours, age at diagnosis 6.8 years), using analysis of variance and logistic regression, both by group, age and gender. Effect sizes (d) and odds ratios (OR) were calculated.

Results: In all domains, the chance of achieving developmental milestones was lower for survivors with a benefit compared to survivors without a benefit. Significant (p < 0.01) ORs ranged from 0.37–0.43 for the milestones in the autonomy domain, 0.26–0.44 in the social domain and 0.38–0.43 in the psychosocial domain. Survivors with a benefit reported worse overall physical and overall mental QoL, than the survivors without a benefit: p < 0.001, d = 1.34 and p = 0.003, d = 0.54 respectively. In addition, they scored worse on 6 out of the 8 domains of QoL: physical (p < 0.001, d = 1.46), social (p < 0.001, d = 0.79) role limitations physical (p < 0.001, d = 0.84), role limitations emotional (p = 0.004, d = 0.52), bodily pain (p < 0.001, d = 0.72), health perceptions (p < 0.001, d = 0.80).

Conclusion: Survivors with a benefit are at risk for multiple problems later in life. Early recognition is warranted. Further research should show whether stimulating the achievement of developmental milestones while growing up will create conditions for a better labour market position and result in a better QoL later in life.

DEVELOPMENTAL TRAJECTORY AND QOL OF SURVIVORS WITH A BENEFIT BECAUSE OF CHILDHOOD CANCER

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Purpose: Young adult survivors of childhood cancer show a less favourable developmental trajectory in terms of social, psychosexual and autonomy development, and worse QoL than young adults without a history of cancer. The aim of the present study is to confirm that survivors with a benefit because of childhood cancer even achieved fewer developmental milestones and experience worse QoL than survivors without a benefit.

Method: Survivors aged 18–30 completed the Course of Life Questionnaire (developmental milestones) and the RAND-36 (QoL). Survivors with a benefit because of childhood cancer (N = 53, 40.4% brain tumours, age at diagnosis 7.3 years) were compared to survivors without a benefit (N = 313, 5.4% brain tumours, age at diagnosis 6.8 years), using analysis of variance and logistic regression, both by group, age and gender. Effect sizes (d) and odds ratios (OR) were calculated.

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Conclusion: Survivors with a benefit are at risk for multiple problems later in life. Early recognition is warranted. Further research should show whether stimulating the achievement of developmental milestones while growing up will create conditions for a better labour market position and result in a better QoL later in life.

RELATION BETWEEN PARENT AND CHILD PSYCHOSOCIAL ADJUSTMENT IN CHILDREN WITH ACUTE LYMPHOBlastic LEUKAEMIA: THE ROLE OF PARENTING STRESS AS A MEDIATOR

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Purpose: Examining the relation of the parent variables well-being, illness cognitions, coping and perceived social support with change in the psychosocial adjustment of children with acute lymphoblastic leukaemia (ALL) during first year of treatment. A proposed mediating role of parenting stress in these relations was explored.

Method: A nationwide multicentered study with a longitudinal design in which at diagnosis sixty-five parents of children (ages 2–17) diagnosed with ALL completed parent adjustment questionnaires (well-being, coping, illness cognitions, parenting stress and perceived social support) and a child psychosocial adjustment questionnaire at diagnosis and after one year treatment. Regression analyses including specific mediation analyses were used to investigate the relationship between parent variables, parenting stress and child outcome.

Results: Parenting stress (Beta: 0.227; p < .01) and parental perceived social support (beta -.805; p < .05) were found to predict change in child behaviour problems. Moreover, point estimates of the mediation analysis showed parenting stress operating as a mediator in part of the relations between parent and child adjustment.

Conclusion: Findings support an early screening of parents to select families at risk for psychosocial adjustment problems.

Exploration of Parents’ Preferences for Information Sharing with Children with Cancer

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Purpose: Despite better survival rates these days, childhood cancer is a major life-event that causes significant distress for families. Open communication and the provision of information appear to be important mediating factors in reducing the negative impact of cancer. Some studies, however, suggest that parents can struggle with information sharing because they have an instinctive need to protect their child and have doubts about the benefits of information sharing. This research investigated parents’ perspectives on information sharing with their child and to provide a greater understanding of the factors which facilitate or hinder parents’ communication with their ill child.

Method: The data were obtained from in-depth interviews with parents (n = 22) of children with cancer from one unit in Ireland in 2009. This data is drawn from a larger study which investigated children’s participation in decision-making from multiple perspectives. Transcripts were analysed using interpretative phenomenological analysis (IPA) which strives to understand experiences from the perspective of the participant whilst allowing the researcher to ask critical questions of the text in order to interpret the participants’ responses.

Results: Parents report varying preferences for sharing information with their children. Some parents want to protect their child from unnecessary worry and so they restrict information, are careful with terms, and carefully monitor all information exchanges between their child and health professionals. Parents feel they are acting in the best interests of the child because they know their child best. When health professionals do not respect parents role as gatekeepers of information, this can cause considerable relationships difficulties. Other parents feel it is essential that their children are involved and hence always encourage and support them to be actively involved in all discussions about their care and treatment.

Conclusion: Parents hold varying perspectives and can play a significant role in facilitating or obstructing information sharing with their child.

Feasibility of Neurofeedback for Reducing Neurocognitive Deficits After a Childhood Brain Tumor

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Purpose: Survivors of a childhood brain tumor experience neurocognitive deficits, including decreased processing speed, attention and memory, resulting in problems with learning and social functioning. Therefore, the need for effective cognitive rehabilitation possibilities in this group of survivors is high. There is growing evidence that neurofeedback, a ‘brain wave’ feedback training in which the brain activity is regulated, is a valuable treatment for children with brain disorders (e.g. ADHD, epilepsy, traumatic brain injury) and could be helpful for pediatric brain tumor survivors. In this pilot study we explored the feasibility and neurocognitive impact of neurofeedback.

Method: Seventeen survivors with cognitive problems were invited to join this pilot-study. Before starting the training a quantitative electroencephalogram (QEEG) was made and a neurocognitive assessment was performed. The QEEG and assessment were repeated after 30 training sessions
PS032

PARENTAL RATINGS OF LATE EFFECTS IN SURVIVORS OF CHILDHOOD BRAIN TUMORS: ASSOCIATIONS WITH RADIOTherAPY, HEALTH-RELATED QUALITY OF LIFE AND INTEllIGENCE

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Purpose: To examine the relationship between parental ratings of late effects after treatment for childhood brain tumors and radiotherapy (RT), the patient’s health-related quality of life (HRQoL) and general intelligence (IQ).

Method: A consecutive sample of 123 patients aged 8 to 40 years from East Denmark, treated for a brain tumor before the age of 15 years between 1970 and 1997. Parents rated whether 15 symptoms and deficits had changed after the therapy. The patients answered an early version of the Minneapolis–Manchester Quality of Life questionnaire (MMQL) and were assessed for IQ by WISC–R or WAIS–R.

Results: The most frequently reported deficits were learning disabilities, attention and memory problems, fatigue, and motor problems, all reported by 50–59% of the parents. The 15 symptom ratings were intercorrelated and a scale counting the number of symptoms reported for each child had a mean score of 6.5 symptoms [range: 0–15]. For the 69 patients treated with RT, the parents rated a mean of 8.4 symptoms, while the mean rating was 4.1 symptoms for the 54 children treated without RT (p < 0.001). The number of symptoms rated correlated significantly with the patients’ Full Scale IQ (r = -0.62), and with the patients’ ratings’ quality of life on all MMQL scales (r ranging from -0.18 to -0.55). Adjusting for IQ attenuated the correlations between parental ratings and quality of life reported by the patients, but several correlations remained significant.

Conclusion: Parental ratings of new problems after treatment for a brain tumor in childhood show a meaningful pattern of associations with treatment parameters (RT), formal cognitive testing (IQ) and the patients’ reported quality of life (HRQoL). To some extent these ratings reflect information that is independent of late effects on IQ and thus parental ratings provide useful supplementary information.

PS033

TREATMENT NON-ADHERENCE IN TEENAGE AND YOUNG ADULT CANCER PATIENTS: A MULTI-INFORMANT, PROSPECTIVE STUDY

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Purpose: There is a definite paucity of studies examining treatment non-adherence (NA) in teenage and young adult (TYA) cancer patients. Furthermore, many of these studies have assessed NA at one time point and/or used only one source of information. Our aims were to (1) examine the adherence difficulties encountered by TYA patients during the 4 months following diagnosis and (2) to examine the association between health professional reports of patient adherence at 2 months post-diagnosis and patient self-reported adherence at 4 months post-diagnosis.

Method: Cancer patients (16–24 years old), diagnosed and treated at a TYA cancer centre in the UK during a 30 month study period were eligible for the study. At 2 months post-diagnosis, a nurse and consultant for each patient reported upon the adherence functioning of their patient, using a scale that reflected the many treatment challenges encountered by TYA cancer patients. Patients completed a comparable adherence scale at 4 months post-diagnosis.

Results: Eighty three percent (84/101) of eligible patients participated. Results from the patient report measure (completed at 4 months post-diagnosis) showed that total NA scores ranged from 0 (100% adherence) to 19 (37% NA), mean 4.99 (10% NA), sd 4.46. Patient demographics (gender, cancer diagnosis, age at diagnosis) were not associated with patient reported adherence. However, consultant perception of patient adherence at 2 months post-diagnosis correlated with patient reported adherence obtained at 4 months (r = .34, p = .002).

Conclusion: During the first few months of treatment, NA may be a problem, with up to 37% of treatment demands not being adhered to. With the lack of consistency in the literature of factors associated with NA, the potential role of consultants in identifying patients at risk of adherence difficulties is highlighted. The authors are currently establishing the validity of these findings using an objective measure of patient adherence.

PS034

THEIMPACT OF CANCER ON THE QUALITY OF LIFE OF HEALTHY SIBLINGS

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Purpose: When a child is diagnosed with cancer the family situation undergoes dramatic changes potentially putting healthy siblings under severe stress. Quality of life of siblings may be affected, but up till now little is known about siblings’ self-ratings of their QoL or about parental perceptions of the siblings’ QoL.

Method: Quality of life was assessed using the parent and child versions of the Child Health Questionnaire (CHQ, Landgraf et al., 1999). 60 parents (48 mothers) and 42 siblings (28 boys) participated. Mean domain scores of the siblings and their parents were compared to mean domain scores of a Belgian reference group of siblings of healthy children and their parents.

Results: Apart from a slightly lower mean score on the Family-Cohesion domain, siblings of children with cancer scored higher on all QoL domains compared to the reference group. Siblings reported significantly better General Health and less Bodily Pain. No age effects were found. Boys reported less Bodily Pain, a better General Behaviour and a better Mental Health.

In contrast, compared to the reference group, parents reported significantly lower QoL on the domains General Health, Parental Impact-Emotional, Parental Impact-Time, Family-Limitations in activities and Family-Cohesion. In the parent ratings no age or gender effects were found.

Conclusion: Siblings reported a good QoL, in many domains better than siblings of healthy children. Parents rated the siblings’ QoL, as lower compared to parents of siblings of healthy children, specifically on family related domains. Counselling families should take into account parental perceptions and possible worries of the impact of cancer on healthy siblings, especially bearing in mind siblings’ self-report of their QoL, which are encouraging.
Method: A mailed questionnaire was sent to 243 families. This questionnaire was filled out by parents. Questions were related to the needs and use of psychological interventions at different times. Reasons for wishing these psychological interventions or not, potential difficulties and satisfaction where also explored.

Results: A total of 110 families (45%) participated. During the first two years of the follow-up, 41% families met a psychologist, most frequently for the treated patient, less for parents and even less for siblings. 53% families mentioned no need for a psychological support. Only 11% children treated came back for psychological support to the unit. No parents or siblings have done it. Families were highly satisfied (75.5%). Their main wishes were to be reassured, to be listened to what they had gone through and talk about the future. The majority of respondent families (65.5%) agreed with the proposition of a systematic psychological interview during this period, following the end of the treatment, mainly because of their persistent fears and feelings of vulnerability and loneliness.

Conclusion: All families usually want to recover a normal life and forget this upsetting experience. Persistent fear and distress may occur and negatively affect the well-being of the family. Even if it seems to be difficult to come back to the hospital, the specific unit appeared as a reassuring place.

Most parents wish to be proposed a systematic psychological assessment during this period.

PS036

FACIAL EXPRESSION RECOGNITION AND SOCIAL-COGNITIVE FUNCTIONING IN SURVIVORS OF CHILDHOOD CANCER

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Purpose: Survivors of childhood cancer exhibit impairments in cognitive and social functioning, including recently-observed deficits in facial expression recognition. Interpretation of emotions portrayed through facial expressions is considered a key component of social interaction. However, exploration of these deficits has been limited by a lack of sensitive measures. Therefore, we developed the Facial Expression Recognition Instrument (FERI) using responsive virtual human technology. The FERI demonstrated good initial validity and now needs to be evaluated against specific measures of social functioning. The objectives of the current study were to determine the associations between the FERI and measures of social and cognitive functioning (processing speed, attention).

Method: Thirty survivors of pediatric cancer and 30 typically-developing children aged 10–16 are currently being recruited (current n = 41). After consent, participants complete the FERI, cognitive testing, and measures of social functioning. Study participation takes approximately 90 minutes for which participants are paid $10. The FERI consists of 48 static faces displaying overt or subtle variations of the six basic emotions: happiness, sadness, anger, fear, surprise and disgust) based on Ekman’s Facial Action Coding System. Participants are asked to identify the correct emotion from these choices.

Results: Currently, 15 survivors of pediatric cancer and 26 typically-developing children have completed study procedures. Preliminary analyses reveal robust correlations between the FERI and measures of social functioning (e.g., PedsQL; r = .46, p < .05), such that deficits in facial expression recognition were associated with poorer parent-rated social functioning. Additionally, the FERI was strongly correlated with measures of cognitive functioning, with deficits significantly correlated with slower processing speed (r = .55, p < .05) and parent-rated attention problems (r = .34).

Conclusion: Preliminary results reveal robust associations between facial expression recognition and measures of social and cognitive functioning. Facial expression may represent a salient intervention target for survivors with social deficits, work that is critical to improving the long-term outcomes and quality of life.

PS037

DEVELOPMENT OF INTERNATIONAL NURSING COLLABORATION: STRATEGIES TO IMPROVE PATIENT OUTCOMES

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Purpose: Oncology nurses require specialized education and training to ensure safe, efficient and evidence based patient care. Collaboration between developed and developing organizations facilitates training and mentoring between expert and novice nurses, supports information sharing, professional growth and improves outcomes.

Concepts of a successful partnership include shared decision making, participation in process improvement and respectful interactions among members.

Method: In 2008, a collaboration between Children’s Cancer Hospital Egypt 57357 (CCHE) and Dana-Farber/Children’s Hospital Cancer Care (DFCHCC) began.

During 2009, an educational nursing conference led by nursing staff from both centers was offered to an international nursing and medical community in Cairo.

Results: The essentials of pediatric oncology nursing were presented, case studies were shared and discussions of best practice were initiated. Further education and clinical support was provided by DFCHCC nursing experts during the opening of the CCHE Hematopoietic Stem Cell Transplant unit and the implementation of a computer order entry system. Future initiatives include a leadership series focusing on communication, coaching, mentoring and goal setting. The International Society of Pediatric Oncology (SIOP) Conference, Boston 2010, will host nurses from Cairo to attend educational sessions, observe patient care, and participate in discussions about clinical and professional practice.

Conclusion: Both organizations are committed to sustaining open communication and working relationships to improve the care and outcome of pediatric oncology patients around the world. Long term goals include: promoting and supporting nursing practice and leadership, developing nursing research, creating an educator’s learning series, and offering fellowship opportunities at both institutions. This international nursing collaboration is a model that can be expanded to other developing organizations.

PS038

FAMILY ADJUSTMENT TO CHILDHOOD CANCER: A SYSTEMATIC REVIEW

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Purpose: The current study sought to examine levels of distress in mothers of children recently diagnosed with cancer. The current study is based upon a larger study of mothers of children newly diagnosed with cancer. Data collection is ongoing.

Method: Participants were 29 mothers of children, ages two to 16 (M = 7.76 years, 48.3% male), who were diagnosed with pediatric cancer six to 18 weeks prior to participation. Mothers were ages 22 to 55 (M = 35.28 years, 55.2% Caucasian). As part of a larger study, mothers completed a demographic form, the Symptom Checklist-90-R (SCL-90-R), and the Impact of Events Scale-Revised (IES-R). Participants were recruited while attending outpatient appointments at the cancer center of a midwestern children’s hospital.

Results: First, the percentage of mothers who reported scores within the clinically significant range on each of the measures of distress was examined. Using a T-score of 63 as a cutoff, 17.2% of mothers met criteria for clinically significant levels of distress on the Global Severity Index (GSI) of the SCL-90-R. Using Creamer, Bell, and Fullla’s (2002) recommended cutoff score of 33 or greater, 27.2% of mothers met criteria for posttraumatic stress disorder. Next, a hierarchical regression was conducted. Theoretically significant (Thompson & Gustafson, 1996) demographic covariates were selected and entered into the regression equation. After controlling for child age and annual family income, global distress, as measured by GSI score, was a significant predictor of posttraumatic stress symptoms in mothers of children newly diagnosed with cancer, F(3, 24) = 15.643, p = .000.

Conclusion: A subset of mothers of children who have recently been diagnosed with cancer are at risk for clinically significant level of distress. Those mothers who are experiencing global distress are at an increased risk to also experience posttraumatic stress symptoms.
PS039

CHILDREN IN REMISSION FROM ACUTE LYMPHOBLASTIC LEUKAEMIA: MENTAL HEALTH AND PSYCHOSOCIAL ADJUSTMENT

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Purpose: To assess the mental health and psychosocial adjustment of children in remission from acute lymphoblastic leukaemia (ALL) compared to healthy controls. Method: Children and adolescents treated for ALL (n = 40; mean age 11.8 years, range 8.5–15.4) and healthy controls (n = 42; mean age 11.8, range 8.11–15.0) were assessed through a cross-sectional approach using the Child Behaviour Checklist (CBCL), the Youth Self-Report (YSR) and the Strength and Difficulties Questionnaire (SDQ). Results: Children treated for ALL showed on average significantly more symptoms compared to healthy controls as measured by the CBCL Total Behaviour Score for mother’s report (P = 0.005), and for father’s report (P = 0.004), as well as for the internalizing and externalizing subscales. Six children had a CBCL score of ≥ 90 percentile, indicative of severe problems, as reported by the mothers, while none in the control group. The SDQ parent self-report for mothers showed significant differences for the emotional symptoms summary scale (P = 0.008). Conclusion: Children in remission from ALL showed on average significantly more problems regarding mental health and psychosocial adjustment compared to healthy controls, as reported by their parents. Adequate rehabilitation and follow-up programmes should be implemented for children in remission from ALL.

PS040

RESTRICTIONS IN DAILY LIFE AFTER RETINOBLASTOMA FROM THE PERSPECTIVE OF THE SURVIVORS

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Purpose: Little is known about the impact of retinoblastoma (RB) on the health status of survivors in terms of disabilities and worries, both of which may restrict participation in activities of daily life. The purpose of this study is to investigate the consequences of RB, the ICF as a principal framework, and to develop a second primary tumour (SPT). Compared with the general population, RB survivors did not differ in rates of employment or marital status. However, special educational services were more frequently offered, and the level of completed education was lower. Conclusion: RB has influenced the lives of most survivors and, even though their prognosis was good, illness-related restrictions are common. Especially fear of developing SPT and of further loss of vision are important life-long problems, and many survivors had special education needs. The ICF might serve as a bridge between families and professionals, because this classification may facilitate early detection of problems.

PS041

COPEING STRATEGIES OF RETINOBLASTOMA SURVIVORS IN RELATION TO BEHA VIORAL PROBLEMS

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Purpose: To assess coping strategies of long-term retinoblastoma (RB) survivors and explore determinants of behavioural functioning, including medical, socio-demographic and coping variables. Method: This population-based cross-sectional study included 117 RB survivors (12–35 years), registered in the Dutch national RB register. Survivors were asked to fill in coping, social support and behavioural questionnaires, and situational characteristics were obtained from medical archives and from an interview. Prevalence rates of coping strategies were computed based on self-reports. One-sample t-tests were applied to analyse differences in the use of coping strategies compared with healthy reference samples. Multiple regression analyses were performed to identify various determinants for behavioural problems within the RB sample. Results: RB survivors differed from their healthy reference group in one coping style, i.e. they showed significantly less emotion-oriented coping behaviour. Adolescents who came from a single-parent family and/or experienced lower social support and used more emotion-oriented coping reported more total problem behaviour. More internalising problems were reported for adolescents who experienced less social support and less acceptance of the disease. For adults, more life events, emotion-oriented coping and lower social support explained more total problem behaviour, especially internalising problems. Conclusion: RB survivors showed less emotion-oriented coping behaviour compared with the reference group. Behavioural problems are best determined by emotion-oriented coping, social support, life events other than RB and acceptance of the disease, and not by medical variables. Therefore, these variables should be taken into consideration during interventions for this group.
**THE RELATIONSHIP BETWEEN PSYCHOSOCIAL FUNCTIONING DURING AND AFTER CANCER TREATMENT AND TREATMENT SEVERITY IN CHILDHOOD CANCER SURVIVORS**

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**Purpose:** Childhood cancer survivors (CCS) are at increased risk for psychological problems during and after cancer treatment. The objective of this study is to understand the course of psychological problems from diagnosis through survivorship and to examine risk factors influencing psychological distress.

**Method:** CCS were recruited during a CCS Clinic (n = 141) visit. The parent (child < 18 years old) or the survivor (> 18 years old) completed a questionnaire about depression, anxiety, behavior problems, anger problems, and sleep problems during four time periods: before diagnosis, during treatment, after treatment, and current status. An overall composite score was generated. Risk factors included diagnosis, age at diagnosis, gender, current age, and cancer treatment severity. Treatment severity was rated using the Intensity of Treatment Rating Scale 2.0.

**Results:** Cancer diagnoses included 57% Leukemia/Lymphoma, 39% Solid Tumor, 2% CNS Tumor, and 3% Other. The average age of diagnosis was 4.2 (range 0.2–14) with treatment severity rated at 1 (6.2%), 2 (32.8%), 3 (35.9%) and 4 (25%). Participants reported at least one item of psychosocial distress before treatment (9.7%), during treatment (28.7%), after treatment (37.9%), and currently (35.0%). Repeated measures analysis of variance was used to assess psychosocial distress over time and possible risk factors. There was a significant effect of time (F = 6.24, df = 3,106, p < .001) and treatment severity was significant at a trend level (F = 2.933, df = 1, 106, p < .09) but did not interact with changes in psychosocial distress over time (F = 2.02, df = 3,106, p = .111). Neither age at diagnosis nor gender was associated with psychosocial distress.

**Before During After Currently**

Behavior problems 4% 4% 12% 13%
Depression 1% 7% 11% 8%
Anxiety 3% 17% 20% 17%
Anger 4% 12% 15% 15%
Sleep problems 4% 14% 13% 12%

**Conclusion:** Psychosocial distress did not decrease following the termination of cancer treatment suggesting a long-term need for psychologists in cancer survivor care.

**H.L.Lu Fe, Pediatric Oncology Unit, Valencia, Spain**

**Pediatric cancer survivors are at risk of developing physical and mental health problems in comparison to peers. We aim to evaluate the long-term sequelae in our population and their repercussion for cognitive, physical and behavioural functioning in order to establish individualized programs to promote healthy behaviours and early detection of chronic health problems.**

**Method:** Prospective transversal study in patients with leukemia and solid tumors (ST) (except CNS tumours) treated in our Unit, > 5 years (y) from cancer treatment, still in the follow-up (FU) clinic, informed consent signed. Survivors completed an in-house questionnaire about health and lifestyle, later reviewed together with the nurse. HU23P4ES.4Q (Spanish-Proxy) was applied, being the psychooncologist the interviewer. Statistical analysis (frequencies, parametric tests) was carried out (SPSS 17.0).

**Results:** Out of 225 patients included, 110 completed HU3 (66 Leukemia, 44 ST), median age at evaluation 19y (range: 6–29y), median follow-up 13y (range: 5–23y); 67% male. Health problems detected in the in-house questionnaire were related to body-image and fertility. Asthenia, back pain, visual and mood problems were frequent symptoms. HU3 Utility Scores were 0.94 (95% CI: 0.89–0.99) in leukemias and 0.93 (95% CI: 0.87–0.99) in ST (p n.s.). Regarding to individual attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition, pain) there were not statistical differences between both groups (at level > 2). Personal scores (Excellent-
SIOP ABSTRACTS

Very Good; Good; Regular-Bad) show minor differences (68%-30%-2% in leukemias; 61%-39%-0% in ST).

Conclusion: 1/Our in-house questionnaire informs about survivors' problems with more detail than the brief interview in the FU-clinic: body-image and fertility are issues of interest for them. 2/HU3 Utility Scores were similar among leukemia and ST survivors. 3/HU3 measures quality of life in a specific cohort of long-term childhood-cancer survivors and reflects their own health-status perception as a good or excellent, with a median long time follow-up after cancer treatment. Supported by: FIS8062307 and CANECARE

OPTIMISM AND PESSIMISM AS PREDICTORS OF CHILDREN'S FUNCTIONING FOLLOWING STEM CELL TRANSPLANTATION (SCT)

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Purpose: Stem Cell Transplantation (SCT) is a stressful experience for children and parents. Children’s functioning prior to transplant may be predictive of long-term outcomes. The current study was designed to examine the extent to which children’s optimism and pessimism prior to SCT predict affective functioning and quality of life 6 months later.

Method: Ninety-three children aged 6–18 (Mean age = 12.7, SD = 3.9) preparing to undergo SCT and their primary caregivers were recruited for a multi-site clinical trial examining the efficacy of a psychosocial intervention during SCT. Prior to randomization and preparative therapy (i.e. baseline), children completed a measure of optimism and pessimism. Parents and children also reported on child affective functioning and quality of life at 6 months post-transplant. We previously discovered that optimism and pessimism prior to SCT predict affective functioning and quality of life 6 months later.

Results: Analyses examined associations of baseline optimism and pessimism with affective functioning and quality of life at 6 months post-transplant. We previously reported significant associations within baseline. As expected, optimism was associated with fewer symptoms of anxiety and depression and better quality of life (r = 3-4), whereas pessimism demonstrated similar correlations in the opposite direction. However, after controlling for baseline functioning, nearly all correlations became non-significant and it appeared that this could be accounted for by stable stability in children’s functioning over time. In contrast, baseline optimism or pessimism remained predictive of positive affectivity and behavioral functioning.

Conclusion: The extent to which children report being optimistic or pessimistic prior to SCT appears to predict variability in how they are functioning following SCT. However, it is possible that these associations over time are primarily accounted for by stability in children’s baseline and later functioning.

INTRODUCING ZORA CAMP4ALL: A VIRTUAL COMMUNITY TO AUGMENT PEDIATRIC CAMPING

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Purpose: Pediatric camping has a positive impact on adolescents with serious illnesses; in fact, camp increases hopeful attitudes by decreasing levels of anxiety related to illness (Briery & Rahban,1999; Turak et al., 2006). Yet, the hopefulness derived from the experience may dissipate when the camper returns to the chronic stress of his/her illness (Hinds, 1988). Since May 2009, in collaboration with Camp For All (CFA), a camp for children with serious illnesses, a 3D virtual environment resembling CFA was created for campers to maintain friendships from camp and explore concepts such as hope and connectedness.

Method: The technology called Zora Camp4All was introduced to 40 adolescents with cancer (N = 16), blood disorders (N = 6) and their siblings (N = 18) during their week at CFA in June 2009. After the week’s completion, they accessed this virtual camp through home or hospital computers. This pilot study’s goals were to discover if Zora Camp4All could: (1) sustain the campers’ hopefulness after their week of camp, (2) sustain the campers’ feeling of connectedness after their week of camp, and (3) promote the campers’ positive technological development (PTD). Hindi™ HS, Lee’s™ SCS-R, and Bersa™ PTD-Q were administered before and after using the program.

Results: The results from this study suggest that Zora Camp4All may contribute to sustaining social connectedness and PTD. The mean PTD increase (M = 2.13, SD = 4.55, N = 40) demonstrates significance (t = -2.95, p < .005) and the mean social connectedness increase (M = 1.08, SD = 2.27, N = 40) is also significant (t = -2.99, p < .005). Increase in hopefulness did not demonstrate statistical significance. Additionally, aspects of the program that contributed to sustainability remain to be determined. Siblings and campers from urban communities scored significantly lower in each of the three areas.

Conclusion: These findings call for future exploration into the field of virtual interventions catered to the developmental needs of adolescents with chronic life-stressors.

SWEDISH AND ICELANDIC PARENT SHORT AND LONGTERM PSYCHOSOCIAL CONSEQUENCES AFTER THEIR CHILD CANCER DIAGNOSIS

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Purpose: To determine the incidence and compare disease-related distress symptoms in Swedish and Icelandic parents of children diagnosed with cancer. Based on comparisons of the national samples we also wanted to identify nation-, site-, and organisational determinants of parent reactions.

Method: 309 parents of 199 childhood cancer (CC) patients who were either in treatment or had finished treatment at one of two sites in Sweden or Iceland participated. Cancer-specific distress were assessed with the 11-dimensional Parental Psychosocial Distress in Cancer questionnaire (PPD-C). PPD-C subscales cover: uncertainty (heightened informational needs), loss of control, self-esteem, anxiety, disease-related fear, loneliness, sleep disturbances, depression, and psychological and physical distress. General distress was assessed by the General Health Questionnaire (GHQ-12). Descriptive, comparative and inferential analyses were completed with analysing outcomes against non-clinical norm data, when possible.

Results: Systematic differences were found between cancer parents of the two national sites regarding all studied dimensions of distress (PPD-C) where Icelandic parents scored significantly higher on 5 of the 11 subscales: uncertainty (p = 0.000), loss of control regarding the parent (p = 0.007); disease-related fear (p = 0.000); sleep disturbances (p = 0.001); and psychological and physical distress (p = 0.003). For remaining subscales of PPD-C and for GHQ outcomes were similar for the two national groups. Distress generally exceeded the level of available comparison data from non-clinical norm group.

Conclusion: Findings confirmed heightened complex reactive distress symptoms in Swedish and Icelandic parents of CC patients. Great subjective needs of information – more prominent in the Icelandic group – about survival and late-effects signal needs of better routines for meeting parental uncertainty. National differences indicate that local/national arrangements regarding care,surveillance and information are influential means for reducing parental distress. Specialised centers appear as better suited to provide the kind of care and parental fellowship where mutual support and sharing information can reduce uncertainty.

BRAIN TUMORS IN CHILDHOOD AND ADOLESCENCE: COGNITIVE, EMOTIONAL AND PSYCHOSOCIAL LONGTERM EFFECTS AND SCHOOL INTEGRATION

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Purpose: Many survivors of brain-tumors in childhood and adolescence experience impairment of neuropsychological functioning and suffer from educational and psychosocial difficulties. The purpose of the study was to identify the influence of...
the late effects of disease and treatment on school performance and to assess the influence of psychosocial resources and stressors to educational success.

**Method:** The cognitive, affective and psychosocial long term outcome, concerning school integration and quality of life was assessed in 38 patients, diagnosed with a brain tumor in childhood under 18 years. The mean time since diagnosis was 10 years. The age of patients at the time of investigation ranged from 8 to 30 years. Neuropsychological testing, medical data, questionnaires and interviews with patients and parents were used.

**Results:** The study indicates that 62% of the patients needed support for developmental aspects in different domains after the end of treatment. Cognitive abilities like making conclusions and memory functions concerning verbal aspects, were clearly impaired in this sample. These results were particularly connected with a higher intensity of treatment with radiation and chemotherapy. The need for special education after therapy increased from 9% to 25%. Patients experienced higher anxiety and stress in relation to school, the more general emotional and behavioural problems existed. Behavioral problems were described more often, if the patient was older during diagnosis.

**Conclusion:** The results of the study show that long term effects like cognitive and socio-emotional impairment are especially relevant to school integration and quality of life. Particularly the statements of patients and parents emphasize the considerable need to prevent and ameliorate these late effects and to offer adequate psychosocial counseling and rehabilitation programs. There is as well a need for more communication of knowledge about consequences of long term effects with teachers at school.

Supported by Luebeck-Hilfe für krebskranke Kinder

**PS050**

**ADJUSTMENT IN ADOLESCENT AND YOUNG ADULT CANCER PATIENTS: COPING, SELF-IMAGE, EMOTIONAL, AND FAMILY DIMENSIONS**

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**Purpose:** The adolescent and young adult with cancer is confronted with a range of stressors resulting from both the treatment of a life threatening disease and the normative challenges associated with this stage of development. This study was undertaken to investigate the impact of these stressors on key developmental domains to include emotional status, self-image, family relationships, and coping with disease related stress.

**Method:** Subjects were 43 male (mean age = 19.44) and 25 female (mean age = 19.35) mixed-diagnosis cancer patients. Mean age at diagnosis was 16.12 years and mean time from diagnosis to assessment was 3.27 years. A non-cancer sample of 26 male and 47 females served as a contrast group for the coping assessment. Subjects completed a battery of validated measures; The Ways of Coping Checklist, Symptom Checklist-90, Offer Self-Image Questionnaire, and the Family Environment Scale. Completed questionnaires were submitted to a battery of validated measures; The Ways of Coping Checklist, Symptom Checklist-90, Offer Self-Image Questionnaire, and the Family Environment Scale.

**Results:** Analyses revealed that both the cancer and non-cancer groups most frequently employed problem-focused coping strategies. The results of a MANOVA testing differences between the two groups was significant (F(5,128) = 13.1, p < .001) as a result of a significant univariate difference on the Blunted Self Scale (F (1,132) = 61.0, p < .001), with patients using this strategy less than non-patients. Only the Avoidance coping scale scores were associated with emotional distress, accounting for 16.9 percent of the variance in Global Distress. Self-image comparisons showed that patients maintained an overall positive self-image in comparison to norms. Consistent with the literature, no clinically significant elevations in emotional distress were noted. Family climate was described by the cancer patients as exhibiting a moderately greater emphasis on religious issues and somewhat less expressiveness.

**Conclusion:** The overall picture resulting from the present study is encouraging. Based on our findings, interventions with this population should promote active problem solving and engagement as opposed to avoidant coping strategies.

**PT002**

**A STEM CELL ORIGIN FOR THE PERICYTES IN INFANTILE HEMANGIOMA**

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**Purpose:** Infantile hemangioma (IH) is a vascular tumor that occurs in 5–10% of infants of European descent. IH can grow dramatically and develops into a disorganized mass of blood vessels. We recently isolated Stem Cells (HemSC) from infant cancer patients as exhibiting a moderately greater emphasis on religious issues and somewhat less expressiveness. HemSC can differentiate into functional endothelial cells when injected into nude mice. This establishes the first cell-based animal model of IH. With our current work we demonstrated that IH blood vessels are aligned with closely associated perivascular cells. We hypothesized that these perivascular cells in IH originate from the HemSC.

**Method:** In vivo we showed that HemSC differentiate into alphaSMA expressing cells by tracking GFP-HemSC late after injection into nude mice. Colonization between GFP and SMA was found in cells adjacent to blood vessels in two different IH models that we devised: injection of HemSC alone and in combination with cord blood endothelial progenitor cells (cEPC).

In vitro we obtained pericytic differentiation of HemSC when cultured in direct contact with cEPC. The phenotype was confirmed by Real Time PCR, as increased expression of calponin 1 mRNA, and by immunohistochemistry for expression of SMA and smMHC. Single cell-derived clonal-HemSC were analyzed for the ability to originate from the HemSC.

**Results:** Hepatotoxicity is a major problem of children receiving cancer treatment. Our purpose was to study the effect of chemotherapy on liver, the organ where most of the chemotherapeutic agents are metabolized. Hepatotoxicity is a major problem of children receiving cancer treatment. We retrospectively collected medical records of 78 children diagnosed with cancer and treated for this in Emergency Hospital Targu Mures, Romania, Department of Pediatric Hematooncology, between January 2001 December 2007. Those children received treatment for acute leukemia (40 patients), and solid tumors (38 patients). We analyzed clinical and laboratory liver function parameters (serum bilirubin, liver enzymes, alkaline phosphatase, serum proteins, serum albumins), noticing liver function abnormalities. We used inferential statistics (chi square test) to determine the difference between frequency of hepatotoxicity in acute leukemia versus solid tumors.

**Conclusion:** Conclusions: From our results hepatotoxicity is highly frequent in all children treated with chemotherapy, but more frequent as severity and number of episodes in leukemia treatments than solid tumors, without a statistically significant difference, possibly by the comparatively small number of cases. Those results are imposing careful evaluation of liver function before starting treatment, considering that this might be strongly affected under chemotherapy. Therefore, after assessment of tumor histology, the next important factor to consider in the selection of chemotherapy regime is organ function.

**Results:** Using the OMS criteria of hepatotoxicity, we noticed: 18 patients with stage 0 hepatotoxicity, 53 episodes of stage 1 hepatotoxicity, 37 episodes of stage 2 hepatotoxicity, 27 episodes of stage 3 hepatotoxicity, 7 episodes of stage 4 hepatotoxicity.

**Conclusion:** Conclusions: From our results hepatotoxicity is highly frequent in all children treated with chemotherapy, but more frequent as severity and number of episodes in leukemia treatments than solid tumors, without a statistically significant difference, possibly by the comparatively small number of cases. Those results are imposing careful evaluation of liver function before starting treatment, considering that this might be strongly affected under chemotherapy. Therefore, after assessment of tumor histology, the next important factor to consider in the selection of chemotherapy regime is organ function.

**Results:** Hepatotoxicity is a major problem of children receiving cancer treatment. Our purpose was to study the effect of chemotherapy on liver, the organ where most of the chemotherapeutic agents are metabolized. Hepatotoxicity is a major problem of children receiving cancer treatment. We retrospectively collected medical records of 78 children diagnosed with cancer and treated for this in Emergency Hospital Targu Mures, Romania, Department of Pediatric Hematooncology, between January 2001 December 2007. Those children received treatment for acute leukemia (40 patients), and solid tumors (38 patients). We analyzed clinical and laboratory liver function parameters (serum bilirubin, liver enzymes, alkaline phosphatase, serum proteins, serum albumins), noticing liver function abnormalities. We used inferential statistics (chi square test) to determine the difference between frequency of hepatotoxicity in acute leukemia versus solid tumors.

**Conclusion:** Conclusions: From our results hepatotoxicity is highly frequent in all children treated with chemotherapy, but more frequent as severity and number of episodes in leukemia treatments than solid tumors, without a statistically significant difference, possibly by the comparatively small number of cases. Those results are imposing careful evaluation of liver function before starting treatment, considering that this might be strongly affected under chemotherapy. Therefore, after assessment of tumor histology, the next important factor to consider in the selection of chemotherapy regime is organ function.
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We noted the effect of propranolol in children with cutaneous capillary hemangioma.

The treatment of these tumors varies depending on the size, location and presence of thrombocytopenia (Kasabach Merritt syndrome) and consumptive coagulopathy. The purpose:

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Method: Aims and Objectives: To determine the efficiency of treatment of propranolol and its safety profile in children affected by a hemangioma. Materials and methods. Children with one or more hemangiomas sized more than 1 cm diameter without any threatening for vital or functional structure for which emergency treatment with steroid is not needed were treated with 2 mg/kg of propranolol after informed consent.

Children with cardiac pathology, and asthma were excluded. Proportion of hemangioma size variation was measured clinically at monthly intervals. Results: 20 patients with hemangiomas were included in the study. Of that 11 patients were on regular follow up. In that male: female ratio was 2:9. 60% of the children were less than 1 year. All patients were directly started on propranolol without steroids. All patients underwent treatment for more than 3 months, and are on regular follow up. 90% patients showed significant reduction in size and vascularity. In which, lesions completely disappeared in 20% of patients. No side effects of note.

Conclusion: Although larger studies are required to confirm, our study concludes that propranolol is a promising therapeutic option in the treatment of hemangioma.

PT003

CHILDHOOD MYELOFIBROSIS: EXPERIENCE AT A SINGLE TERTIARY CARE CENTER IN INDIA

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Purpose: Myelofibrosis, a chronic myeloproliferative disorder, is rare in childhood. Literacy evidence for both primary and secondary myelofibrosis in childhood is in the form of case reports or small case series. Investigators have reported variable natural history and outcomes in these. In this communiqué, we describe 10 cases of myelofibrosis diagnosed and managed at our center over 16 years.

Method: Case records of patients with myelofibrosis accrued at the Pediatric Oncology unit of All India Institute of Medical Sciences (AIIMS) over a 16 year period from 1988 to 2004 were retrieved. Data concerning symptoms, clinical features, lab investigations, diagnosis, management and outcome of all these patients was recorded.

There were 2 and 8 cases respectively of primary and secondary myelofibrosis. All patients presented with fever, pallor, hepatosplenomegaly and/or lymphadenopathy. Hodgkin’s lymphoma (n = 4), neuroblastoma (n = 1), thrombocytopenic thrombocytopenia (n = 1) and retropertioneal-mass (n = 1) were causal in 7 patients while diagnosis could not be established in a sole case of secondary myelofibrosis.

Results: Patients were managed with appropriate chemotherapy and supportive care. However, outcome was dismal. Only a sole patient with HD (case 9) is alive and well.

Conclusion: We emphasize variable clinical-laboratory-spectrum of myelofibrosis, highlight management constraints and concerns in a developing country and that prognosis/outcome depends upon apt management of underlying condition. We underscore the need of including HL in the list of pediatric malignancies causing consequent poorer outcome.

PT004

PROPRANOLOL: A PROMISING THERAPY FOR HEMANGIOMA IN CHILDREN

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Purpose: Hemangiomas, the most common benign tumors of infancy present with a broad spectrum of clinical behavior ranging from benign, slow growing tumors to aggressive, destructive lesions. They can cause high-output cardiac failure or cause thrombocytopenia ( Kasabach Merritt syndrome) and consumptive coagulopathy. The treatment of these tumors varies depending on the size, location and presence of complications. Standard treatments include cortico steroid therapy, vincristine, cytophosphamide, and α-interferon but these treatments cause frequent side effects. We noted the effect of propranolol in children with cutaneous capillary hemangioma studied by Le et al.® Labre`ze et al. Hence we undertook a study to find out the efficacy of propranolol in the treatment of hemangioma.

Method: AIMS and Objectives: To determine the efficiency of treatment of propranolol and its safety profile in children affected by a hemangioma. Materials and methods. Children with one or more hemangiomas sized more than 1 cm diameter without any threatening for vital or functional structure for which emergency treatment with steroid is not needed were treated with 2 mg/kg of propranolol after informed consent.

Children with cardiac pathology, and asthma were excluded. Proportion of hemangioma size variation was measured clinically at monthly intervals. Results: 20 patients with hemangiomas were included in the study. Of that 11 patients were on regular follow up. In that male: female ratio was 2:9. 60% of the children were less than 1 year. All patients were directly started on propranolol without steroids. All patients underwent treatment for more than 3 months, and are on regular follow up. 90% patients showed significant reduction in size and vascularity. In which, lesions completely disappeared in 20% of patients. No side effects of note.

Conclusion: Although larger studies are required to confirm, our study concludes that propranolol is a promising therapeutic option in the treatment of hemangioma.

PT005

NUHS EXPERIENCE IN VETOPEC CHEMOTHERAPY REGIMEN FOR RECURRENT/PROGRESSIVE SOLID TUMORS

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Purpose: To report our experience on use of VETOPEC chemotherapy regimen.

Method: A detailed retrospective chart review of all progressive/relapsed patients who were treated with VETOPEC was performed.

Results: VETOPEC regimen comprised of vincristine 0.05 mg/kg (days 1, 14), etoposide 2.5 mg/kg/day (days 1–3), cyclophosphamide 30 mg/kg/day (days 1–3). Fourteen patients were treated with VETOPEC: six retinoblastomas (2 – bilateral Stage IV, 2 – unilateral Stage IV, 2 – Stage V); three medulloblastomas (Stages T1M0; T2M1; T4M0); one supratellar primitive neuroectodermal tumor (Stage T4M2); one mediatinum germ cell tumor (Stage IV); one Kaposi’s sarcoma (Stage IV), one embryonal rhabdomyosarcoma (Stage I) and one Wilms’ tumor (Stage IV). Seven patients (42.85%) were treated with VETOPEC regimen (3 to 8 cycles) for their primary disease whilst remaining seven patients received (1 to 11 cycles) for relapsed/progressive disease. Combined therapies for primary disease were surgery and chemotherapy (VETOPEC, Infant Brain Protocol, others) for eight patients; chemotherapy (VETOPEC, BEP protocol) alone for two; one treated with combined chemotherapy (Infant Brain Protocol ), surgery and radiation; one with combined chemotherapy (PNET III) and radiation; and one with surgery alone.

Median relapse time from primary disease was 0.82 years (0.28 - 7.55 years). Median follow-up time was 1.23 years (0.12 - 7.77 years). Three patients had complete response whilst another two had partial response. At last follow up, seven patients had progression of disease of which four died of disease, two lost to follow up and one alive with disease. Three patients (21.42%) were alive without evidence of disease, three were lost to follow up and one was alive with disease and continues on VETOPEC chemotherapy. 5-year overall survival rate for cohort is 48.2% (95% CI, 11.4–85.0).

Conclusion: VETOPEC is a reasonable chemotherapy choice for treatment in patients with previously treated relapsed solid tumors.
previously been shown to give a highly accurate estimate of the AUC and might therefore be used to optimise the tobramycin therapy. The aim of the present study was to retrospectively evaluate the applicability of a limited sampling strategy based on one concentration measurement for estimation of the tobramycin AUC in clinical practice.

**Method:** Tobramycin concentration data (C1h) were obtained in the clinical routine care from 38 febrile paediatric cancer patients (median age: 4.3 years; range: 0.16 to 18.9 years; median dose: 6.8 mg/kg) during a total of 54 treatment courses. The comparison group consisted of concentration measurements (C1h) from twenty-three paediatric cancer patients (median age: 9.1 years; range: 1.8 to 18.0 years; median dose: 8.0 mg/kg) included in a previous pharmacokinetic study using standardised drug administration with carefully controlled blood sampling. Tobramycin was administered as a short time (5 min) infusion in all patients. Blood sampling was performed using the central venous access.

**Results:** Significantly higher (p = 0.009) tobramycin concentrations (C1h normalised by the dose in mg/m²) were obtained in the clinical routine care as compared to in the standardised pharmacokinetic study. Deviations in the blood sampling time point one hour post drug administration might contribute to the higher concentrations found in the clinical setting.

**Conclusion:** Educational efforts regarding blood sampling is recommended in order to use the limited sampling strategy for estimation of the systemic drug exposure of tobramycin.

**PT007**

**HEMATOLOGICAL TOXICITY AND SECONDARY MALIGNANCIES IN PEDIATRIC ONCOLOGY, EVALUATION OF 349 COURSES OF DEXRAZOXANE IN CHILDREN**

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**Purpose:** To Evaluate the hematological toxicity and incidence of secondary malignancies as a children with 5 rate lymphoblastic leukemia in a pediatric oncology unit in mexico receiving chemotherapy with daunorubicin and dexrazoxane.

**Method:** We evaluated 141 children with acute lymphoblastic leukemia diagnosed between 2005 and 2010 at the centro estatal de cancerologia in xalapa, state of veracruz in Mexico. After the administration every course of chemotherapy including daunorubicin and dexrazoxane in a dose 20 to 1 in relation to anthracyclin, we evaluate the nadir of hemoglobin,leukocytes,neutrophils and platelets and the incidence of secondary malignancies.

**Results:** We had 141 patients, 78 male and 63 female and 349 courses of chemotherapy with dexrazoxane and daunorubicin were administered. we did not found any case of secondary malignancy and about the hematological toxicity we found according to the nci criteria of toxicity a 40% of anemia Grade I, Leukopenia Grade II in 40%, neutropenia Grade 4 in 80%, and the most severe toxicity in platelets were Grade 4 in 20% of cases. there were no mortality related to this treatment.

**Conclusion:** Dexrazoxane is a drug used to prevent anthracycline-cardiotoxicity with some information in literature about the risk of hematological toxicity and secondary malignancies. We found that is safe to use dexrazoxane in children with no significant morbidity and mortality and without cases of secondary malignancies.

**PT008**

**EFFICACY OF INFLUENZA A(H1N1) VACCINATION IN CHILDREN WITH CANCER.**

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**Purpose:** To assess the ability of Influenza A(H1N1v) vaccine to elicit appropriate immune response among children with cancer receiving chemotherapy.

**Method:** Following informed consent 32 children (aged 1–18) with solid and haematological malignancies on chemotherapy or within six months from the last therapy were included. All patients received a dose of Influenza A(H1N1v) vaccine (Novartis FOCETRIA 0.5ml); two doses were administered to children <10-year-old three weeks later. Hemaggulutinin-inhibition (HI) antibody titre was determined on day 0 (pre-vaccination), on day 21 and on day 42 for children who received the second dose. Immune response was measured as geometric mean titres (GMT) and rising in HI titres. At day 0 the neutrophil, lymphocyte and CD4/CD8 counts were obtained to evaluate the possible role of these factors on the vaccine response.

**Results:** GMT of HI titres pre and post vaccination increased in all patients but two children and no significant differences were observed at day 42 for children aged <10 and at day 21 for children >10-year-old. In children <10-year-old seroconversion (HIx4) rate was 46.7% at day 21 and 81.3% at day 42; 87.5% rate was observed in children >10 at day 21. Seroprotection (HI > 40) was 60% (day 21), 87.5% (day 42) under 10 years old and 93.7% (day 21) in children aged >10. No significant differences were observed when seroconversion and seroprotection were compared with adult healthy controls. The data were further analyzed for the effects of lymphocyte, neutrophil and CD4/CD8 counts on HI titres at day 21. Seroconversion was not influenced by the above parameters. No serious side effects were observed.

**Conclusion:** Vaccination induces protective levels of antibody in immunocompromised children. The second dose administered at three weeks was followed by seroprotection in children aged 1–10.

**PT009**

**MALIGNANT DISEASE AND THE EFFECT OF TREATMENT ON SOMATIC DEVELOPMENT IN CHILDREN WITH CANCER**

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**Purpose:** In the current study we aimed to evaluate somatic development of children with various malignancies.

**Method:** The retrospective study was conducted on a sample of 75 children with various malignancies who were diagnosed and treated in the Pediatric Clinic Tg-Mures during 2001–2008.

**Results:** Group included 75 patients (42 boys and 33 girls) with a mean age of 6.8 years at the onset of the malignant disease. Of the 75 patients, 40 were diagnosed with acute leukemia, 14 with lymphoma and 21 with solid tumors. At the onset of the malignant disease, 39 patients (52%) had the weight appropriated to the age below percentile 25, among which 17 patients (23%) had weight below percentile 5, which is maintained under intensive cytostatic treatment (24%), but it improves at the end of the cytostatic treatment. The height appropriated to the age was at the onset of the disease under percentile 25, to 37 patients (49.3%), and the percentile 5 to 10 patients (13%), indicating the chronic malnutrition. Under intensive chemotherapy treatment, the height of children has stalled, but improves at the end of therapy.

**Conclusion:** 1. Prevalence of malnutrition was 23% in malignant disease onset and lasts under intensive treatment, and then improves at the end of treatment.
2. Lower height of children at the onset of the disease tumor is in no way caused by malignancy, but protein-energy malnutrition in chronic preexisteing disease.
3. Prevention, early correction of the protein-calorie malnutrition in children with cancer is essential for survival, knowing that malnutrition is an adverse prognostic factor for survival in cancer.
PT011

ASSESSING THE UTILITY OF A TRANSITION PROGRAM: A SURVEY OF PARENT PARTICIPANTS

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Purpose: An educational visit at the completion of therapy is offered to patients and families at our institution. The Transition Visit (TrV) includes: review of treatment, disease recurrence surveillance plan, discussion of potential late effects and receipt of a printed individualized "transition book" summarizing this information. The utility of the program has not been assessed.

Method: We conducted a mailed survey of the 121 parent-participants in the program. Respondents reported their recollection of the TrV, their perception of the program, its timing, content and impact on well-being.

Results: Of 121 surveys, 49 were returned. The mean age of the patient at the time of TrV was 8.5 years (range 2–22 years), mean time from visit 2.1 years (range 1–3 years), 36/49 who returned the survey remembered the TrV. Almost all felt the visit was somewhat to very helpful (n = 35), 6/36 reported that the visit was upsetting (n = 3) or very upsetting (n = 3). The book containing a treatment summary and follow-up plan was recalled by 34/36 (94%). Of the 33 who remembered the book, all reported it to be helpful, and 17/33 reported reduced anxiety associated with access to this written information. The "Late Effects" section of the book was reported to be the most frequently utilized section (30/33). 88% of respondents endorsed the timing of the TrV to be within 3 months of completion of therapy; 12/33 reported that psychosocial provider support at or after the TrV might have been helpful. Only 10/33 shared the book with their pediatrician.

Conclusion: A Transition Visit is helpful and may decrease anxiety for parents as their children enter into follow-up. At two years off-therapy, parents report accessing individualized information about late effects. Involvement of psychosocial professionals during the transition period might reduce anxiety, and communication with primary care providers needs improvement.

PT013

GLOBAL PERSPECTIVES ON PEDIATRIC ONCOLOGY & NEURO-ONCOLOGY TRAINING: CAREER DEVELOPMENT OF INTERNATIONAL PEDIATRIC ONCOLOGY FELLOWS TRAINED IN SYDNEY

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Purpose: The career development of Pediatric Oncology fellows from low or middle income countries (LMIC) training in high income countries has not been examined previously. This study examines their expectations, career development and the extent to which their fellowship influenced or equipped them to contribute to the development of pediatric cancer medicine in LMIC.

Method: Fifteen international fellows from LMIC trained in Pediatric Oncology and Neuro-Oncology at Children’s Hospital at Westmead, Sydney (CHW) between 1990 and 2009. Thirteen fellows consented to participate in semi-structured interviews exploring their personal and family backgrounds, educational history, fellowship experience at CHW and subsequent career pathway after leaving CHW. The study was approved by the Human Research Ethics Committee at the University of Sydney. All interviews were audiotaped with consent and transcribed for analysis.

Results: All subjects completed early schooling and their primary medical qualification in their country of birth: India - 6, Philippines - 3, Malaysia - 2, other - 2. Subjects commenced at CHW 6 to 15 years (median, 11yrs) after medical graduation. Ages ranged from 27 to 62 yrs (median, 41 yrs) and duration ranged from 9 months to 36 months, (median, 15mo). Among the 10 subjects who have completed fellowships at CHW, 7 have returned to their home countries and are involved in busy pediatric hematology/oncology practices in a range of funding settings. Several factors emerged as significant in fellows' decisions to return to their country of origin including extended family, fellowship funding from country of origin, and interval between graduation and accepting fellowship appointment.

Conclusion: The pediatric oncology department at CHW prepares international fellows for a range of subsequent appointments including practice in LMIC settings. Fellows would benefit from an expanded knowledge by their host of their specific needs and career goals, particularly where future practice in LMIC is envisaged.
PT014
DELAY AND CAUSES OF DELAY IN THE DIAGNOSIS OF CHILDHOOD CANCER IN AFRICA
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Purpose: Few studies have investigated delays in diagnosis and treatment among children and adolescents with cancer. Although this has been investigated a few times in more developed countries, it has never been subject of study in South-Africa. Early diagnosis is fundamental as it allows timely treatment and prevents unnecessary complications.

Aim: to identify any delay in diagnosing childhood cancer and the causes of this delay

Method: combined prospective and retrospective study: 126 patients were included through review of the medical charts and 68 through interviews with the parents of the patients. Patients were diagnosed between 2000 and 2009

Results: The median total diagnosis delay was 34 days (2–1826). The median patient delay was 5 days (0–457). The median physician delay was 20 days (0–924). The female: male ratio of the study population was 1:1.37. Gender did not have a significant influence on the total diagnosis. The mean age at the start of the symptoms was 5.9 years old (std.dev. = 4.0064).

Conclusion: The most common misdiagnoses seem to be different infections and constipation, which are most often treated with antibiotics. There is considerable delay in diagnosing childhood cancer in South Africa with a physician delay of 20 days on average. The findings of our unit should be correlated with other South African centres. An urgent need is to address the issue of awareness in childhood cancer and education of nurses and doctors in warning signs should become a national priority.

PT015
TRAINING PEDIATRIC ONCOLOGISTS FOR DEVELOPING COUNTRIES: THE EXPERIENCE OF THE ASSOCIATION OF PEDIATRIC HEMATOLOGISTS/ONCOLOGISTS IN CENTRAL AMERICA AND DOMINICAN REPUBLIC (AHOPCA)
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Purpose: The lack of pediatric hematologists/oncologists in AHOPCA impedes development of pediatric cancer control programs in the region. The objective of the AHOPCA fellowship program in Guatemala is to provide sub specialty training in pediatric hematology/oncology for full-trained pediatricians working in Latin America.

Method: We describe a fellowship training demonstration program in Guatemala, at the Unidad Nacional de Oncologia Pediatria initiated in 2003. Based on an estimate of the number of pediatric oncologists practicing in Central America, we calculated the number needed by country assuming that the ideal number of pediatric oncologists was 1 per 20 newly diagnosed pediatric cancer patients per year. The current number of pediatric oncologist needed in the region is 66. The program consists of 3 years of clinical training, covering the theory and clinical practice of the specialty. The program includes didactic teaching, direct patient care responsibilities, daily discussions of clinical cases with local and international experts, participation in seminars, medical meetings, and self-guided learning using the educational web site www.cure4kids.org. Trainees rotate in pathology, radiotherapy, floor cyrometry, and at St. Jude’s Children’s Research Hospital (SICRH) in Memphis, TN and Ospedale San Gerardo in Monza, Italy. This initiative is partially funded by the International Outreach Program of SICRH, and the National Cancer Institute of the USA. The program is accredited by the School of Medicine of Universidad Francisco Marroquin.

Results: Six fellows have completed the program: two from Ecuador, and one each from Honduras, Guatemala, Nicaragua and Dominican Republic. All are working at pediatric oncology centers in their home countries. Five fellows are currently in training.

Conclusion: Pediatric hematologists/oncologists can be trained successfully in Central America. This demonstration project has reduced by 10% of the current shortage or pediatric hematologists/oncologists can be used as a model for other institutions in Latin America to implement similar activities.

PT016
A COMPARISON OF LIPOPOLYSACCHARIDE-BINDING PROTEIN (LBP) WITH C-REACTIVE PROTEIN (CRP) AS EARLY INFECTION INDICES IN PEDIATRIC ONCOLOGIC PATIENTS
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Purpose: Comparative evaluation of LBP and CRP as early markers of bacterial infection in febrile paediatric oncologic patients.

Method: We prospectively studied 70 febrile episodes in 70 patients (32 boys; mean ± SD age 6.7 ± 5.1 years) and 20 afebrile controls. At fever onset and after 48h infection indices (LBP, CRP) were measured and cultures from biological materials were collected. Febrile episodes were classified in 3 groups: (a) bacterial, (b) viral infections, (c)fever of unknown origin. and were compared with the control group.(d)

Results: LBP values at fever onset were significantly different among the 4 groups and were higher in the group with bacterial infection (47.5 vs 29.5 vs 42.5 vs 18.8ng/ml, p = 0.001), while the relative CRP values were 33.2 vs 10.9 vs 23.7 mg/L, p = 0.012, respectively. Furthermore LBP values at 48h were higher in children with positive blood culture vs positive culture from other biological material vs negative cultures (52.0 vs 48.7 vs 40.3mg/ml, p = 0.020). When comparing LBP (cut-off level > 35 ng/ml) and CRP (cut-off level > 10 mg/L) in distinguishing between bacterial and viral infections, LBP had a better sensitivity than CRP (78.9% vs 71%), while their specificities and positive predictive values were similar (LBP:84.6% and 93.7%; CRP:84.6% and 93.1%) respectively. Moreover, LBP performed better than CRP in distinguishing between bacteremia and the absence of bacterial infection (LBP sensitivity:72.72%, specificity:50%, negative predictive value (NPV):75%; CRP sensitivity:54.54%, specificity:44.44%, NPV:61.53%).

Conclusion: LBP seems to be a more reliable early bacterial infection marker than CRP in febrile paediatric oncologic patients, especially suggestive of the presence of bacteremia.

PT017
DELAYS IN DIAGNOSING CANCER IN CHILDREN PRESENTING VIA EMERGENCY DEPARTMENTS IN THE WEST OF SCOTLAND: A RETROSPECTIVE CASE NOTE REVIEW
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Purpose: Identify which patients admitted to a haemato-oncology service via an Emergency Department (ED) experienced significant delays in diagnosis.

Identify areas of delay: Patient, Primary Care or Hospital Induced.

Identify which patients admitted to a haemato-oncology service via an Emergency Department (ED) experienced significant delays in diagnosis.

Identify staff groups for a targeted education programme.

Method: Between 2005–2008, all haemato-oncology patients admitted via ED were identified using the unit’s admissions database. Delay was defined as either 2 or more visits to the ED or a 30 day interval from symptom onset, prior to diagnosis.
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Results: The service saw 258 new diagnoses between 2005-2008. 86 patients were admitted via the ED, 13 patients excluded as notes were unobtainable. The remaining 73 patients were divided into 3 groups:
1. Leukaemia, n = 30, median age 41.5 months, presentation: lethargy, pallor, bruising, limp.
2. Solids, n = 31, median age 62.5 months, presentation: nocturnal pain, hip pain, limp, abdominal mass, anorexia, weight loss and lethargy.
3. Brain tumours, n = 12, median age 70 months, presentation: headache, vomiting, weight loss, lethargy and seizures.

Overall median time to diagnosis: 60 days (IQR 28-150)

Delay was identified in 28 (36%) patients: leukaemia n = 6 (21%), solids n = 14 (50%), brain tumour n = 8 (29%).

Causes of delay:
Hospital and primary care combined (52%)
Primary care (35.7%)
Hospital (7%)
Primary care and patient combined (3.6%).

Time of presentation to the ED was significant: more children attended out of hours in the delay group.

Conclusion: Early diagnosis allows treatment initiation and may improve prognosis. Symptoms are alleviated allowing a good relationship between the treating team and patient/family to develop. Almost 1/3 of children experienced a delay in their diagnosis; solid tumours being the most common group. Primary care and ED staff were identified as targets for education and a programme has commenced. “Red Flag” guidance for ED staff is now included in their induction programme and outreach education to Primary Care physicians has started.

PT018
RADIOLOGY INTRAPARAVERTEBRAL NEUROGENIC TUMORS OF THE SPINE IN CHILDREN

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Purpose: to identify the main features of neural crest tumors using radiological methods of diagnosis

Method: an analysis of 108 (100%) children aged from 2 weeks to 15 years with intraparavertebral neurogenic tumors 78(72,9%), of them are benign neurogenic tumors 19 (24,4%), malignant neurogenic tumors 58 (75,6%); and tumors of the spine in children 29 (27,1%) of them are benign neurogenic tumors 6 (21,4%), malignant tumors 22 (79,6%). All children (100%) carried out X-ray chest cavity, ultrasound abdomen, CT 35 (25,2%), spine MRI 39 (28,1%).

Results:
- Neurogenic tumors in children revealed cervical 5(6,4%), thoracic 34(43,6%), lumbar 37(47,4%), sacral 2(2,6%)
- Study of the vertebrae was located in cervical level of the spine 3(10,3%), thoracic level 8(27,6%), lumbar level 4(13,8%), sacral level 14 (48,3%)

Group with neurogenic tumors were located in the paravertebral areas, adjacent to the vertebrae 78(100%), has intra-and paravertebral components, interconnected through the intervertebral foramen 78 (100%), bone pressure 45(57,6%), increased distance between the transverse processes of vertebrae 38(48,7%), oval shape 61(78,2%), calcinates 56(71,8%).

Conclusion: Radiology neurogenic tumors and tumors of the spine in children revealed at any level of the spinal column. Neurogenic tumors have the right form, pressure atrophy of vertebrae. Tumors of the spine in children are irregular in shape, with vertebrae destruction.

PT019
INTERNATIONAL NETWORK OF TELECONSULTATION SUPPORT ACTION

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Purpose: The International Network of teleconsultation Support action (iSA) Project aims to create a pilot cooperative medical support network coordinated by Son Dureta University Hospital (Palma, Spain) to provide web based diagnosis and therapeutic support in adults and pediatric oncology and Infectious diseases.

Method: The first part of the project has consisted of building clinical workgroups. The second stage has launched the iSA web tool www.theisaproject.eu. This tool makes possible internet based exchange of CTs, MR and microscopic images (Anatomic Pathology), videos and reports. The iSA network of hospitals is divided into two main groups: 1: the iSA leading team in charge of providing specialized expertise and support, with the University Hospital Son Dureta (Palma, Spain), Instituto Valenciano de Oncologia (Valencia, Spain), Hospital Vall d’Hebron (Barcelona, Spain), Hospital San Joan de Deu (Barcelona, Spain).2. The petitionary centers are “Desarrollo 2000 en Africa” (Equatorial Guinea), Hospital Regional Docente de Trujillo (Peru), Instituto Nacional de Cancerologia (Mexico), CIMP International (Kenya), College of Health Sciences of the University of Nairobi (Kenia.)

Results: We analyze interconsultation results by considering indicators such as number of consultations per month, communication impact in each case and analyze educational and academic achievements. The iSA web tool may be a feasible tool to make specialized clinical knowledge and biomedical technologies accessible to researchers and health workers in Partner countries where medical expertise and technological resources are deeply needed.

Conclusion: The iSA Project seeks a major impact on the quality of health assistance at hospital in Cooperation Partner Countries for the benefit of patients with cancer and severe infection diseases. It has showed evidence to justify investments on human resources, technology and infrastructures in each center. This project is an action supported by a grant of the Seventh Framework Programme of the European Union.

PT020
A NOVEL MODEL OF TWINNING: OUTREACH PROGRAMS IN THE BORDER REGION

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Purpose: The impact of twinning programs in improving pediatric cancer care in Low Income Countries (LIC) has been demonstrated. Twinning represents cooperation between centers in developed countries and LIC, whereby knowledge and organizational skills are shared and pediatric oncology units are established in a culturally sensitive manner and adapted to local health care systems. Border towns have a particularly high need for development of such programs. In 2007, St. Jude (SICRH) and Rady Children’s Hospital San Diego (RCHSD) initiated an outreach project with the Hospital General in Tijuana (HGT), Mexico.

Method: A modified SICRH assessment revealed the following: basic laboratory, pathology, and blood bank services; patients treated by an adult hematologist in a general pediatric ward; untrained nurses; improper chemotherapy preparation; no treatment plans; incomplete medical records; inadequate supportive care and psychosocial programs.

A 5-year strategic plan was designed focused on hiring professionals, providing intensive education, and improving infrastructure. A bilingual pediatric hematologist/oncologist based at RCHSD was appointed to supervise and visit the HGT weekly.

Results: After 1.5 years, accomplishments include: opening of an isolated pediatric oncology unit, training of nurses and staff, and the establishment of a multidisciplinary team led by a pediatric oncologist. Ninety-eight patients now benefit from accurate diagnosis and treatment plans; access to pediatric subspecialties, supportive care, infection control, specialized nurses, dedicated pediatricians, a trained pharmacist; and psychosocial and nutritional support programs. In 2008, the Pediatric Oncology Program at HGT received accreditation by a federal insurance program, ensuring full coverage for the patients. Ongoing initiatives include: a shelter, a campaign in “ Early Detection of Childhood Cancer”, calculation of survival rates, completion of the “ Prevention of Abandonment” program and enhanced education and subsidies for families.
Conclusion: Projects along the border constitute a unique model of twinning. Proximity permits close follow-up and more rapid establishment of programs, benefiting children along the border.

PT021
POLY-CHROMATIC FLOWCYTOMETRY TO IDENTIFY NOVEL BIOLOGICAL MARKERS ASSOCIATED WITH TUMOR INDUCED ANGIOGENESIS IN PEDIATRIC SOLID TUMORS.

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Purpose: Poly-chromatic flowcytometry (PFC) has allowed a more comprehensive understanding of cellular biology of rare blood cell subsets with regards to isolation and characterization of circulating progenitor cells (CPCs) versus endothelial progenitor cells (EPCs) and their role in tumor angiogenesis. We designed a pilot study to test a novel PFC strategy to detect CPCs and EPCs in pediatric patients with solid tumors.

Method: Peripheral blood was obtained from aged matched control children and pediatric patients with solid tumors (cases). Mononuclear cells were stained to simultaneously detect EPCs, namely endothelial colony forming cells (EFCFs; CD31+CD34brightCD45dimAC133+CD14+CD41a–CD235a-LIVE/DEAD Violet+), and two distinct hematopoietic, myeloid-lineage, circulating progenitor cell (CPC) subsets, one pro-angiogenic (CD31+CD34brightCD45dimAC133+CD14+CD41a–CD235a-LIVE/DEAD Violet+) and another anti-angiogenic (CD31+CD34brightCD45dimAC133–CD14–CD41a–CD235a-LIVE/DEAD Violet–) for both diagnosis and after treatment, then compared to normal healthy controls.

Results: Thirty-four normal children with no chronic illness (3–21yrs) were recruited to the study. There was no significant difference in the EFCF and CPC concentrations in the 24 controls by age or sex. Seventeen cancer patients (cases) with varying malignant solid tumors including brain tumors (3–21yrs) were recruited and samples obtained at baseline prior to starting therapy and after a regimen of chemotherapy-radiotherapy. The ratio of the pro-angiogenic CPCs to non-angiogenic CPCs was significantly elevated in cases at day 0 compared to controls and decreased to normal levels after a treatment regimen (p<0.0001). In addition, EFCF levels were statistically significant in the pediatric cancer patients at day 21 as compared to controls (p<0.001).

Conclusion: We have shown for the first time that the novel PFC strategy is capable of detecting rare blood cell subsets “in real time” in patients. This pilot study now requires expansion to include patients with a uniform group of malignant solid tumors who will be prospectively treated, to validate CPCs and EPCs as novel biological markers of response to cancer therapy.

PT022
CLINICAL SIGNIFICANCE OF SERUM GLYPICAN 3 AS THE NOVEL DIAGNOSTIC MARKER

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Purpose: Glypican 3 (GPC3) has been reported the usefulness as a more sensitive marker than alpha fetoprotein (AFP) for hepatocellular carcinoma. However, the correlation of pediatric malignant tumors and GPC3 is unknown. In this study, clinical implications of GPC3 for pediatric patients were widely assessed.

Method: Immunohistochemical examination (tGPC3, tAFP) and serum expression level (sGPC3, sAFP) were evaluated for 60 pediatric solid tumors including 13 neuroblastoma associated tumors, 16 renal tumors, 8 hepatic tumors, 16 germ cell tumors and 7 other tumors since 2002. Serum levels of GPC3 (sGPC3) were analyzed by a sandwich ELISA method.

Results: 60 cases, 9 cases (15.0%) showed sGPC3(+) and 35 cases (58.3%) showed sAFP(+) in the present cases. Of 8 cases of hepatoblastoma, 6 cases showed sGPC3(+) and 35 cases showed sAFP(+) including 2 cases of yolk sac tumor showed sGPC3(+)/sAFP(+). Most cases of mature teratoma or immature teratoma showed sGPC3(+) and sAFP(+) (5/5). On the other hand, 9 cases showed sGPC3(+) and 35 cases showed sAFP(-), and in one case of undifferentiated sarcoma with the sGPC3(+) and sAFP level decreased according to the decrease of tumor by the treatment.

Conclusion: Serum GPC3 level was high in the cases of hepatoblastoma, germ cell tumors and the cases under 1 year age. Serum GPC3 level may be considered to be physiologically high both 1 year old from our data. In the pediatric malignant solid tumors demonstrating sGPC3(+) and sAFP(+) over 1 year such as the present case with undifferentiated sarcoma, serum GPC3 level might be an independent novel tumor specific marker.

PT023
IMMUNOSUPPRESSIVE THERAPY WITHOUT HEMATOPOIETIC GROWTH FACTOR SUPPORT IN PEDIATRIC ACQUIRED APLASTIC ANEMIA

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Purpose: Sibling HLA-matched hematopoietic cell transplantation (HCT) is considered optimal initial therapy for children with acquired aplastic anemia (AA) and immunosuppressive therapy (IST) is reserved for children without a sibling donor, primarily due to the risk of secondary clonal evolution. Hematopoietic growth factor exposure during IST may increase the incidence of clonal evolution. We describe response, survival and incidence of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) in children with AA who received IST without hematopoietic growth factor exposure and compare outcomes with those who received upfront HCT.

Method: A population based retrospective review of all children treated for AA in British Columbia between 1991 and 2007 was completed. All IST patients received a standardized regimen of cyclosporine, anti-thymocyte globulin and corticosteroids with no hematopoietic growth factor exposure.

Results: Fifty-one patients (22 female; 29 male) with a median age of eight years were included, of which 45 (88%) received IST as initial therapy. Partial and complete IST response were achieved in 82% and 64%, at a median of 55 days and 7.6 months, respectively. In a sub-group, granulocyte telomere length at diagnosis or following incomplete IST response was less than the first or tenth percentile for age in 78% and 100%, respectively (n=9). Incidence of AML or MDS in children who received IST or sibling HCT as initial therapy was 2% and 0%, respectively, at median 55 months follow-up. Five year actuarial survival was 96% and 100% for IST or HCT as initial therapy, respectively.

Conclusion: In this large, population based pediatric cohort, we show that IST without hematopoietic growth factor exposure results in excellent response, low incidence of AML/MDS and survival comparable to sibling HCT. We conclude that IST should be considered as first-line therapy in pediatric AA, regardless of donor availability for sibling HCT.

PT024
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) IN CHILDREN WITH CANCER

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Purpose: Reversible Encephalopathy Syndrome (PRES) is a neurologic complication that may occur during childhood cancer treatment. It is characterized by seizures, headache, altered mental status, cortical blindness and typical transient lesions on Magnetic Resonance Imaging (MRI). PRES is most often reported in patients with acute leukemia and series in solid tumors are scarce. A review of PRES in childhood cancer patients is not available.

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Method: We describe seven childhood cancer patients with clinical and radiological symptoms of PRES and reviewed all well-documented PRES cases reported during childhood cancer treatment. The review has been performed using PubMed databases (National Library of Medicine, Washington, DC).

Results: Fifty-six children with PRES, including our seven cases, were identified. Mean age at onset was 9 (range:2–17) years. Primary diagnoses were acute lymphoblastic leukaemia (n = 31), acute myeloid leukaemia (n = 5), non-Hodgkin lymphoma (n = 7) and solid tumors (n = 13). PRES patients presented with seizures (n = 50), altered mental status (n = 20), visual disturbances (n = 24) and/or headaches (n = 17). PRES was associated with hypertension in 49 patients. 86% of the patients had both clinical and radiological reversible symptoms. Four patients developed epilepsy, in one patient ataxia remained and one case had a persistent mydriasis. The onset of PRES could not be related to a certain type of drug, as various chemotherapy regimens were used for the treatment of the different cancers.

Conclusion: Although PRES has predominantly been described in leukemia patients, it occurs in children with solid tumors as well. Tumor-related or treatment-related hypertension seems to be the most important etiologic determinant. A variety of symptoms are reported, of which seizures are the most frequent. To avoid unnecessary therapy delay, it is important to recognize the characteristic radiological picture, for which MRI (using FLAIR imaging) is the diagnostic tool of choice. Although reversibility has been a hallmark of PRES, neurologic symptoms remain in ~10% of the cases.

PT025

IS FINE NEEDLE ASPIRATION CYTOLOGY A GOOD DIAGNOSTIC MODALITY FOR SOLID TUMOURS?

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Purpose: A tissue diagnosis is essential in solid tumours. In our set up and what would be true in all developing nations, the procedure of getting a biopsy done and obtaining a report takes a week to 10 days, resulting in a delay in treatment, as compared to a fine needle aspiration cytology (FNAC) where the result is available within 24 hours. The most important factors in the use of cytology are (i) experience of the cytopathologist, (ii) the similarity of small round cell tumours and (iii) the possibility of a sub-optimal FNAC sample.

Method: The cytology results of children with a solid tumour undergoing a diagnostic FNAC were compared with the subsequent histopathology report from a biopsy/surgical excision. Data was collected from January 2004 to December 2009.

Results: There were 114 patients. In 2 cases the aspirate was acellular. An accurate diagnosis was obtained in 97 patients. FNAC was false negative in one patient: cytology being reactive hyperplasia: biopsy being reported as anaplastic large cell lymphoma. In 6 patients the diagnosis was incorrect: 2 neuroblastomas were reported as Wilms tumour; 2 Ewings sarcoma patients diagnosed as rhabdomyosarcoma; one hepatoblastoma reported as hepatocellular carcinoma & one atypical mesoblastic nephroma reported as clear cell sarcoma kidney. There was mild discordance in 8 patients. A round cell tumour was diagnosed and the FNAC was unable to characterise the type of tumour as immunocytochemistry could not be done due to technical constraints.

Conclusion: FNAC is a simple, swift & reliable method of establishing a diagnosis in solid tumours. The efficacy is 92%. It needs to be corroborated with clinical and imaging findings. Similarity of round cell tumours is the biggest challenge. The usefulness of this diagnostic modality has improved with the advent of routine immunocytochemistry & could achieve near 100% with cytogenticstics.

PT027

100% FRESH? A QUALITY AUDIT ON SOLID TUMOUR BIOPSY SPECIMENS

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Purpose: Increasingly, cytogenetic abnormalities in solid tumours of childhood are of diagnostic and prognostic importance. These biological markers require molecular methods for their detection, usually on fresh tissue samples. Fresh tissue is also important for tissue banking for future research. The aims of this audit are to report the incidence of solid tumour biopsies without fresh specimens at diagnosis and to identify factors that may be contributory.

Method: All solid tumours registered from January 2009 to January 2010 in the Children’s Cancer Foundation Solid Tumour Registry were included. A retrospective chart review via computerized records was done.

Results: There were 84 paediatric solid tumours, benign and malignant, diagnosed from January 2009 to January 2010. Of these, the top 3 solid tumours were CNS tumours, neuroblastomas and retinoblastomas. 65 tissue specimens were sent in total over this period. 20% of tissue biopsies did not have any fresh specimens at diagnosis. This resulted in significant diagnostic delay for 2 neuroblastoma patients. Only 50% of neuroblastoma patients had a full molecular diagnosis made on the first biopsy. The type of tumour, method of biopsy, time of biopsy and operator were not significant factors. We postulated that the lack of knowledge of the need for fresh specimens, lack of a formal workflow and poor communication were contributory factors.

Conclusion: The suboptimal rate of fresh tissue specimen collection is of concern in this era of molecular methods for diagnosis and prognosis. A Clinical Practice Improvement Project to address this problem is timely.

PT026

CATHETER-RELATED BLOODSTREAM INFECTIONS IN CHILDREN WITH CANCER ADMITTED WITH FEVER

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Purpose: Most children with cancer need a central venous catheter (CVC). CVCs are thought a major risk factor for bloodstream infections. A prospective study was conducted (April 2008 to December 2009) to determine the frequency of catheter-related bloodstream infections (CRBSI).

Method: All children hospitalized with fever had concurrent blood cultures drawn from a peripheral vein and from their CVCs. CRBSI was defined as growth of microbes from a blood sample drawn centrally at least two hours before microbial growth was detected in a blood sample obtained from a peripheral vein.

Results: 373 admissions with fever were registered. A positive blood culture was found in 77 episodes. Seventeen of these episodes were classified as contamination which was defined as a single positive blood culture with a common skin contaminant. Five cases were excluded because of insufficient data regarding the blood culture origin. A concurrent peripheral blood culture could not be obtained in three cases and in one case blood cultures could not be obtained centrally. In 20 of the remaining 51 bloodstream infections, no microorganism was grown from the peripherally obtained blood culture; however, one or more microorganisms were grown from the centrally obtained blood culture. In seven cases microorganisms were only grown from the peripherally obtained blood culture. Of the remaining 24 bloodstream infections, thirteen showed growth of microbes from a centrally obtained blood culture at least two hours before growth of the same microbes was detected on the blood culture from a peripheral vein. Escherichia coli, Klebsiella oxytoca, and coagulase-negative staphylococci were most commonly occurring in the cases of CRBSI whereas Staphylococcus aureus and non-hemolytic streptococci were most commonly found in the non-CRBSI.

Conclusion: Out of 373 admissions with fever 77 cases with a positive blood culture were found. 33 (39%) of these cases were CRBSI.

PT002

SEXUALITY AMONG CHILDREN AND ADOLESCENTS WITH CANCER: NURSES AND SOCIAL WORKERS PERCEPTION

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Purpose: Sexual health plays an important part in the patient’s quality of life, especially during the crucial adolescent years. Since one of the nurses’ main goals is to preserve and improve the patient’s quality of life, the topic of sexual health must be addressed in an optimal way.

To understand the personal professional perception (PPP) of pediatric oncology and community nurses on the topic of sexuality in children/adolescents, and their behaviors and management of sexuality care.

Method: The sample included 33 participants; hospital pediatric oncology nurses, community nurses, and pediatric oncology social workers. Ten nurses (30%) had a post graduate education in oncology. The survey questionnaire included two major sections: The first part focused on nurses feeling regarding their personal professional perception (PPP). The second part focused on the nurses’ behavior and activities in the management of sexuality care.

Results: A statistically significant positive correlation was found between PPP and management of sexuality care \( p < 0.01 \). As the nurse feels more comfortable and less embarrassed providing care on sexuality issues for children and adolescents oncology patients, she initiates and promotes conversation or patient education on this subject. No statistically significant difference has been found between the nurses’ education level and PPP, and also between management sexuality care \( p > 0.05 \).

Conclusion: The sexual perception of the nurse is shaped through her entire life by her personal beliefs, culture, education, and life experiences. Her post graduate oncology education is not the main factor that influences her sexuality perception and her obligation to provide sexual health care.

In order to promote and implement sexual health care on a daily basis, pediatric oncology nurses should receive special education, focusing on children and adolescents with cancer.

PU003

SEXUALITY AMONG CHILDREN AND ADOLESCENTS WITH CANCER: NURSES AND SOCIAL WORKERS PERCEPTION

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PU004

HEMATOPOIETIC STEM CELL TRANSPLANT DISCHARGE RESTRICTIONS: WHAT IS BEST PRACTICE IN THE HOME?

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Purpose: Hematopoietic Stem Cell Transplant patients require multiple intravenous infusions for supportive care throughout the transplant process. These infusions include parental nutrition, intralipid, narcotics, blood products, multi-coverage antibiotics, antifungal and antiviral agents, and immunosuppressants. Cyclosporine, the most common immunosuppressant used, requires adherence to a strict schedule to maintain appropriate drug levels. Although patients have double lumen central catheters (CVC), nurses are challenged to administer the medications efficiently. At Children’s Hospital Boston, cyclosporine is infused over at least two hours every 12 hours through a designated lumen which restricts use of the CVC four hours a day or more. If cyclosporine could safely be infused through the same lumen as continuous nutrition and narcotic, it would allow more flexibility in the administration and timing of other infusions through the opposite lumen. To revise current practice, an evidence based review was conducted.

Method: A literature review was completed and no information was found related to compatibility of cyclosporine with other infusions. Expert opinion of pharmacists from Children’s Hospital Boston and Brigham and Women’s Hospital, Boston stated there was not sufficient information to support compatibility. Novartis Corporation, the manufacturer, stated that it is not specified in the Box Warning and is up to the prescribing provider and institutional policy and procedures.

Results: Benchmarking with other pediatric stem cell transplant centers was conducted by contacting colleagues through the APHON BMT bounce list. Three questions were asked that addressed infusion of cyclosporine and compatibility practices. Eleven centers responded. Nine of these centers do not infuse cyclosporine concurrently with parental nutrition.

Conclusion: The objective of the review was to verify if there was information to support the safety of administrating Cyclosporine and Parental Nutrition concurrently through the same lumen of the CVC. Based on the evidence, this practice could not be supported and validates we are currently following best practice.

PU006

NURSE PRESCRIBING IN CHILDREN'S CANCER SERVICES: THE WAY TO IMPLEMENTING NATIONAL GUIDANCE?
SIOP ABSTRACTS

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Purpose: There has been little research into the potential and possible impact of nurse prescribing in the field of children’s cancer nursing. The publication of “Improving Outcomes for Children and Young People with Cancer” (IOG, NICE, 2005) was seen as an opportunity to explore to what extent non medical prescribing could assist staff within the principal treatment centre in implementing the IOG.

Method: The study used literature review as the research methodology to gain knowledge, identify gaps and inconsistencies and create new knowledge and ideas to assist in answering the original research question. Comprehensive searches of the literature were conducted with strict inclusion and exclusion criteria. The CASP (PHRU, 2007) critical appraisal tool was used to assess the rigor and relevance of each of the short listed studies. Twelve papers were selected for analysis and synthesis.

Results: Five themes were found within the selected studies, these themes were then used to help answer the original research question. The IOG was used as a framework to structure the discussion focusing on the sections that involve the prescription of medicines or blood products within the different care settings. Findings from the study confirmed that nurse prescribing does have the potential to assist in the implementation of the IOG for children and young people with cancer, within the greater potential within the day care and community settings. Prescribing rights can also enhance the skills of the nurse in the key worker role, particularly within palliative care. The importance of acknowledging constraints and ensuring that each organisation put into place adequate planning and support mechanisms was highlighted.

Conclusion: This study provides a starting point for the exploration of the potential and impact of nurse prescribing in children’s cancer services, further primary research is recommended in this field in the future.

PU007

THE CHEMO HUDDLE: A STRATEGY TO MINIMIZE ERRORS AND MAXIMIZE CHEMOTHERAPY SAFETY

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Purpose: The administration of chemotherapy in the pediatric population is a high risk process, requiring safety checks throughout each stage of prescribing, dispensing, and administration. While computerized physician order entry (CPOE) has eliminated many potential and actual errors, many institutions currently use multiple computer applications, or concurrent computer and paper systems, to process chemotherapy orders. Systems that are not integrated pose a safety risk, requiring innovative applications, or concurrent computer and paper systems, to process chemotherapy orders. Changes included retiming of medications, dosing adjustments, and (10/90) of chemo orders. In a second review, changes were made in 10% (34/345) of the initial review revealed that changes or clarification of administration guidelines. Several strategies were subsequently developed increase safety and strengthen confidence in the chemotherapy process. One strategy is the chemotherapy “ huddle”, in which nursing and pharmacy meet daily to review chemotherapy orders. During the huddle, clinicians ensure that medications, number of doses, and administration dates/times are accurate and assigned correctly. An audit tool is completed to track corrections and changes. The huddle takes 5–15 minutes to complete.

Method: The chemotherapy huddle was implemented in January 2009. Two months later, a review of 90 chemotherapy patient days was conducted to determine the rate of adjustments/changes to orders during the huddle. Recently a second audit of the period between October and December 2009 was conducted, where 345 chemotherapy days were reviewed.

Results: The initial review revealed that changes or clarifications were made in 11% (10/90) of chemo orders. In a second review, changes were made in 10% (34/345) of orders. Changes included retiming of medications, dosing adjustments, and clarification of administration guidelines.

Conclusion: Our institution is moving toward a CPOE system which will integrate several applications to process pediatric chemotherapy orders. In the interim, the hemo chemotherapy has proven to be a successful strategy to identify potential errors and improve communication among pediatric oncology care providers.

PU008

PATIENT CARE GUIDE FOR NURSES IN A HEMATOLOGY AND PEDIATRIC ONCOLOGY UNIT

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Purpose: It is imperative for nursing staff responsible of children and adolescents with cancer or blood diseases, to emphasize that nursing care required by these patients is very different from that needed by adults who suffer same diseases. There is ample and solid evidence that physical, emotional and cognitive development of children and adolescents, together with different aspects of their pharmacodynamics and pharmacokinetics, dictate a different approach from the care and treatment indicated in adults. It is essential that this fact is clear during the learning process of nurses, and also during knowledge recycling process for professional nurses that are not used to work with children and adolescents. This work intends to create a guide that includes a theoretical agenda to adequately perform treatment and how to face possible complications patients could present, either caused by treatment or by their pathologies. It intends also to improve the quality of training to nursing students and employees who have recently joined units with these characteristics.

Method: We have consulted bibliography of existing publications on nursing care for children and adolescents under treatment. We have also looked for medical publications that may help us to better understand the most frequent pathologies in these patients, and the indicated therapeutic procedures. Spanish data bases CUIDEN and ENFISPO were consulted, as well as MEDLINE. Numerous medical literature and publications oriented to improvement of nursing care have been discussed, both in Spanish and English.

Results: We found more publications of this type in English than those in Spanish. Themes included in this guide have been selected after particular issues expressed by former students and nurses formed in our unit. We consider them most important to improve quality in patients care.

Conclusion: As a result, the guide includes nine different topics.

PU009

UNCERTAINTY AND INTENTION OF PARENTS OF CHILDREN WITH CANCER REGARDING EXPLANATIONS OF THE DISEASE NAME AND CONDITION TO THEIR CHILDREN

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Purpose: Currently, 70–80% of patients with childhood cancer achieve remission. In Japan, despite the trend toward informing children of the disease name, the decision to give such explanations is primarily made by their parents. A survey we conducted in 2003 that qualitatively investigated the intention of parents of children with cancer on explaining the disease name and condition to their children indicated that uncertainty was an important factor affecting these parents’ Intention. I clarified uncertainty and intention of parents of children with cancer regarding explanations of the disease name and condition to their children.

Method: The questionnaire survey was conducted on parents of children with cancer who had not received explanations of the disease name and condition as well as parents of children with collagen disease (control group).

Results: The following three factors (comprising 14 items) were identified as factors related to the uncertainty of parents regarding explanations of the disease name and condition to their children: glare of clarity regarding method h, glare of information regarding explanations of the disease, disease name, and condition h, and gavagueness of necessity h. Compared to the control group, parents of children with cancer had significantly higher scores for glare of clarity regarding method h and glare of information regarding explanations of the disease, disease name, and condition h, and many of these parents responded that gexplanations of the disease name and condition must be given but I can not bring myself to do it h, and gl intend to explain the disease name and condition after my child enters junior high or high school h.

Conclusion: These results suggest that parents of children with cancer in Japan face great uncertainties regarding explanations of the disease name and condition to their children, and tend to postpone these explanations.
PU011

REHABILITATION FOR CHILDREN WITH LATE EFFECTS AFTER CANCER

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Purpose: Aim: There has been major progress in the treatment of children with cancer which makes more people survive the disease. The price for survival is late effects, which is a result of the disease and the treatment. Children who are still in development are extra vulnerable to the treatment that is given by cancer disease. Many children and adolescent will have the need for preparing and a cooperative approach to benefit from the best possible function- and master abilities after the disease.

Method: To map the needs of the patient for cooperative follow up, the project nurse have had conversations with children/adolescent who have finished the treatment, and their parents. In addition, all the children and adolescents that had finished their treatment in the years 1998–2006, got health related Quality of life Questionnaires, KINDL, ILK, SDQ and ASEBA. Both the children and their parents were asked to answer the questionnaire. This was used to map the needs for more follow-up. Approximately 50 per cent of the ones that answered the questionnaire got an offer for the collaborative team. 16 children were referred to the collaborative team at the children hospital center. The team workers were neurologist, psychologist, physiotherapist and a specialist educator.

Results: In this project about 50% needed help from the different professionals because of late effects after cancer. The children can have the ordinary follow-up at the medical center. Training and rehabilitation can happen in the children’s community by the different professionals.

Conclusion: In Norway the professionals such as teacher, community nurse and doctor, physiotherapist and others is joining a working group with the parents of each child. They can make an individual plan for the child’s rehabilitation and training.

PU012

HOW TO INFLUENCE THE SAFETY CULTURE - IN A PAEDIATRIC UNIT

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Purpose: Social life have been reported to be negatively affected by being diagnosed with and treated for cancer during childhood. Children undergoing cancer treatment report missing school and contact with friends as a major concern. One of the few studies on school attendance among children treated with cancer found a positive relation between health-related quality of life (HRQOL) and school attendance. Recommendations on social life during childhood cancer treatment varied between hospitals in Sweden. Due to lack of general national recommendations and inconsistent routines families kept the children from school and social interaction with other people without any medical reason. The aim was to form national recommendations for social life in children undergoing cancer treatment accepted by the pediatric oncologists in Sweden.

Method: The national network of Consultant nurses in paediatric oncology in Sweden evaluated existing local recommendations on social life and arranged multiple meetings, local as well as national, with physicians and nurses discussing social issues.

Results: After ten years of consistent questioning by the Consultant nurses some kind of national consensus was achieved. Suggestions on recommendations concerning important parts of social life were formed and presented to the pediatric oncologists. Agreement on national recommendations for social life among children on cancer treatment concerning society, school attendance and Varicellae was attained during the development of the Swedish Pediatric Society. 15 recommendations concerning social life were formed and presented to the pediatric oncologists in Sweden.

Conclusion: The Swedish national recommendations for social life are based on the general state of the child, not blood cell counts. Furthermore, recommendations concerning Varicellae are less strict overall. Forming national recommendations concerning other social aspects continue.

PU013

FAMILY CENTERED CARE AND THE IMPLEMENTATION OF BEDSIDE REPORT

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Purpose: It is well documented in the literature that including families of patients in all aspects of care improves satisfaction and decreases errors. The transfer of clinical information during nursing shift report is an opportunity to increase patient safety and enhance family centered care. Nurse-to-nurse report at the bedside, in the presence of the patient, puts the patient central to all care activity information (Anderson and Moskowitz 2006).

Method: At Children’s Hospital Boston (CHB), we recently implemented a bedside report system on the pediatric oncology and stem cell transplant units. One nurse from each unit was chosen to lead the change. Nurses were educated and several tools developed in the months leading up to the pilot to prepare for the change. A parent education sheet was developed to inform families and encourage them to participate. The pilot officially began in September 2009. Our bedside report process consists of nurse to nurse verbal report at the patient’s bedside, and includes a safety check, a visual inspection of infusions, and a patient identification verification. Patients and caregivers are encouraged to use this time to ask questions and/or make suggestions regarding the patient’s plan of care for the next shift.

Results: After 6 weeks, each unit conducted a staff survey to evaluate bedside report. The majority of responses were positive, with only 14.3% of staff disagreeing that this process should be implemented permanently. This survey also helped us to identify areas where the process could be improved.

Conclusion: Overall, bedside report has improved patient safety and communication through the interception of errors and the dialogue between nurses and families at change of shift. Other units at CHB are currently modeling the process to implement bedside report.
and all interviews were analysed with qualitative content analysis. Performed in three support group meetings in concordance with focus group method. Siblings had similar thoughts about survive or die and all of them the child died have to live and cope with the grief. Sister would survive or die. Thoughts of fatal outcomes repressed. For siblings when they felt anticipatory grief and grief regardless of age or sex on whether the brother or experienced anticipatory grief directly after diagnose of cancer. Despite age have experience of being a sibling of a child with cancer, during or after treatment or death. Tel Hashomer Ramat Gan 52621, Israel

Method: The Clinical Nutrition Department together with the International Outreach Program at St. Jude Children’s Hospital initiated a training program for pediatric oncology dietitians from around the world. The purpose of this program is to share information and foster cooperation. In the 3-week program, dietitians have a chance to observe St. Jude dietitians working in hematology, leukemia, solid tumors, neuro-oncology, and the bone marrow transplantation unit. Food Service and Infectious Diseases rotations can be accommodated upon request.

Results: Continuation of the program after dietitians return to their home countries is accomplished via webcast through Cure4Kids (www.cure4kids.org). The Clinical Nutrition Department and International Outreach Program provide assistance for air travel, hotels, and meals.

Conclusion: The main obstacles we have identified in our efforts are financial problems, language barriers, and differences in job descriptions.

PU015

THOUGHTS OF DEATH AND GRIEF RELATED TO THE EXPERIENCE OF BEING A SIBLING OF A CHILD WITH CANCER

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Purpose: To describe siblings’ thoughts about death and grief related to the experience of being a sibling of a child with cancer, during or after treatment or death.

Method: The subjects of the study were with 35 siblings, 19 had a brother or sister who was alive and 16 had lost their brother or sister. The method uses a life world approach, twenty were single interviews and fifteen were performed in three support group meetings in concordance with focus group method and all interviews were analysed with qualitative content analysis.

Results: Death has been a possibility for the siblings since the cancer diagnosis and they felt anticipatory grief and grief regardless of age or sex on whether the brother or sister would survive or die. Thoughts of fatal outcomes repressed. For siblings when the child died they have to live and cope with the grief. Conclusion: Siblings had similar thoughts about survive or die and all of them experienced anticipatory grief directly after diagnosis of cancer. Despite age have sibling more experiences in common and this made them more equal. Death was unthinkable and they were in no way prepared for a fatal outcome.

PU016

PERCEPTIONS OF PEDIATRIC HEMATOLOGY PHYSICIANS AND NURSES ABOUT GASTROSTOMY

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Purpose: Malnutrition is commonly seen in children with cancer, both at the time of diagnosis and during continuation of intensive treatment protocols. Nutritional status has a prognostic effect upon outcome in children with cancer: malnutrition may affect the tolerance of chemotherapy, diminish immunity, and increase infections and the risk of co-morbidities. Enteral or parenteral nutritional support may be used in such patients, but of the complication associated with TPN, gastrostomy should be considered. Hypothesis: Physicians and nurses in the department of hemato-oncology in the Sarfa children’s hospital are apprehensive about gastrostomy insertion and therefore avoid using it.

Conclusion: In this study we have shown that the medical team is apprehensive about the use of gastrostomy but project their concern on the parents. Expending physicians and nurses knowledge and guidelines strategies may improve decision-making regarding feeding gastrostomy.

PU017

LIKE EVERYONE ELSE, BUT WITH CANCER – EXPERIENCES FROM A TEENAGE GROUP AT A PAEDIATRIC UNIT.

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Purpose: On a paediatric cancer unit the teenage patient is rare. A nurse caring for these patients usually meet them in a bed covered in a blanket. They do not socialize, since they cannot see other teenagers on the unit. Teenagers want to hang out with others in the same age. Having cancer disrupts the normal life for the teenager. We wanted to create a place where teenagers can meet other teenagers in the same situation.

Method: Letters of invitation to night meetings for teenagers with cancer were sent. The criteria’s were; cancer patients 13 years and up, on treatment or just off treatment; a best friend could join. No parents were allowed. Two staff from the unit attended and supervised, at least one nurse so patients with ongoing chemo could join the meeting. The meetings had themes e.g. “Nintendo wii” night, celebrities visiting, spa. Meetings were unstructured, more like a café. They could talk if they want or they could be there and watch.

Results: During a 10 year period we have had monthly meetings, except during summer. The number of teenagers participated was between 5 -15. Some teenagers came now and then, some every meeting. Participating teenagers expressed that they found these meetings valuable. They felt good to meet other teenagers in the same situation. Here they were normal, like everyone else. After attending the meeting the teenager kept contact with each other e.g. “Facebook”. We also evaluate if they still want invitations. The result showed that even for those teenagers not attending the meetings a letter of invitation makes them feel good, they know they have a place to go to if they want and it was comforting.

Conclusion: In a paediatric unit, “teenage meetings” can be one way to meet some of teenage cancer patients needs.

PU018

NEEDS OF MOTHERS TAKING CARE OF CHILDREN WITH CANCER

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Purpose: Children with cancer are mainly treated by hospitalization in Japan. Initial therapy needs a long-term hospitalization from one to six months. Mothers stay at the
hospital and take care of their children during hospitalization. The paper clarify the needs of such mothers, what they demand for the care and treatment.

**Method:** Forty five mothers who experienced caring for hospitalized children.

**Questions:** What mothers needs for the care and treatment with their children.

**Results:** The problems cited by mothers are worry about hospitalized children’s brothers and sisters, insufficient environment for caring, and physical burden of mothers, etc. The needs cited by mothers are improvement of nurses l language and attitude toward children, relaxation of hospital rules, secure of manpower especially for the nursery stuff to support children’s life as well as counselors to consult about illness and care, which is an establishment of support system.

**Conclusion:** Mothers usually concern about their children’s ill progress and hardly care about their own life and health. The results show that mothers care more about their children’s life, support for their siblings, and care with enough time than their own health.


**PU019**

**PSYCHOSOCIAL HEALTH IN CHILDREN AND ADOLESCENTS SURVIVING CANCER**

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**Purpose:** To explore psychosocial health in children and adolescents surviving cancer three years after diagnosis compared with healthy controls, as assessed by adolescents themselves, their parents and teacher.

**Method:** Fifty children and adolescents diagnosed with cancer between January 1, 1993 - January 1, 2003, treated at the Paediatric Department St. Olav’s University Hospital, Trondheim, Norway were included in this case-control study. Psychosocial health was assessed by the Strengths and Difficulties Questionnaire (SDQ) (self report, parent and teacher report), as well as the Achenbach System of Empirically Based Assessment questionnaire (ASEBA) (teacher report).

**Results:** Children surviving cancer had more emotional symptoms, higher total problem scores and poorer academic performance, than their peers. Emotional problems were consistently reported by parents, teachers and adolescents themselves, especially in children with brain tumours and among survivors with late effects, but also in children surviving leukaemia. Mean scores on the parent report were considerably higher on the emotional symptom scale both in children with brain tumours (p = 0.005 vs. control) as well as in children with leukaemia (p = 0.01 vs. control).

**Conclusion:** We conclude that when planning long-term follow-up care, rehabilitation of children and adolescents with cancer should take into account their psychological functioning and the need to develop adequate supportive interventions and programs for long-term follow-up care. Child and adolescent psychiatric professionals should be part of the professional collaborative team planning and performing such follow-up care.


**PU020**

**PSYCHOSOCIAL STRENGTHS ENHANCING RESILIENCE IN ADOLESCENTS WITH CANCER**

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**Purpose:** Resilience helps adolescents with cancer to be more positive about their future. This study explored the methods of enhancing resilience in adolescents with cancer.

**Method:** A case study was used with a pattern-matching logic that data were compared with the self-sustaining process. Permission from three agencies and the informed consent from participants were obtained. Semi-structured interviews lasted between 30 and 50 minutes while waiting for the result of a blood test, and were audiotape-recorded and transcribed verbatim. Nine patients aged 11 to 18 years were 5 males and 4 females, and diagnosed with acute lymphoblastic leukemia, acute myelogenous leukemia, and non-Hodgkin’s lymphoma within the last 2 years. Five had been newly diagnosed and 4 had experienced relapse.

**Results:** The adolescents moved through the self-sustaining process and felt themselves hopeful and competent, though some differences were found in the subcategories between the two groups. They also developed psychosocial strengths that consist of positive attitude, purpose, confidence, connection with friends, and more understanding of life by achieving the self-sustaining process. Differences were seen in the development process of the strengths between the groups. It seemed to be unsteady in the newly diagnosed during inpatients. A positive attitude as early inpatients may lead them to have their hope for recovery and gain strengths in the future. The process appeared to be steady in the other one. Purpose in the early period may be an important guide for them to cope with cancer and lead to improve their strengths.

**Conclusion:** To enhance resilience, the strengths may be important for them at certain stages and to the individual with social support. For them, their mothers and friends were considered the key persons. Further studies are still needed in adolescent survivors and in those with a poor prognosis of quality of life.


**PU021**

**DOCTORS’ PERCEPTIONS OF PROMOTING AUTONOMY IN CHILDREN WITH CANCER**

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**Purpose:** Children with cancer in Japan are hospitalized for cancer treatment over six months and their behaviors would become passive through days with surgical operations and/or other painful procedures. To examine doctor’s perception on prompting autonomy in children with cancer who have to undergo intrusive treatments.

**Method:** Self-report questionnaires were administered to pediatric oncologists and pediatric surgeons (n=20). The questionnaires were sent back by mail or hand. The ethics committee of the School of Nursing Chiba University examined research plan and it was approved.

**Results:** Fourteen questionnaires returned. Doctors reported that the most important opportunity is the time of explanation on the disease with the child. And they also considered explanation of the reason for admission is important. And some doctors thought that asking the child directly about his/her physical conditions and letting him/her have chance to have choice are more important. But they also think it’s very difficult to promote autonomy when the treatments is ineffective and the child has to be shifted to palliative care. In the case of children old enough to understand his/her disease, all doctors answered that discussing on his/her disease promotes his/her autonomy. 10 doctors, moreover, answered that they preferred to tell the child the name of the disease, while 3 of them don’t consider the discussion without the parent’s agreement. Furthermore, for the adequate age of a child who could understand the disease and treatment, some doctors considered it over 4-years, while others considered children in primary school as suitable for discussion. All doctors reported that the attendance of the nurse was necessary when they informed a child and his/her family.

**Conclusion:** They think that psychological support for children by nurses is essential during the explanations of diagnosis and treatments and it’s expected for family of the child, as well.


**PU022**

**LETTING GO - WHEN CHILDREN DIE**

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**Purpose:** Each year about 130 children admitted to the Centre of Pediatric Oncology in Münster, Germany, face a diagnosis of cancer. In spite of an overall favorable cure rate, there will still be some children who cannot be cured. What then is the nurse’s role in caring for those terminally ill children? Means of supporting those children and their families will be presented, a number of farewell and mourning rituals will be described, and legal aspects will be explained. Interdisciplinary co-operation and pro-active management are essential in this process. Aspects to be considered include the time, way and extent to which the “Bridging-Team” may participate, the time when the family should take their child home for his/her last days, and ways of granting a child’s last wish. Further, means of assistance will be detailed which can be provided when a child enters the final phase.
**Purpose:** The topic of “Death” is still taboo in our society, but is ever present for staff at Pediatric Oncology departments. It is hard to let go again and again. And: the task is not complete when a child dies. This is the time when a process of intense grieving begins. Establishing fixed rituals such as days of remembrance offers parents and caregivers alike the possibility to reflect on what has happened.

**Conclusion:** In summary, many ways of supporting the ill child and his/her family during the end-of-life phase have been developed over the years. Offering this kind of support, however, involves facing the various aspects of letting go – before and after a child’s death.

**PU024**

**PATIENT SAFETY AND PROTOCOLS CONNECTED**

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**Purpose:** To improve the implementation of the existing nurses’ protocols by using a risk matrix, that categorizes the protocols in terms of patient safety.

**Method:** Quality of care and patient safety is considered very important amongst health professionals, but still a great variety in the care is obvious. Protocols are considered to diminish the uncertainties and variability, but implementation is difficult. During an internal audit at the children’s oncology ward it became clear that many nurses do not even know a particular protocol is present and if so where they can find it. This might increase errors and incidents.

**Results:** All protocols and standard operating procedures relevant for the children’s oncology ward are categorized according to the four different groups of the risk matrix. Green are the protocols that have no consequences. Yellow are the protocols that have minimal damage. Orange are the protocols that cause average damage and the red protocols are causing severe damage or death. Different implementation strategies follow directly out of the different categories. For the “green” protocols, nurses receive an email. For the “yellow” protocols nurses receive an email and they have to sign a list that proves that they have read it. The “orange” protocols are also supported by an oral presentation. The “red” protocols are tested by practical experience by every nurse. The Safety Committee decides which category procedure is agreed. This is done by consensus on risk, the measure of frequency and severity of the complication. All new protocols are discussed and weighed in this way.

Beginning in 2010, this risk matrix was introduced.

**Conclusion:** Due to demonstrate that nurses work of protocol and unambiguous accountability for the actions that should reduce chances of error.

**PU025**

**NEEDLELESS POSITIVE-PRESSURE MECHANICAL VALVE CONNECTORS: ARE THEY SAFE?**

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**Purpose:** To determine whether the introduction of a needleless positive-pressure mechanical valve connector in adult and pediatric hematology-oncology units influenced the rate of catheter-related bloodstream infections (BSI).

**Method:** A mechanical valve (MV) connector system (CLC2000®) was introduced and replaced miscellaneous conventional open systems (COS) with a standard Luer-Lock removable cap. The objective of this change was to reduce the use of heparin flushes in tunneled catheters (Hickman®). The retrospective analysis included patients with Hickman catheters, inserted during two different periods. The catheter-related BSI rate was observed during 6 months for each system and reported as number of BSI per 1000 catheter days. Microbiological characteristics of bacteremias occurring during each period were compared. The hospital policy for care of Hickman catheters did not change over both study periods.

**Results:** During the COS-period, 39 Hickman catheters were inserted in 15 children and 24 adults with a total dwell time of 1544 and 1899 catheter days respectively. During the MV-period 60 Hickman catheters were placed in 13 children and 47 adults with a total dwell time of 1181 and 3223 catheter days respectively. Both in the pediatric and adult population, the rate of catheter-related BSI during the MV period was significantly higher than during the COS-period: resp. 11 vs 1.29 infections per 1000 catheterdays (p < 0.009) and 12.4 vs 6.32 infections per 1000 catheterdays (p < 0.019).

During the MV-period, the percentage of polymicrobial BSIs increased from 0 to 84.6% in children and from 8.3% to 21% in adult patients.

**Conclusion:** A significant increase in the rate of BSI was found among hematology and oncology patients with newly inserted Hickman catheters concomitantly with a change from a conventional open-system to a mechanical valve connector. The risk and type of BSI are clearly associated with the catheter cap design which promotes microbial contamination.

**PU026**

**IDENTIFICATION AND MANAGEMENT OF THROMBOSIS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBlastic Leukemia RECEIVING ASPARAGINASE THERAPY AT DANA-FARBER CANCER INSTITUTE**

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**Purpose:** Asparaginase is a chemotherapeutic agent commonly used in the treatment of pediatric acute lymphoblastic leukemia (ALL). An untoward effect of asparaginase depletion may include the development of a deep vein thrombosis (DVT) or sagittal sinus thrombosis as a result of reduced synthesis of antithrombin III. Although these events are rare, they necessitate interruption and potential discontinuation of asparaginase therapy, which may impact overall disease free survival (DFS).

Method: Patients present with a variety of symptoms depending on the location of the thrombosis. A patient with an extremity DVT may exhibit pain, swelling, erythema, venous dilatation, decrease peripheral pulses, or increased extremity circumference. A patient with a central nervous system thrombosis may present with severe headaches, photophobia, behavioral changes or seizures. If a thrombosis is suspected, prompt diagnostic studies including ultrasound, magnetic resonance imaging or computed tomography venogram are indicated. Following diagnosis of a clot, children begin anticoagulation therapy with low molecular weight heparin in consultation with the anticoagulation team.

Results: After 4–6 weeks of therapy the thrombus is re-evaluated. Once the thrombus is resolved or re-cannulated, asparaginase therapy is reinstituted. Anticoagulation therapy during asparaginase depletion requires close monitoring ensuring a platelet count greater than 50,000 and a low molecular weight heparin level between 0.5–1 IU/ml (standard of care). Children may require platelet transfusions and Anti-thrombin III (ATIII) replacement.

Conclusion: Asparaginase has proven to be a potent antileukemic enzyme resulting in asparaginase depletion in the treatment of ALL. Close monitoring of the thrombosis and anticoagulation therapy have altered the course of asparaginase use. Ultimately, most children who experience a thrombotic event are able to complete 30 weeks of asparaginase therapy according to the DFCI ALL protocol.

**PU027**

**RESPECT FOR CHILD AND FAMILY INTEGRITY IN A HOSPITAL**

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**Purpose:** It is important to understand what integrity means for a child and family in a hospital in order to avoid unnecessary suffering and to promote child’s health. The study emanates from the caring science that has been developed at the Department of Caring science, Åbo Akademi University, Finland. The theoretical perspective constitutes of integrity; suffering and caring. Study seeks answers to questions: What characterizes child and family integrity in the child healthcare context? What experiences parents have in child and family integrity in the hospital?

**Method:** The study is a qualitative study and the data was collected with a parent questionnaire. Eleven parents in a parents’ association responded and questions were analyzed according to the content analysis.
Results: Child and family integrity is characterized as respect for the unique human beings dignity, integrity that respects the child and family’s space and integrity that supports participation. I was based on: the human beings dignity was confirmed, the family space was respected and the child and the parents were invited to participate in the hospital community. The parents described also offending and poor experiences.

Conclusion: Respect for the child and family integrity requires understanding that the child and the family are vulnerable in the hospital. It also requires that the individual respects the child and family integrity in the hospital. This research helps the caring personnel to give quality care to the child and the family and to alleviate their suffering in the hospital. The caring personnel acquire an increased knowledge of promoting child and family health and sense of well-being.

PU028

DEVELOPMENT OF THE SUPPORT PROGRAM FOR NURSES WORKING WITH OTHER PROFESSION IN THE CARE OF CHILDREN WITH CANCER AND THEIR FAMILIES

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13Fukuoka Prefectural University, Child Nursing, Fukuoka, Japan

Purpose: Nursing care for children with cancer and their families in Japan presents various problems. Many nurses have limited experience in the care for children with cancer and there are no benchmarks for providing such care. Nursing Care Guidelines Study Group of Japanese Society of Pediatric Oncology Nursing started working on developing the guidelines in 2006. Aims of this program are: 1) to support nurses who care for children with cancer and their family, 2) to contribute in overcoming difficulties that nurses face, 3) and to improve the quality of life of children with cancer and their families.

Method: Contents of the guidelines:
We made the guidelines in 2008. The guidelines consist of the following 9 chapters:
(1) telling the diagnosis or explanation about the disease -informed consent/assent, (2) symptom management, (3) examinations and treatment, (4) hospital environment, (5) rehabilitation/habilitation to school and society, (6) support for long-term survivors, (7) care of the end of life, (8) support for families, (9) mental health of pediatric oncology nurses. Each chapter has guiding principles at the top of the chapter.

Revision of the guidelines:
In a pediatric oncology nursing seminar about informed consent/assent, participated nurses were asked by questionnaire about their experiences and thoughts on informed consent/assent for the children.

Results: We received answers from eleven nurses. Nine nurses described that after physician told the children and their families the diagnosis and left from the room, nurses are involved in children and parents by asking their concerns. Nurses performed the role based on their own thoughts. It is needed to discuss nursing role in team approach.

Conclusion: Now the Study Group is working on support program for nurses. In addition it will be needed examination through using the guidelines in clinical setting and improvement of the guidelines with evidence based on research.

PU030

USE OF A TV CONFERENCE SYSTEM TO LINK THE HOSPITAL CLASS WITH THE REGULAR SCHOOL CLASS OF A CHILD UNDERGOING CHEMOTHERAPY

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Purpose: The aim of this study was to establish a TV conference system to link a child undergoing chemotherapy, who was enrolled in a hospital class, with his classmates in his regular school, and to examine the possibilities of class development through bidirectional communication.

Method: Research period: June 2008 to October 2009.2 The 2 classes in the regular school and in the hospital were linked by optical broadband network on the conference system over a period of 5 months.

Results: 1. The participant was a 9-year-old boy who was undergoing a year of chemotherapy following radiotherapy for a brain tumor. He was enrolled in B hospital class during treatment. At the time of admission a year earlier, he was confined to bed and had difficulty walking. 2. Intervention began at the point where he transitioned from bedside learning to walking to the hospital classroom. The TV system was linked for the boy and his classmates talked via the TV screen. Such weekly sessions as reading time and recorder playing were held. In total, 9 sessions were held. 3. Evaluation by the participant: Initially, the boy felt awkward, but was happy to be able to see friends from his class. After leaving the hospital, he had no problems in relations with friends, and enjoys playing soccer and participating in other activities with them.

Conclusion: The establishment of this bidirectional system strengthened communication between the school and hospital. In addition, the fact that the child was able to participate in classes in his regular school via the system facilitated friendships and reduced psychological isolation from the school, enabling him to form an image of returning to school after leaving hospital. Experiences such as talking and
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playing music together using this system were evaluated as contributing to the boy’s smooth reentry into his regular school.

PU031

USE OF ORAL LIQUID DISPENSERS FOR THE PREVENTION OF WRONG ROUTE ERRORS: 1 YEAR FOLLOW-UP

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Purpose: After the occurrence of three wrong route errors on the pediatric hematopoeis-oncology ward, the use of oral liquid dispensers (O.L.D.) was introduced. These purple colored syringes are incompatible with intravenous equipment, due to the tip-connection design. As purple has become the “oral and enteral” European standard color, its color gives a reflection to the nurses to use the correct route. In addition to the use of oral liquid dispensers, new purple coded nasogastric extension lines with O.L.D. entrance were implemented.

Method: Due to the importance of this project, the use of O.L.D syringes was introduced in the entire pediatric department, including neonatology and the maternity ward.

Results: A poster campaign in the hospital and several educational sessions for all staff members highlighted this important change in practice. Some additional practical problems were observed. As feeding lines were not always compatible (e.g. on neonatology), additional lines were designed and developed in order to fulfill all needs. The project was highlighted several times on a national level to promote and enhance the safety culture in the pediatric departments. As a consequence, many hospitals started to implement it’s use. In our hospital, there was regular feedback of the project. After one year of implementation, no wrong-route errors were reported so far.

Conclusion: By using oral liquid dispensers, we were able to reduce the number of wrong route errors, so far. Especially in pediatric oncology wards where children have many lines and the risk for wrong route errors is real, we hope, by further expansion and promotion of this project, to avoid this important kind of errors.

PU032

QUALITY OF LIFE AND FAMILY FUNCTIONING OF SIBLINGS OF A CHILD WITH CHILDMOOD CANCER

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Purpose: The aim of the present study was to describe QOL and family functioning of siblings of a child with childhood cancer who had completed hospitalized-based chemotherapy, and to determine the informed state of the siblings.

Method: This study was performed at a pediatric oncology outpatient clinic of university-hospital in Hyogo, Japan. A questionnaire sheet regarding QOL (PedsQL), family functioning (FACESKG), and siblings’ knowledge of disease was distributed to 17 siblings.

Results: Thirteen siblings returned the questionnaire sheet. The mean age of the siblings was 12.8 with a range of 8–18 years. Six siblings (46.2%) experienced family separation or a change of family member, such as moving to a grandparent’s house, while their ill sibling was hospitalized. The scores of PedsQL were Physical functioning 86.2, and total 87.2. Significant differences were found between Social functioning and Duration of hospital stay (Spearman rs = 0.68; i.e., a longer hospital stay was associated with worsening QOL). Regarding family functioning, ten of 13 siblings perceived their family life as chaotic. Types of family cohesion varied but there was no enmeshed type. Regarding siblings’ knowledge of the ill child’s disease, 3 siblings (23.1%) had been informed of the diagnosis. No significant differences were found between siblings who were or were not informed, either in siblings’ ages or sibling’s age at time of diagnosis. All of the informed siblings were siblings of a child with acute lymphoblastic leukemia.

Conclusion: Siblings expressed good QOL; however, the duration of hospital stays may have negatively affected siblings’ long-term QOL. Most siblings perceived their family life as chaotic, perhaps due to the influence of cancer in a family member. Further investigation is needed regarding the informed state of the siblings.

PU033

PILOT COMPARISON OF COST AND NURSING INTERVENTIONS BETWEEN AN OUTPATIENT AND INPATIENT CHEMOTHERAPY REGIMEN IN PEDIATRIC PATIENTS

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Purpose: Improvements in antiemetic and fluid hydration delivery have allowed for certain chemotherapy regimens to be administered as an outpatient. Yet, there are no clear data detailing objective cost and work savings for outpatient chemotherapy. We propose a pilot study evaluating cost and nursing interventions for patients receiving vincristine, cyclophosphamide with/without dactinomycin (VAC or VC).

Method: Single institution retrospective medical record review of patients under 21 years of age who received any outpatient courses of VAC or VC from May 2007 to March 2010. For patients who received both inpatient and outpatient therapy, we compared treatment cost and number of defined nursing interventions.

Results: Nine patients received at least one course of outpatient VAC or VC. There were 6 females. Median diagnosis age was 13 years (range 14 months – 18 years). Seven patients had rhabdomyosarcoma and 2 with Ewing’s sarcoma. Four patients received only outpatient chemotherapy while at MDACC. Total number of courses evaluated include inpatient VAC (22 courses), outpatient VAC (14), inpatient VC (4), and outpatient VC (10). Mean cost inpatient VAC was $14,975 compared to outpatient VAC ($10,534). Mean cost for inpatient VC was $6,710 compared to outpatient VC ($4,305). Number of nursing pages printed for inpatient admission was 57 compared to 4 pages for outpatient. Mean number of inpatient nursing note entries was 10.9 (range 4–19) compared to 6.9 entries (range 4–12) for outpatient. Four patients were admitted following chemotherapy due to toxicity (3 for fever/neutropenia and 1 for mucositis) but only 1 admission followed outpatient therapy.

Conclusion: Our preliminary findings indicate that outpatient VAC or VC is safe and with demonstrated cost savings and decreased number of nursing forms to be completed resulting in work savings. Further study is needed to confirm these preliminary findings in a larger cohort and with other chemotherapy regimens.

PU034

A MULTIDISCIPLINARY APPROACH TO IMPLEMENTING PEDIATRIC ONCOLOGY CLINICAL TRIALS.

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Purpose: Pediatric oncology research studies are becoming more complex. Meeting the emotional and clinical needs of patients and families while maintaining the integrity of the research study can be a challenge for the bedside clinical staff. In an effort to standardize our approach to pediatric oncology clinical research we developed a process of protocol implementation that considers compassionate safe clinical care and quality research practice.

Method: Based on our experiences with the Children’s Oncology Group (COG) ANBL-0032 protocol for the treatment of high risk neuroblastoma, a multidisciplinary group was convened that included Physicians, Advanced Practice Nurses, Research Coordinators, Research Nurses, Nurse Educators, Nursing Informatics, Staff Nurses and Pharmacists with the goal of standardizing the approach to protocol implementation. Each member of the group held a distinctive role in the execution of the protocol and therefore provided a unique perspective. The group reviewed the experiences surrounding the first two patients enrolled on the protocol at our institution.

Results: Based on the feedback from prescribers, nursing, pharmacy and research staff along with family input we identified gaps in knowledge and what was perceived as “fractured care” by families and staff. Utilizing the findings from the debriefing, the group developed reference materials and system processes with the purpose of...
Conclusion: A multidisciplinary collaborative approach that considers individual contributions made by each member of the research team is an effective process of protocol implementation in pediatric oncology clinical research.

Results:

Method:

Participants, the logistic support consisting of computers, cameras, printers and the teachers(s) in optimal pedagogical practice and technical use of the system.

The child

PU035

BEDNET: ON-LINE SCHOOL EDUCATION FOR CHILDREN AND YOUNGSTERS WITH MEDICAL NEEDS

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Method:
The Bednet service cooperates with the parents, the school, the local educational guidance centre and the medical staff before and during the full service period. Each child is individually supported by a trained mentor who coaches the teachers(s) on oral and educational practices and technical use of the system.

Participants, the logistic support consisting of computers, cameras, printers and internet connections. Through a webcam, the child has visual and auditory contact with the teacher and classmates. Printer and scanner are used to exchange documents.

The system can be used during classes and out-of-class activities to interact with teachers and peers. It enables social contacts and collaboration by lack of face-to-face contact. Bednets interface is very intuitive and transparent in use.

Results:

Until February 2010 a total of 30 patients used this service. Some of them (11) attended two school years. Distribution of type of school was as follows: primary school, n = 22 and secondary school, n = 19.

Conclusion: "Bednet" reduces the learning gap caused by the illness and re-establishes/maintains social contacts of sick children with the "outside world". The use of the program increased progressively since its start but is restricted due to financial limits.

PU036

NAUSEA AND VOMITING PERSPECTIVES OF CHILDREN RECEIVING MODERATE TO HIGHLY EMETOGENIC CHEMOTHERAPY TREATMENT

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Method:

A prospective, cohort design was used to describe children’s coping and primary caregiver’s and nurse’s interventions regarding CINV. A convenience sample of 40 school-age children with a cancer diagnosis receiving moderate or highly emetic chemotherapy at a children’s hospital in the southern area of the United States was used for this study.

Results:
The KIDCOPE questionnaire, which groups responses into positive and negative strategies, was used to determine children’s coping strategies and primary caregivers and nurse to describe interventions used for CINV before, during, and after moderate or highly emetogenic chemotherapy.

Method:

A prospective, cohort design was used to describe children’s coping strategies and primary caregivers and nurse’s interventions regarding CINV. A convenience sample of 40 school-age children with a cancer diagnosis receiving moderate or highly emetic chemotherapy at a children’s hospital in the southern area of the United States was used for this study.

Results:
The KIDCOPE questionnaire, which groups responses into positive and negative strategies, was used to determine children’s coping strategies and primary caregivers and nurse to describe interventions used for CINV before, during, and after moderate or highly emetogenic chemotherapy.

Method:

Nonparametric analysis was used to evaluate whether the coping strategies differed significantly across the three time periods.

Conclusion:

A description of coping strategies used by children and interventions offered by primary caregivers and nurses to manage CINV allows for an increased awareness of symptom management techniques. This information will allow for more effective interventions to be developed and utilized by knowledgeable health care providers.

PU039

PROBLEM OF CHILDREN WITH CANCER IN LATER CHILDHOOD OBTAINED BY INVESTIGATION TO THEIR MOTHERS

Noriko Nakagaki, Nami Jindo, Hiromi Suzuki, Rie Sawada

Japanese Red Cross Toyota College, Child Nursing, Toyota, Japan

Method:

A prospective, cohort design was used to describe children’s coping strategies and primary caregivers and nurse’s interventions regarding CINV. A convenience sample of 40 school-age children with a cancer diagnosis receiving moderate or highly emetic chemotherapy at a children’s hospital in the southern area of the United States was used for this study.

Results:
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Method:

Nonparametric analysis was used to evaluate whether the coping strategies differed significantly across the three time periods.

Conclusion:

A description of coping strategies used by children and interventions offered by primary caregivers and nurses to manage CINV allows for an increased awareness of symptom management techniques. This information will allow for more effective interventions to be developed and utilized by knowledgeable health care providers.
Study is not advanced systematically because treatment is given priority though in the hospital, there is a class. Moreover, it is placed from the continuation of a situation should away for the friend and a long term in the isolated situation. Conclusion: It is necessary to examine the ideal way of the cooperation of the class in the hospital and the local school. This research received the Japan Red Cross nursing society research subsidy in 2009

PU040

HOME SWEET HOME: A FOUR WHEEL HOSPITAL

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Purpose: Among health interventions the hospitals have developed home-based care for children undergoing repeated and lengthy hospitalizations for chemotherapy, treatment of infectious complications and other toxicities. The hospital on four wheels was founded to avoid long hospital stays whenever possible. At home, blood sampling, infusions, antibiotic therapies, chemotherapy, pain therapy as well as PVC maintenance can be safely performed, both in patients receiving curative treatments, as well as in terminally sick patients receiving palliative care.

Method: The home care team consists of a supervising attending, a physician delivering home care, a nursing coordinator, nurses, and a psychologist. The involved nurses are on staff at the Hem-Onc Division and perform home visits outside their working hours. The following needs can be satisfied: post-chemotherapy blood tests, transfusions, post-transplant follow-up, routine PVC flushes and dressing changes, nutritional support, IV antimicrobial therapies, and terminally ill patients. The program starts with an interview with the family and the child is then enrolled by the nursing coordinator reachable for the physician, after outlining a treatment plan.

Results: During the last 12 months, 18 pts were treated, median age being 112 months (range 11–205); 617 visits were done to perform: 210 blood tests, 171 doses of antibiotics, 61 other IV therapies, 29 PRBC and 67 Pt transfusions, 2 courses of chemotherapy, 18 IV pain treatments, 22 PVC flushes, 103 NPT. 3 terminally ill pts received all palliative care until death at home, close to their loved ones.

Conclusion: Nothing can better demonstrate our experience than this sentence “Since I started home care, the quality of my life has improved, I have more time to spend with the people I care for, such as family and friends, I’m surrounded by my things, which belong to my life and not to a sterile and neutral place as the hospital.” Nicola, 16-year-old patient.

PU041

CLINICAL RESEARCH NURSING IN PEDIATRIC ONCOLOGY: TOOLS OF THE TRADE

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Purpose: Clinical trials have long been a part of pediatric oncology nursing. The pediatric oncology nurse at the bedside is charged with collecting quality research data while meeting the clinical and emotional needs of children with cancer. The Children’s Oncology Group (COG) study ANBL-0032 for the treatment of high risk neuroblastoma is a complex research protocol with multiple data collection points and investigational medications. In an effort to enhance the bedside nurse’s ability to provide expert clinical care and research practice to patients being treated on ANBL-0032, we developed a series of tools and programs designed to facilitate documentation, provide protocol education and ensure consistent delivery of study medications.

Method: Nurses from the pediatric oncology and stem cell transplant units collaborated with nurses from the pediatric clinical research unit to create resources that ensure the success of the clinical trial.

Results: The tools developed include nursing management plans that guide nursing care and data collection, educational in-services, protocol summary sheets and quick reference sheets for side effects management and drug delivery. Since these patients can be cared for on three different units, these tools have been essential in providing consistency in nursing practices surrounding monitoring and drug delivery. Staff has demonstrated knowledge of the protocol by recognizing and managing side effects and by providing patient and family education.

Conclusion: bedside nurses are the front line data collectors in pediatric oncology clinical trials, providing detailed resources and education directly related to the nursing care of patients involved in pediatric oncology clinical trials assist the nurse in providing safe, compassionate clinical care while maintaining the integrity of the research protocol.

PU042

DEVELOPMENT OF PROVIDER TOOLS TO IMPROVE THE PROCESS OF RESEARCH IMPLEMENTATION: HIGH RISK NEUROBLASTOMA PROTOCOL ANBL0032

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Purpose: The Children’s Oncology Group ANBL0032 protocol for the treatment of high risk neuroblastoma is a complex research trial with a multifaceted treatment plan. In order to ensure that all aspects of the protocol are executed, a group of advanced practice nurses from Children’s Hospital Boston/Dana Farber Cancer Institute (CFIC) developed templated order sets and prescriber reference tools. The goal was to improve communication across the inpatient and outpatient settings, increase standardization of patient care, decrease errors in cytotoxicity/antibody administration and supportive care orders, and ensure accurate and timely data collection.

Method: A multidisciplinary group (nurse practitioners, staff nurses, pharmacists, nursing informatics, and clinical research coordinators) was created to review feedback from staff and parents. The group identified knowledge gaps and recognized areas of “fractured care.”

Results: Tools developed included templated admission orders, templated inpatient progress notes, electronic admission and discharge notifications, and an inpatient protocol reference binder. The templated inpatient orders decreased order entry errors and sped the patient admission process. A daily source document was developed to systematically document and collect required protocol data. Not only did this decrease the amount of time needed to review patient charts for toxicity data, it also expedited the reporting of adverse events. In an effort to improve communication across the care continuum, electronic admission and discharge notifications provided key information to oncology team members. This increased communication contributed to family perceptions of seamless care. Finally, a reference binder was developed to facilitate course by course management for individual patients.

Conclusion: Critical analysis of these tools and processes continue with the goal of increasing knowledge and decreasing “fractured care” so as to provide expert clinical care with exceptional research practice. As pediatric oncology research continues to become increasingly complex, provider specific tools can be an effective way to streamline patient care and improve patient outcomes.
transition process an evidenced based review was conducted. The review focused on identifying the best practice for transitioning HSCT patients to the outpatient setting.

**Method:** A review of the literature was completed and yielded no articles related to pediatric HSCT patients and transition of care. Additional databases, American Society of Blood and Marrow Transplantation and Center for Disease Control were reviewed. No recommendations were identified. Next steps were to benchmark with other Pediatric HSCT Programs

A questionnaire was developed with 13 specific questions which focused on clinic flow, patient/family education, and nursing assignments and was sent to the APHN Bounce List as well as other HSCT experts.

**Results:** The six responses provided the following information; transition process of patients varies among programs, inpatient teams provide all pre-discharge teaching, and the outpatient team may be less familiar with post transplant guidelines.

**Conclusion:** The objectives of the review were to provide consistent information to patients and families and to develop opportunities to periodically update providers with changes in practice. By benchmarking with other HSCT programs, we are now able to make recommendations to improve our transition process.

**PU 044**

**NEED OF INFECTION CONTROL NURSE IN PAEDIATRIC ONCOLOGY WARD: EXPERIENCE FROM A DEVELOPING COUNTRY**

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**Purpose:** Infection remains the leading cause of death and most frequent cause of serious complications causing delays in treatment and inferior outcomes in children with cancer undergoing aggressive chemotherapy. Life threatening infections in patients with cancer include bacteremia caused by gram negative aerobic bacilli, fungemia, bacterial pneumonia, and fungal pneumonia. The primary objective of this retrospective analysis was to evaluate the incidence of positive blood culture, one of the important measures of infection control, in the pediatric ward one year before (2008) and one year after (2009) posting a Specialist Infection Control Nurse in the ward. The secondary objective was to identify the common infectious organisms isolated from blood in pediatric ward.

**Method:** Data of total number of 3263 patient (age group 1 month to 15 years) admissions in the pediatric ward of Tata Memorial Hospital from Jan 2008 to Dec 2009 were analyzed for this study and retrospective data of blood culture was collected from patient record files and Hospital Information System.

**Results:** In 2008 – Total number of organisms isolated from blood cultures of 336 samples in 1622 admissions was 91 (Gram –ve 38)[Pseudomonas 20], Gram –ve 4, Fungal-3, ). In 2009 – Total number organisms isolated from blood cultures of 1276 samples in 1641 admissions was 45 (Gram –ve 38[Pseudomonas 7], Gram –ve 7). In above data maximum organism was isolated in 2008 were pseudomonas 20 and in 2009 were pseudomonas 7. In above data maximum organism was isolated in 2008 were pseudomonas 20 and in 2009 were pseudomonas 7. After analysis, it was observed that infection rate had reduced from 91 (6.80%) in 2008 to 45 (3.52%) in 2009.

**Conclusion:** This study shows the importance of nurse’s role in prevention of infections in admitted children with cancer. A nurse with proper knowledge in infection control measures can minimize complications by providing road to faster, smoother and safe recovery.

**PU 045**

**OUTCOMES ASSOCIATED WITH PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS SURGICALLY IMPLANTED PORTS DURING INDUCTION THERAPY FOR PATIENTS WITH ACUTE LYMPHOBlastic LEUKEMIA**

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**Purpose:** Central venous access devices (CVADs) are essential to pediatric oncology patients for administration of chemotherapy and supportive care. It is estimated that upwards of 25% of CVADs become occluded and 60% of those occlusions are caused by thrombosis (Genentech, 2005). CVAD related thrombotic events are of clinical importance as they can result in treatment delays and disruption in patient care.

**Method:** While conducting an evidence based project at Children’s Hospital Boston (CHB) examining best practice for diagnosing thrombotic CVAD occlusions inconsistencies were identified in Alteplase (tPA) administration and frequency of use. Our institutional guidelines were found to be in agreement with the review of literature and benchmarking with other institutional standards, but were not consistently being followed by providers.

**Results:** Review of the tPA dispensing data at our institution between October 2007 and October 2008 identified 22 oncology patients who had received more than 6 doses of tPA to treat occluded lines. CHB occlusion algorithm recommends a contrast line study be performed if no blood return is obtained after two doses of tPA are administered. Neither our literature review nor our institutional occlusion algorithm recommends how often a line should be evaluated after multiple doses of tPA.

**Conclusion:** After identification of this problem, the decision was made to conduct a multidisciplinary re-education plan regarding prescribing and administering thrombolytic agents including pharmacy, nursing, physician and family re-education components. These findings will enhance and support consistent best practice standards at our institution and will add to the growing body of knowledge about pediatric oncology nursing practice associated with thrombotic events and use of thrombolytic agents.

**PU 047**

**THE NEED FOR NURSING CONTINUING EDUCATIONAL PROGRAM TO PROMOTE TRANSITION OF ADOLESCENTS AND YOUNG ADULTS WITH CANCER**

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**Purpose:** Adolescence is an important transitional phase from child to adult-oriented medical system. However, previous research showed that AYA with chronic illness including cancer had the family relations and psycho-socio-emotional problems in addition to health/illness problems which often disturbed transitional process. To meet care needs of AYA with cancer and facilitate the transitional process, continuing education for pediatric nurses in Japan were needed to be developed.

**Method:** Based on the focus group discussion with clinical nurses, we developed the content of continuing educational program to facilitate the transitional process of AYA.
with chronic illness including cancer. In this educational program, AYA must have
decision making abilities and were capable of living/working independently. This
educational program aimed at providing basic knowledge of adolescents’
development, skills to assess transitional stages of AYA, and plan to facilitate
transition process to adult-oriented medical system which would meet AYA’s
developmental and medical needs. Sixteen lectures (90 minutes/lecture) and
workshops were provided over 5 days period in August and October in 2009 and
February in 2010.
Results: Thirty nurses participated in this program. All of them were females and had
more than 3 years of clinical experiences in the field of pediatric nursing. All of
them experienced difficult cases of AYA with chronic conditions including cancer. All of
them did not have the standardized protocol to initiate preparations for transition in
their facilities. All lectures were rated as important and relevant to clinical practice.
Through the workshop and presentations by participants, it was revealed that
multidisciplinary team work be the key to facilitate the transitional process.
Conclusion: Participants’ evaluations showed that the effectiveness of this program
which deepen their knowledge and motivated to initiate supportive care for the
AYA population because of the increasing number of childhood cancer survivors,
continuing educational programs about AYA and transition should be developed
further.

PV001
LANGUAGE AND COMMUNICATION CHALLENGES EXPERIENCED BY CHINESE AND SOUTH ASIAN PARENTS OF CHILDREN WITH CANCER LIVING IN CANADA

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Purpose: There is compelling evidence indicating that newcomers to Canada, with
limited English proficiency and low health literacy, face systemic, linguistic and
cultural barriers in accessing health information and treatment services. This poster
highlights the role of language and communication in the healthcare experiences of 50
first generation Chinese and South Asian immigrant parents of children with cancer in
Canada.
Method: A constructivist grounded theory approach (Charmaz, 2006) was used. The
findings are part of a larger study of the caregiving experiences of first generation
Chinese and South Asian parents of children with cancer. Parents of children at least
six months post-diagnosis were recruited from six Canadian pediatric oncology
centres. Interviews were conducted in English, Cantonese, Mandarin, Urdu, Punjabi
or Hindi and transcribed into English. Analysis involved line-by-line, focused and
theoretical coding to establish categories and themes. Constant comparison was used
to examine relationships within and across codes and categories. Interviewing
continued until no new themes emerged.
Results: Language and communication challenges had an important impact on
immigrant parents’ ability to access health information, services and resources. The
following key themes emerged: i) difficulty understanding complex medical
terminology (preference for the use of simple language and visual aids/diagrams by
healthcare providers); ii) miscommunication impacting satisfaction with care;
iii) limited (or not readily available) access to formal interpreter services; iv) desire to
communicate in native language whenever possible; and v) limited availability of
linguistically and culturally-appropriate information and resources in the hospital,
community and online.
Conclusion: The ability to communicate effectively plays an essential role in parents’
healthcare experiences for pragmatic and social purposes. Language and
communication challenges can heighten systemic and cultural barriers experienced by
immigrant parents of children with cancer. The provision of culturally and
linguistically sensitive services could help to support immigrant families in their
caregiving role.

PV002
PEDIATRIC ONCOLOGY IN DEVELOPING COUNTRIES: SURVIVAL PROBLEMS

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Purpose: To report the different types of malignancy in children in Egypt, as a model
of developing country, and to study the survival of these cases and compare it with that
of Western countries.
Method: All children with malignant tumors treated in Alexandria University
Hospitals over a period of 20 years were reported. The different types of malignancy were studied, categorized and compared to other
developing countries.
The survival of these cases was recorded and analysed. This survival rate
was compared to that in the Western Countries. Possible causes of the low survival were reported and studied including defects in the
supportive care.
Results: A total number of 1277 cases of malignancy in children was reported. They
were treated in the Pediatric Surgery, Pediatric haematology/Oncology, Pediatric
Neurosurgery and Pediatric Orthopedic Departments. A study of the influence of age
and sex was presented. The five years survival rate of all malignant tumors of
these Egyptian children was 38.9%. This was much lower than that in the USA&UK
which was reported in many studies to be from 60–75%. There were different causes of
this low survival including delayed presentation and lack of optimum specialized
Pediatric Oncology Centers.
Conclusion: The survival of children with cancer in Developing countries including
Egypt is much lower than that in Developed countries. Among the important causes of this low survival are: the delayed presentation of cases
and lack of specialized Pediatric Oncology Centers as well as deficiency in the
supportive care.
Many efforts and measures should be applied to achieve more safety, more supportive
care and better survival.

PV003
PERFORMANCE OF A BRIEF SCREENER OF PARENTAL EMOTIONAL BURDEN FOLLOWING PEDIATRIC HSCT

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Purpose: Parents of children undergoing hematopoietic stem cell transplantation
(HSCT) may face a psychological burden as they manage intense treatments and
uncertain outcomes. This study assesses the performance of a brief measure of
emotional functioning from a health-related quality of life instrument as a predictor of
parental psychiatric status, as compared to the Structured Diagnostic (Clinical)
Interviews for DSM-IV Axis I Disorders (SCID).
Method: As part of a multi-center, pediatric HSCT study, parents (N = 165)
completed the Child Health Ratings Inventories-General Health module at study entry,
which contains a 7-item parental emotional functioning domain. Before their child’s
HSCT, 108 parents also completed specific SCID modules for current anxiety,
depression and adjustment disorder. Based on the DSM-IV criteria for these disorders,
a composite variable was created for threshold (i.e., presence of full symptomatology
with impairment) or subthreshold (i.e., near presence) levels of any of the disorders
assessed. Receiver operating characteristic (ROC) analysis was used to assess how the
7-item emotional functioning domain predicted parental psychiatric status, as
identified by the SCID. Additional variables—including lifetime psychiatric
medication use, psychiatric history, and socioeconomic status—were considered if
they improved prediction and the “area under the ROC curve” (AUC).
Results: Half of parents (51.5%) completing the SCID had at least one of the selected
Axis I disorders at threshold or subthreshold levels. The AUC for the 7-item emotional
functioning domain plus one question about parents’ lifetime psychiatric medication use
was 0.73; the sensitivity was 87% and the specificity was 50%.
Conclusion: Use of a brief emotional functioning screener may identify parents with
selected Axis I disorders, which would facilitate further evaluation and intervention.
The good sensitivity of this screener ensures that parents with these disorders will
likely be identified. Although lower specificity may necessitate additional evaluation in
parents without these disorders, the psychological burden of HSCT may justify
further evaluation.

PV004
PATIENT SATISFACTION QUESTIONNAIRE FOR LONG TERM CHILDHOOD CANCER SURVIVORS: PRELIMINARY ANALYSES OF RELIABILITY AND VALIDITY ON 78 PATIENTS

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Purpose: To report the different types of malignancy in children in Egypt, as a model
of developing country, and to study the survival of these cases and compare it with that
of Western countries.
Method: All children with malignant tumors treated in Alexandria University
Hospitals over a period of 20 years were reported. The different types of malignancy were studied, categorized and compared to other
developing countries.
The survival of these cases was recorded and analysed. This survival rate
was compared to that in the Western Countries. Possible causes of the low survival were reported and studied including defects in the
supportive care.
Results: A total number of 1277 cases of malignancy in children was reported. They
were treated in the Pediatric Surgery, Pediatric haematology/Oncology, Pediatric
Neurosurgery and Pediatric Orthopedic Departments. A study of the influence of age
and sex was presented. The five years survival rate of all malignant tumors of
these Egyptian children was 38.9%. This was much lower than that in the USA&UK
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this low survival including delayed presentation and lack of optimum specialized
Pediatric Oncology Centers.
Conclusion: The survival of children with cancer in Developing countries including
Egypt is much lower than that in Developed countries. Among the important causes of this low survival are: the delayed presentation of cases
and lack of specialized Pediatric Oncology Centers as well as deficiency in the
supportive care.
Many efforts and measures should be applied to achieve more safety, more supportive
care and better survival.
Purpose: Our aim is to illustrate the validity of a patient satisfaction questionnaire for long-term childhood cancer survivors.

Method: Patients were 78 childhood cancer survivors recruited at the Pediatric Hematology-Oncologic Clinic, University of Padova. All patients were Caucasian with a mean age of 19.70 years (SD = 3.02) and equally distributed by gender with 39 girls and 39 males. Mostly patients were affected by haematological disorders (N = 43), while 24 had different types of solid tumours.

A 30-item questionnaire assessing patient satisfaction was given to the patients, out of therapy from an average of 9.11 years (SD = 2.96). Also socio-economic and medical data were collected.

Results: We ran a Varimax rotated factor analysis (principal components, orthogonal rotation, 4 factors extraction) on the total 30 items to create psychometrically robust dimensions. We identified 4 dimensions explaining totally 58.15% of variance. The first factor was “Medical communication and technical quality of care” (N item = 11; alpha = 0.90; 24.18%); the second factor was “Accessibility and physical environment satisfaction” (N item = 11; alpha = 0.84; 14.30%); the third factor was “Interpersonal manner” (N item = 4; alpha = 0.71; 10.41%) and the last factor was “Empathy” (N item = 4; alpha = 0.65; 9.24%). The majority of the alpha coefficients for the 4 dimensions represent good internal consistency. The identified dimensions were all correlated to each other, showing a good construct validity of the questionnaire. We ran also Pearson correlations or Variance analysis to see the for the 4 dimensions represent good internal consistency. The identification was confirmed by a promising research tool to give direct voice to childhood cancer survivors about their experience with the health service.

PV005

LONG TERM FOLLOW UP PROGRAM - MODEL OF CARE

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Purpose: In 2009, the Victorian Government in Australia announced the Statewide Cancer Action Plan. Within this plan, provision and funding was allocated to the Paediatric Integrated Cancer Service to develop and implement a Long Term Follow Up (LTF) Program for survivors of childhood cancer.

Method: The LTF program has a strong client focused approach with an emphasis on wellness and health promotion and has been developed based on the experiences of pediatricians, General Practitioners and specialists utilizing the skills and knowledge of a variety of Paediatric specialists and referring to Pediatricians, General Practitioners and specific specialist services in both metropolitan and regional areas.

Conclusion: The poster will outline the key components of the Long Term Follow Up model of care, which is available to all survivors of childhood and adolescent cancer in Victoria, Australia.

PV006

PREDICTORS OF ADHERENCE TO LONG TERM FOLLOW UP CARE IN CHILDHOOD CANCER SURVIVORS

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Purpose: To identify variables associated with adherence to follow-up after completion of therapy in patients treated at Texas Children’s Cancer Center (TCCC).

Method: A retrospective chart review of all patients diagnosed and treated for pediatric cancer between 1998 and 2001 at TCCC (n = 1177) was conducted. Medical records were reviewed and demographic, clinical, psychosocial, and socioeconomic characteristics were compared between the patients who continued to attend appointments and those who were lost to follow-up (defined as missing the requested next follow-up appointment for more than 6 months). Frequencies and proportions for categorical variables were compared by Fisher’s exact test and Chi-square analyses, and mean values for the continuous variables were compared by t-test or ANOVA.

Logistic regression analyses were used for multivariable comparisons.

Results: Of the 1,177 charts identified, 488 who survived cancer and not referred to another institution for follow up formed the study population. Notably 258 (52.8%) were lost to follow-up. Those who attended regularly, were on average, 1.6 years younger at diagnosis compared to the lost to follow-up group (5.9 years vs. 7.5 years, respectively, p = 0.001). In univariate analyses African American race, brain or solid tumor diagnosis, surgery as the sole therapy, single-parent household, living in an apartment, mobile home or a trailer at the end of treatment were associated with a greater likelihood of being lost to follow-up (p ≤ 0.05). In multivariable analyses, having surgery as the sole therapy (OR 1.9, 95%CI 1.1–3.1), and single parent household (OR 2.8, 95%CI 1.7–4.6) were independently associated with being lost to follow up.

Conclusion: In this pilot study a variety of patient and clinical characteristics were associated with non-adherence to follow-up care. Prospective studies are planned to confirm and expand these results. Future research goals include designing intervention strategies to improve the quality of long term care and adherence for survivors of pediatric cancer.

PV007

RARE CASES OF BIOLOGICALLY ACTIVE GONADAL TUMORS IN INFANTS AND CHILDREN

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992 SIOP ABSTRACTS

**Purpose:** The study aimed at reporting the biologically active gonadal tumors recorded in children in the last ten years with their rare unique presentations and the modalities of treatment.

**Method:** All children with hormonally active gonadal tumors admitted and treated in the Pediatric Surgery Department, University of Alexandria, Egypt were reported. They were studied concerning their demographic data, different clinical and imaging presentations and the modalities of treatment.

**Results:** Among recorded cases with testicular tumors, over a period of ten years, five cases with hormonally active gonadal tumors were reported. They were two boys and three girls with the age range from 7 months to 6 years. The boys were seven and 5 years and 7 months old and presented with premature puberty in the form of suprapubic hair and enlarged penis. Ultrasoundography verified the presence of a localized unilateral testicular tumor. The treatment was unilateral orchectomy. The histopathological diagnosis was Leydig Cell Tumor in the two cases. The girls were three in number and their ages were 4 years, 6 years, and 7 months. The first girl presented with suprapubic hair and enlargement of both breasts and the second one presented with suprapubic hair and a large abdominal cyst. However, the third girl (7 months old), presented with a rare and unique manifestation namely, severe bleeding per vagina. Ultrasoundography verified the presence of unilateral ovarian swelling in the three girls (cystic in one and solid in the other two).

The treatment was unilateral oophorectomy in the three cases and the histopathological diagnosis was Juvenile Granulosa Cell Tumor in the three cases. Follow up of all cases for three years revealed vanishing of all the secondary sexual characteristics with good quality of life and satisfaction of the parents.

**Conclusion:**

1. Biologically active gonadal tumors in infants and children are very uncommon.
2. Their main presentation is precocious pseudopuberty.
3. High index of suspicion is needed to avoid delay in the diagnosis.
4. They are benign tumors and unilateral gonadectomy is curative.

**PW004**

**THORACOSCOPIC TOTAL RESECTION OF NEUROGENIC TUMOURS IN CHILDREN: REVIEW OF 45 CASES**

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**Purpose:** Neurogenic tumours (NTs) arise in the posterior mediastinum, and comprise one third of all mediastinal tumours in children. 60% of these mediastinal NTs, are malignant with neuroblastoma being the most common tumour type. Minimally invasive resection of solid tumours is controversial because of concerns about inadequate resection and local recurrence.

The purpose of this study was to evaluate the feasibility and safety of thoracoscopic resection of neurogenic tumors in children.

**Method:** We performed a review of the literature and we collected all cases treated by thoracoscopic techniques from 1990 to 2007. Of all patients clinical data, surgical data and the postoperative patient history were reviewed including the size of the tumour, its localisation, and its presumed stage. The patient database included the following age group: 1 year old girl, referred to our paediatric surgery unit because a TAC revealed the presence of an oval neuroblastoma gene. The patient was positioned in a modified prone position with the affected side elevated and a combination of 3–5 mm instruments were used to perform the total resection of the tumour in one setting. The mean operating time was about 120 minutes and the hospital stay ranged from 4 to 12 days. All patients were followed up for a mean period of 17.3 months. There were no local recurrences or distant metastases documented.

**Conclusion:** In our series, thoracoscopic resection of NTs is a feasible and safe procedure. This painless technique allows shorter hospital stay in most cases, offer cosmetic advantages and avoid complications related to standard surgical incision. However these findings should be studied in the context of a large cooperative trial.

**PW006**

**LAPAROSCOPIC SURGERY EXPERIENCE FOR PEDIATRIC MALIGNANT SOLID TUMORS: A CASE SERIES**

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**Purpose:** Recently laparoscopic surgery in children is gaining ground due to the technical and instrumental advances. But, minimally invasive surgery for malignant pediatric tumours still remains controversial and only limited experiences were reported.

**Method:** We retrospectively analyzed 10 laparoscopic surgery cases for pediatric malignant solid tumors performed at our institute between April 2005 and January 2010.

**Results:** Complete tumor resection was performed in all cases. Six patients underwent laparoscopic adrenalectomy for neuroblastoma (n = 5), and adrenal neuroblastoma and laparoscopic tumor excision for thyroid or parathyroid or renal tumors. Two patients underwent laparoscopic partial hepatectomy for hepatoblastoma. Remaining two patients underwent laparoscopic salpingo-oophorectomy for yolk sac tumor and laparoscopic tumor excision for thyroid or parathyroid or renal tumors. All patients were followed up for a mean period of 17.3 months. The mean follow up period varied from 6 to 24 months. In all cases, the patients showed good clinical and radiological improvement.

**Conclusion:** Laparoscopic surgery for pediatric malignant solid tumors provides an alternative to conventional open surgery. It allows a technically feasible treatment modality and fully provides advantages of minimally invasive surgery. Long term follow up is mandatory to validate oncologic safety.

**PW007**

**PAPILLARY THYROID CARCINOMA OF CHILDREN: TREATMENT AND RESULTS**

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**Purpose:** Spontaneous pneumothorax is a rare complication of pediatric malignancies affecting the lung. We report a patient who developed recurrent spontaneous pneumothorax while undergoing intensive chemotherapy for poorly differentiated metastatic sarcoma.

**Method:** A 16 year-old boy with widespread metastatic disease from retropertioneal tumour was admitted to our hospital. The diagnosis of poorly differentiated sarcoma was established, with multiple intrapulmonary and hepatic metastases.

**Results:** Two days following insertion of a central venous catheter in the right subclavian vein and two days after the start of the chemotherapy (vincristine-ifosfamide-doxorubicin-etoposide) the patient developed acute respiratory distress. Chest X-ray revealed complete right-sided pneumothorax, and the boy was transferred to the Pediatric intensive care unit. A chest tube was inserted with complete clinical and radiological resolution in the following days. Iatrogenic pneumothorax was postulated, as it was on the same side as central venous catheter insertion. Ten days later the patient complained of acute chest pain and progressive shortness of breath, with right marginal pneumothorax evident on X-ray. Chest CT demonstrated subpleural bulla. Pleurocatheter drainage was placed with complete respiratory recovery.

**Conclusion:** In children and adolescents with cancer spontaneous pneumothorax is mainly related to pleuroparenchymal metastases. Other potential mechanisms include bronchopulmonary fistula as a manifestation of undetected metastasis, chemotherapy-induced rapid cell lysis and necrosis of peripherally located metastatic pulmonary nodules, enlargement of a rapidly growing and necrotizing tumor, chemotherapy-induced impairment of repair processes, and/or persistent local infection. This case illustrates that the presentation may be dramatic. A high degree of suspicion is necessary for prompt diagnosis of this emergency situation and proper therapeutic interventions.

**PW008**

**RECURRENT PNEUMOTHORAX COMPLICATING POORLY DIFFERENTIATED SARCOMA - CASE REPORT**

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2. School of Medicine, University of Rijeka, Croatia, Department of Pathology, Rijeka, Croatia

**Purpose:** Recurrent spontaneous pneumothorax is a rare complication of pediatric malignancies affecting the lung. We report a patient who developed recurrent spontaneous pneumothorax while undergoing intensive chemotherapy for poorly differentiated metastatic sarcoma.

**Method:** A 16 year-old boy with widespread metastatic disease from retropertioneal tumour was admitted to our hospital. The diagnosis of poorly differentiated sarcoma was established, with multiple intrapulmonary and hepatic metastases.

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**Conclusion:** In children and adolescents with cancer spontaneous pneumothorax is mainly related to pleuroparenchymal metastases. Other potential mechanisms include bronchopulmonary fistula as a manifestation of undetected metastasis, chemotherapy-induced rapid cell lysis and necrosis of peripherally located metastatic pulmonary nodules, enlargement of a rapidly growing and necrotizing tumor, chemotherapy-induced impairment of repair processes, and/or persistent local infection. This case illustrates that the presentation may be dramatic. A high degree of suspicion is necessary for prompt diagnosis of this emergency situation and proper therapeutic interventions.
Purpose: To develop adequate strategy diagnostics and treatment of children papillary thyroid carcinoma (PTC).

Method: 258 children (4–16 yeras) 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 at 109 (84%). 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 therapy. As a rule, surgery to the malignant tumours more than 1 sm. in diameter, radical operation on lymphatic collector of a tumour more than 1 sm. in diameter, radical operation on a lymphatic collector of a malignant tumour were performed.

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Conclusion: Treatment PTC of children have to be aggressive (Thyroideectomy as monofocal tumours in the size more than 1 sm. see with obligatory removal central limph dissection, and under indication removal of tumour more than 1 sm. in diameter, radical operation on a lymphatic collector of a tumour).

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 tumour more than 1 sm. in diameter, radical operation on a lymphatic collector of a malignant tumour were performed.

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UNCOMMON PRESENTATIONS OF MALIGNANT RENAL TUMORS IN CHILDREN - THE SINGAPORE EXPERIENCE

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Purpose: Malignant renal tumors comprise 6% of all childhood cancers. Although most children present with abdominal masses; congenital anomalies, clinical syndromes and paraneoplastic syndromes are known to be associated with these tumors. We reviewed our institution’s experience with malignant childhood renal tumors, highlighting patients who had uncommon presentations.

Method: With Institutional Review Board (IRB)’s approval, clinical charts from patients who had undergone surgery for malignant renal tumors between 1 June 1997 and 31 March 2009 were reviewed. Data related to patient’s demographics, clinical presentation, investigations, operative details, pathology, adjuvant therapy and treatment outcomes, were analyzed.

Results: Twenty-three children, with median age of 27 months, underwent surgery for renal tumors. Seventeen patients (74%) had Wilms tumors. Five had rhabdoid tumors and one had renal cell carcinoma. The most common presentation was an abdominal mass (n = 19). The classical triad of abdominal mass, pain and haematuria was only seen in 4 patients. One child presented with diabetic ketoacidosis and prolonged fever. A Wilms tumor was incidentally discovered when the child was screened for intraabdominal sepsis. A child with rhabdoid tumor presented with hypoglycemia. One child, with ruptured Wilms tumor, presented with acute hemoperitoneum. Only one abdominal sepsis. A child with rhabdoid tumor presented with hypoglycemia. One child presented with diabetic ketoacidosis and prolonged fever.

Conclusion: We report a high incidence of this rare childhood malignancy from a German paediatric university hospital and our experience of excellent outcome when different treatment options are applied to each individual case. Literature review of current treatment is presented.

CLASSIFICATION OF INTRACAVAL TUMOR THROMBUS IN WILMS TUMOR FACILITATES PLANNING AND RESECTION: THROMBECTOMY OR CAVECTOMY

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Purpose: Wilms’ tumor with tumor extension into the vena cava is not uncommon at presentation. The tumor thrombus can be classified as infrarenal, retroperitoneal, and suprahepatic and intracaval on imaging. Resection of these can be challenging and is usually deferred till after preoperative chemotherapy. Typically, these thrombi are not adherent to the endothelium and readily lend itself to removal. We present our institutional experience of surgery for nonarticular tumor thrombus.

Method: Dual phase multislice CT scan was performed in all patients for classifying the thrombus extent. Patients with renal vein thrombus only and intraatrial thrombus were excluded. Two patients had infrarenal hepatic tumor thrombus; one each had suprahepatic and retrohepatic thrombus. Based on the extent, venogram was performed only in patients with retrohepatic and suprahepatic thrombus which revealed complete caval occlusion in the former with extensive collateral circulation and partial occlusion in the latter. All patients had received preoperative chemotherapy.

Results: Vascular control (suprahepatic or infrarenal) was achieved in all patients. Cavotomy coupled with milking of the suprahepatic component was performed for thrombus extension. The patient with complete occlusion had thrombus densely adherent to the caval wall. He also had tumor extending into the ureter and the bladder. Encouraged with the presence of extensive collaterals on preoperative venogram,
cavectomy was performed. Vescicotomy was also done to remove the bladder extension. There was no perioperative mortality or complications in any patients. Three patients are receiving postoperative chemotherapy and the patient with cavectomy is free of disease after first follow-up.

Conclusion: Classification of the extent of thrombus by thorough imaging helps in determining the need for additional investigation before surgery. Venograms help in identifying collaterals especially in the retrohepatic and suprahepatic thrombus, which will be helpful for proper planning of surgical resection. With this careful and considerate approach a safe excision could be performed.

PX001
TOMOTHERAPY IN A THREE YEAR OLD FOR THE TREATMENT OF NASAL EWINGS SARCOMA
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2Children’s Hospital of Western Ontario, Pediatric Oncology, London, Canada

Purpose: Ewing sarcoma of the nasal cavity is rare and difficult to treat. We present a 3 yr old female who was diagnosed with an unresectable localized Ewings sarcoma of the nasal cavity involving the hard palate. Treatment consisted of IE/VAC chemotherapy and local radiation to a total dose of 54 Gy in 30 fractions given at week 13.

Method: In order to cover the tumor adequately, limit the dose received by critical structures and reduce side effects as much as possible, we developed radiation treatment plans using tomotherapy and intensity modulated radiation therapy (IMRT) and compared them.

Results: With tomotherapy the minimum dose received by the PTV was 51 Gy and the maximum was 56 Gy. 99% of the PTV received the prescription dose of 54 Gy. In contrast, the IMRT plan delivered minimum and maximum doses of 8.5 Gy and 58 Gy respectively and 90% of the PTV was covered by the prescription dose. The tomotherapy plan yielded lower maximum doses to the optic nerves, brainstem and lenses and was equivalent to the IMRT in terms of maximum doses to the eyes, the optic chiasm and the parotids. Tomotherapy also yielded lower mean doses to the lenses, brainstem, optic chiasm, inner ear and parotids. The IMRT plan, on the other hand, had lower maximum doses to the inner ears and lower mean doses to the eyes and whole brain.

Conclusion: Tomotherapy yielded a superior plan in terms of target coverage and side effects as much as possible, we developed radiation treatment plans using tomotherapy and intensity modulated radiation therapy (IMRT) and compared them.

Conclusion: The use of brachytherapy after chemotherapy and conservative surgery, permits preserving normal bladder functioning, without compromising the oncologic outcome, and avoiding the potential toxicities and sequelae related to radical surgery and external beam radiotherapy.

PX002
SECONDARY BREAST CANCER AFTER LOW-DOSE RADIOTHERAPY FOR LUNG METASTASES OF WILMS’ TUMOR - A CASE REPORT
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Purpose: Presentation of a case with secondary breast cancer after low-dose chest irradiation for lung metastases of Wilms’ tumor in childhood.

Method: We report a thirty-three years old female treated for Wilms’ tumor, stage I at the age of 3 with nephrectomy and chemotherapy with Actinomycin D and Vincristine (SIOP VI protocol), three years later lung metastases were diagnosed and treated with chemotherapy according to protocol CAYVADIC (Actinomycin D, Cytoxan, Vincristine, DTIC) and whole lung radiation with total dose of 13,2 Gy in 1.2 Gy daily fractions.

Results: The patient was regularly followed at the Pediatric clinic, after the age of 18 at the outpatient clinic for late effects at the Institute of Oncology, Ljubljana. In February 2010 breast MRI discovered a suspicious formation, 12X16 mm in diameter, in the left breast, not seen on mammography. US guided fine needle aspiration biopsy revealed breast cancer.

Conclusion: Regular clinical follow-up, self breast examination and diagnostic imaging are mandatory in the follow-up of patients treated even by low-dose chest irradiation for childhood cancer. It seems that breast MRI is the most reliable diagnostic procedure with high sensitivity and no radiation burden.

PX003
BRACHYTHERAPY AFTER CHEMOTHERAPY AND PARTIAL CYSTECTOMY: AN EFFECTIVE, CONSERVATIVE AND FUNCTION PRESERVING APPROACH FOR BLADDER RHABDOMYSARCOMA
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2Hospital Exequiel Gonzalez Cortes, Pediatric Surgery, Santiago, Chile
3Hospital Luis Calvo Mackenna, Pediatric Surgery, Santiago, Chile
4Clínica Alemana de Santiago, Pediatric Oncology, Santiago, Chile
5Hospital Exequiel Gonzalez Cortes, Pediatric Oncology, Santiago, Chile

Purpose: Report our experience in the conservative management of bladder rhabdomyosarcoma, emphasizing the oncologic and functional outcome.

Method: Between 2000 and 2008, 6 patients have been treated with partial cystectomy after chemotherapy (VAC protocol). Brachytherapy (BT) catheters insertion (2–4 catheters) encompassing the tumor bed was performed simultaneously to the primary surgery. Low dose rate BT was administered with afterloaded Ir-192. The dose delivered to the clinical target volume was 55 Gy. The first two cases of the series where treated with BT (20 Gy) and 40 Gy external beam irradiation (EBRT). Bladder function was evaluated clinically and with abdominal ultrasound (US) and urodynamic studies.

Results: All patients were males. Median age at diagnosis was 2.4 years (2–5 years). Surgery required ureteral reimplantation in 2 cases. All resections were R1. At a median follow up of 5.5 years (18 months–9 years), all patients are alive with no evidence of disease. Only one patient (treated with BT+EBRT) relapsed locally, and was successfully rescued with chemotherapy and radical cystectomy. All the remaining patients have clinically normal bladder function at the last follow-up. Renal function is preserved and no anatomical abnormalities or elevated post-voiding residue has been detected with US. In the four BT only patients, urodynamic studies were performed, and all were within normal range.

Conclusion: The use of brachytherapy after chemotherapy and conservative surgery, permits preserving normal bladder functioning, without compromising the oncologic outcome, and avoiding the potential toxicities and sequelae related to radical surgery and external beam radiotherapy.

A001
GENETIC POLYMORPHISMS OF TPMT IN THE INDIVIDUALISATION OF THE DOSE OF 6-MERCAPTOPURINE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA PATIENTS TREATED WITH LALSHOP PROTOCOL
Elisabet Lopez-Lopez1, Idola Martin-Guerrero2, Borja Santos3, Nagore García de Andoin1, Purificacion García-Miguel1, M Angeles Pinan5, Africa García-Orad2, Aurora Navajas1
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5University Hospital La Paz, Oncohaematology, Madrid, Spain
6University Hospital Crues, Haematology and Haemotherapy, Bilbao, Spain
7University Hospital Crues, Oncohaematology, Bilbao, Spain

A002
TRANSIENT HYPERGLYCEMIA IN CHILDREN WITH ACUTE LYMPHOBlastic LEUKEMIA DURING INDUCTION CHEMOTHERAPY: PREVALENCE AND RISK FACTORS
Moldovan Diana1, Baghiu Maria Despina2, Horvath Adrienne3, Chinescan Mihaela4, Balas Alina1
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THE ROLE OF THE MTHFR POLYMORPHISMS IN CRETAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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THE FREQUENCY OF MTHFR POLYMORPHISMS AND TOLERANCE TO METHOTREXATE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

Vijay Gandhi Linga, Meenal Chandgothia, Jayanthi Sriramabhathalas, Dorra Babu Patchva, Krishna Mohan Mallavarapu, Radhika Parimukyala, Pragnya Coca, Narendra Thota, Sadasivudu Gundeti, Senthil Rajappa, Raghunadharao Digumarti

THIOPURINE METHYL TRANSFERASE ACTIVITY LEVELS IN PAEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA POPULATION IN KERALA, SOUTH INDIA

Priyakumari Thankamony, Lakshmi S, Elizabeth K.E, Jasmine A.S, Radhakrishnna Pillai M

INCIDENCE OF TEL/AML1 AND BCR/ABL GENE REARRANGEMENTS IN PAEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA IN KERALA SOUTH INDIA

Priyakumari Thankamony, Lakshmi S, Elizabeth K.E, Jasmine A.S, Radhakrishnna Pillai M

TRAC ELEMENT LEVELS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA AT DIAGNOSIS AND THEIR CORRELATION WITH RESPONSE TO THERAPY AND RISK OF FEBRILE NEUTROPENIA


PREVALENCE OF GENETIC POLYMORPHISM IN MERCAPTOPURINE AND METHOTREXATE METABOLIZING ENZYMES IN CHILEAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

Farfan Mauricio, Carolina Salas, Torres Juan, Maria Santolaya, Milena Villarroel, Kopp Katherine, Gaston Rivera, Jorge Morales

PREVALENCE OF GENETIC POLYMORPHISM IN MERCAPTOPURINE AND METHOTREXATE METABOLIZING ENZYMES IN CHILEAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

PREVALENCE OF GENETIC POLYMORPHISM IN MERCAPTOPURINE AND METHOTREXATE METABOLIZING ENZYMES IN CHILEAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

CENTRAL NERVOUS SYSTEM PRESENTATIONS OF ACUTE LYMPHOBLASTIC LEUKAEMIA: PERSPECTIVE FROM A TERTIARY CARE PEDIATRIC HOSPITAL

Priyanka Sharma, Purvi Kadakia, Archana Swami, Nitin Shah, Mukesh Desai, Bharat Agarwal

UPDATING OF MANAGEMENT OF INFECTIOUS COMPLICATIONS OF CHEMOTHERAPY PRECAUTION AT CHILDREN WITH ACUTE LEUKAEMIA

Margarita Peshikova, Elena Basharova, Elena Zhukovskaya

PATTERN AND DETERMINANTS OF CENTRAL NERVOUS SYSTEM RELAPSE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA IN A RESOURCE LIMITED SETTING

Ketan Kulkarni, Ram Kumar Marwaha, Deepak Bansi, Amita Trehan

CHILDHOOD T LINEAGE ACUTE LYMPHOBLASTIC LEUKAEMIA: PROGNOSTIC SIGNIFICANCE AND MANAGEMENT EXPERIENCE AT A TERTIARY CARE CENTER IN NORTH INDIA

Laxman Singh Arvy, Padmanjali KS, Sudha Sawal, Renu Saxena, Manorama Bhargava, Ketan Kulkarni, Melissa Adde, Ian Magrath

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Laxman Singh Arvy, Padmanjali KS, Sudha Sawal, Renu Saxena, Manorama Bhargava, Ketan Kulkarni, Melissa Adde, Ian Magrath
A014 DISSEMINATED TUBERCULOSIS DISEASE IN TWO ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS IN CHEMOTHERAPY

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A015 PREDICTION OF MINIMAL RESIDUAL DISEASE STATUS AT THE END OF ALL-MB 2008 PROTOCOL REMISSION INDUCTION BY EARLY BLAST REDUCTION PARAMETERS

Alexander Popov1, Grigory Tsaur1, Tatiana Verzhbitskaya2, Olga Streneva2, Olga Khlebnikova1, Alexander Solodovnikov2, Egor Shorikov1, Leonid Saveliev3, Larisa Fechina1

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A016 DETECTION OF EPSTEIN-BARR VIRUS INFECTION USING NESTED POLYMERASE CHAIN REACTION IN ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

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A017 CENTRAL NERVOUS SYSTEM COMPLICATIONS DURING ACUTE LYMPHOBLASTIC LEUKEMIA CHEMOTHERAPY IN CHILDREN

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A018 AVASCULAR NECROSIS OF THE BONE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE INSTITUTION EXPERIENCE

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A019 IS CRANIAL RADIATION REALLY REQUIRED FOR ALL PEDIATRIC PATIENTS IN TODAY AGE?

A020 THE FREQUENCY OF THIOPURINE METHYL TRANSFERASE POLYMORPHISMS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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A021 ACUTE LEUKEMIAS IN CHILDREN: THE EXPERIENCE AT KANTI CHILDREN’S HOSPITAL,NEPAL

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A022 BIOMOLECULAR SUBSTRATE OF PAEDIATRIC ACUTE LEUKEMIAS AND ITS IMPACT ON OUTCOME

Balint Lorediana1, Andrada Licinia Oprisoin2, Oana Ciocarlic3, Smaranda Arghirescu2, Anca Isa4, Bogdana Zoica5, Valentin Ordodi5, Ileana Pocild6, Lalislanu Riti7, Margit Serban2

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A023 LEUKOMOGENESIS AS A NEW APPROACH TO INVESTIGATE THE CORRELATION BETWEEN UP REGULATED GENE 4 (URG4) AND SIGNAL TRANSDUCTION GENES IN LEUKEMIA

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A024 SURVIVAL ANALYSIS OF CHILDREN WITH T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Shweta Bansal1, Suresh Advani2, Anupama Borker3, Anjana Sainani3, Indoo Ambulkar3, Vaishali Khudkhudia4, Surendra Shingnapurkar5, Sonal Bhatt6

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ACUTE MYELOID LEUKEMIA IN INFANTS: EXPERIENCE OF A SINGLE INSTITUTION

Margarita Baka1, Marina Svrčnoglo2, Despina Bouhoutsi3, Maria Varvoutsi4, Apostolos Poutsiakis2, Dimitrios Doganis2, Helen Duna2, Helen Kozantziou1, Theodora Anastasiou1, Helen Kosmidis2

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B008

IS IT REALLY A RELAPSE OF BURKITT LEUKEMIA OR THE EFFECT OF GRANULOCYTE-COLONY STIMULATING FACTOR?: FALSE POSITIVITY OF MAGNETIC RESONANCE IMAGING

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B005

PROFILE OF PATIENTS DIAGNOSED WITH BIPHENOTYPIC ACUTE LEUKEMIAS AT THE PHILIPPINE GENERAL HOSPITAL. PEDIATRIC CHARITY WARDS IN 2006 TO 2008

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IMPACT OF FAB CLASSIFICATION AND CYTOGENETICS ON OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKEMIA

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B009

IS IT POSSIBLE TO TREAT PEDIATRIC ACUTE MYELOID LEUKEMIA IN A DEVELOPING COUNTRY?

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WHERE WE STAND IN TREATING ADVANCED STAGE HODGKIN’S LYMPHOMA?
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Name: Shima Nassif, Alaa EL-Haddad, Farida Gadallah
Affiliation: National Cancer Institute, Cairo University, Pediatric Hematology-Oncology, Cairo, Egypt
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Title: Case Report on Coomb's Negative Autoimmune Haemolytic Anemia in Hodgkin's Disease from Yangon Children Hospital, Myanmar

Abstract: Aye Khing and HtayHtay Tin from Yangon Children Hospital, Haematology-Oncology Unit, Yangon, Myanmar, report a case of Coomb's negative autoimmune haemolytic anemia in a child with Hodgkin's disease. This is the first report of such a case from Myanmar.

Keywords: Coomb's negative, Autoimmune haemolytic anemia, Hodgkin's disease, Myanmar.
COMPLEX RADIODOGANOSTICS OF MALIGNANT TUMORS OF SCAPULA IN CHILDREN

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IMMUNOHISTOCHEMICAL ANALYSIS OF HEPARANASE IN NON METASTATIC EWING SARCOMA

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COMPLEX RADIODOGANOSTICS OF MALIGNANT TUMORS OF HIPBONES IN CHILDREN

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THE TREATMENT OF CHILDREN WITH PRIMARY METASTATIC EWING SARCOMA FAMILY TUMORS

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THE TREATMENT OF CHILDREN WITH PRIMARY METASTATIC OSTEOSARCOMA

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EVALUATION OF THE PHARMACOKINETICS OF HIGH DOSES OF METHOTREXATE ADMINISTRATION (HD-MTX) IN PEDIATRIC PATIENTS

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EXPLORE BEHAVIOUR IN T-CELLS

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RISK STRATIFICATION BASED ON PROGNOSTIC FACTORS AT DIAGNOSIS RELATED TO SURVIVAL OF WILMS TUMOR

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RELAPSED WILMS TUMOR- A FIVE YEAR EXPERIENCE FROM A TERTIARY CARE PEDIATRIC HOSPITAL

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SUCCESSFUL TREATMENT OF MALIGNANT RENAL RHABDOID TUMOR IN A 17-MONTH OLD INFANT

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NEUROENDOCRINE MARKERS IN HUMAN NEUROBLASTOMAS

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MOLECULAR PROGNOSTICATION IN NEUROBLASTOMA AND ITS CORRELATION WITH HISTOPATHOLOGICAL ASPECTS

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H007

WAIT AND SEE STRATEGY IN LOCALIZED ADRENAL MASSES IN INFANTS

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A COMBINED CASE OF MULTIFOCAL NEUROBLASTOMA AND NEPHROBLASTOMATOSIS IN A 5-YEAR OLD GIRL

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RESULTS OF NEUROBLASTOMA TREATMENT IN ONE CENTER

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INCIDENCE, TREATMENT AND FOLLOW-UP OF HYPERCALCEMIA AND CIS-RETINOIC AFTER AUTOLOGOUS TRANSPLANT IN NEUROBLASTOMA, PINDA-CHILE

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H001

A MOLECULAR APPROACH TO THE PARTICIPATION OF FIFTEEN BIOMARKERS OF THE RBI GENE IN THE DEVELOPMENT OF RETINOBLASTOMA TUMOR IN MEXICAN PEDIATRIC PATIENTS

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H002

THE RESULTS OF THE CONSERVATIVE TREATMENT OF ADVANCED RETINOBLASTOMA

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H003

THE TREATMENT RESULTS OF RETINOBLASTOMA IN DOKUZ EYLUL UNIVERSITY HOSPITAL

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H001

CYTOGENETIC CHARACTERIZATION OF BONE MARROW METASTASIS FROM PRIMARY ALVEOULAR Rhabdomyosarcoma of the BREAST

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RHABDOMYOSARCOMA IN CHILDHOOD: CLINICAL PROFILE IN TWO HOSPITALS
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J003

PRIMARY METASTATIC SOFT TISSUE SARCOMA OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY
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RHABDOMYOSARCOM ARISING IN GIANT CONGENITAL MELANOCYTIC NEVUS
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ALVEOLAR SOFT PART SARCOMA : A RARE ENTITY WITH DISTINCTIVE MORPHOLOGICAL AND GENETIC CHARACTERISTICS
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J006

METASTATIC RHABDOMYOSARCOMA: EXPERIENCE IN A PEDIATRIC ONCOLOGY CENTER
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J007

MALIGNANT Rhabdoid Tumor of the Retropharynx in an Infant
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J008

RHABDOMYOSARCOMA OF THE TONGUE
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J009

PRIMARY RHABDOMYOSARCOMA OF THE OVARY WITH INTRA-ABDOMINAL RUPTURE
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K001

LAPAROSCOPIC LIVER RESECTION FOR TREATMENT OF HEPATOBLASTOMA IN CHILDREN
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K002

ANATOMIC LAPAROSCOPIC HEMIHEPATECTOMY IN CHILDREN (CLINICAL CASE)
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K003

PLANNING FOR MAJOR HEPATIC RESECTIONS AND LIVER TRANSPLANTATION FOR HEPATOMBLASTOMA
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LIVER TUMOURS: A SINGLE CENTER EXPERIENCE IN ARGENTINA
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PRIMARY OVARIAN TUMORS IN A TERTIARY CARE HOSPITAL
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UNDIFFERENTIATED EMBRYONAL SARCOMA OF THE LIVER: TWO CASES REPORT
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SELF-LIMITING STERNAL TUMORS OF CHILDHOOD (SELSTOC)
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SUCCESSFUL RESULTS WITH A MODIFIED EORTC PROTOCOL FOR TWO CHILDREN WITH MELANOMA AT HOSPITAL INFANTIL DE MEXICO
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OVERVIEW OF PATIENTS WITH CNS ATYPICAL TERATOMI RHABDOID TUMORS
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THYROID FUNCTION IN CHILDREN TREATED FOR MEDULLOBLASTOMA
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NEUROCYSTICERCOSIS AND POSTERIOR FOSSA NEOPLASM: CO-EXISTENCE OF DUAL INTRACRANIAL PATHOLOGY
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DISSEMINATED TUMORS OF THE CENTRAL NERVOUS SYSTEM WITHOUT A CLEAR PRIMARY LESION: A RARE PRESENTATION.
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RANDOMIZED MULTINATIONAL TRIAL ON PATIENTS WITH CHILDHOOD CRANIOPHARYNGIOMA (KRIANOPHARYNGEOM 2007) - UPDATE AFTER 27 MONTHS OF RECRUITMENT
Hermann L. Müller1, Ursel Gebhardt2, Sabine Schröder3, Fabian Pietsch3, Rolf-Dieter Kortmann4, Isabella Zwiener4, Andreas Faldum5, Monika Warmuth-Metz6, Torsten Pietsch7, Gabriele Calaminus8, Reinhardt Kolb2, Christoph Wiegand9, Niels Sörensen9
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Faruk Guclu Pinart1, Aydur Oguz1, Ceyda Karadeniz1, Arzu Okur1, Ayni Sarac2, Kemali Buyukaner2, Huseyin Bora3, Aylar Poyraz2

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TEMOZOLOMIDE IN RELAPSED OR RESISTANT PEDIATRIC BRAIN TUMORS: 13 CASES FROM A SINGLE CENTER
Hacı Demir1, Canan Akışın1, Hacı Ahmet Demir1, Ali Varan1, Bilgehan Yalçın1, Sihiyesa Oacak1, Tezir Kutlu1, Minever Büyükkumuşçu1
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DOUBLE AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION FOLLOWED BY CONVENTIONALLY FRACTIONATED LOCAL IRRADIATION IN CHILDREN WITH UNFAVOURABLE BRAIN TUMORS
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M009
TREATMENT RESULTS IN PATIENTS WITH ATRT. SINGLE INSTITUTION STUDY
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M010
THE ROLE OF YOUNG AGE AS A POSSIBLE PROGNOSTIC FACTOR IN CHILDHOOD HIGH GRADE ASTROCYTOMA
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M014
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M015
OPTIC NERVE LOCALIZATION OF INTRACRANIAL GERM CELL TUMORS
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INTRA-OPERATIVE MRI FOR PAEDIATRIC BRAIN TUMOURS - INITIAL EXPERIENCE WITH A DEDICATED HIGH-FIELD (3T) SYSTEM.

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ATYPICAL TERATOID/RHABDOID TUMOR OF THE BRAIN WITH METACHRONIC MALIGNANT RHABDOID TUMOR OF THE KIDNEY - CASE REPORT

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M018

HEALTHY HEROES: LIVING THE CURE. AN INNOVATIVE INTERVENTION FOR CHILDHOOD BRAIN TUMOR SURVIVORS

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M019

TREATMENT OF NON-MIDLINE GERMINOMAS WITH A COMBINATION OF CHEMOTHERAPY AND REDUCED DOSE AND VOLUME IRRADIATION: A REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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M020

2 BROTHERS WITH ASTROCYTOMA – CASE REPORT

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N001

A BRAZILIAN SINGLE CENTER EXPERIENCE ON AUTOLOGOUS STEM-CELL TRANSPLANTATION IN CHILDREN AND ADOLESCENTS

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N002

SUPPORTIVE CARE PRACTICES: A SURVEY OF PEDIATRIC BLOOD AND MARROW TRANSPLANT CONSORTIUM INSTITUTIONS

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N003

CO-TRANSPLANTATION OF HAPLO-IDENTICAL MESENCHYMAL STEM CELLS AND PERIPHERAL BLOOD STEM CELLS. PLATFORM FOR IMMUNE THERAPY IN HIGH RISK PEDIATRIC HEMATOLOGICAL MALIGNANCES

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N004

GONADAL FUNCTION AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: THE SINGLE CENTER EXPERIENCE

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THE OPTIMAL TIME FOR HEMATOPOIETIC STEM CELL MOBILIZATION IN CHILDREN WITH SOLID TUMORS - SINGLE CENTER EXPERIENCE

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N006

PHARMACOLOGIC DRUG INTERACTIONS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): DESCRIPTIVE STUDY IN A CHILEAN COHORT (2006–2009)

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INFECTIONS IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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COMPARISON OF OUTCOME FOLLOWING MATCHED SIBLING TRANSPLANT FOR APLASTIC ANEMIA: THE CAIRO-BOSTON EXPERIENCE

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NIMOTUZUMAB EXPANDED ACCESS PROGRAM FOR CHILDREN AND ADOLESCENTS WITH BRAIN TUMORS. TOXICITY AND LATE EFFECTS INTERIM RESULTS OF PROLONGED USE.

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BEVACIZUMAB IN PEDIATRIC ONCOLOGY: SAFETY CONCERNS

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TOXICITY OF BEVACIZUMAB IN CHILDREN AND ADOLESCENTS WITH PROPOOR-PROGNOSIS NON-CN5 SOLID TUMORS

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SOLID TUMORS INCIDENCE IN CHILDREN IN THE KYRGYZ REPUBLIC

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ONCLOGIC PATIENTS IN THE SECTION OF PEDIATRICS OF THE HOSPITAL OBRERO #3 OF SANTA CRUZ-BOLIVIA FROM 2001 TO 2008

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SEARCHING UNAPPARENT RELATIONSHIPS BETWEEN ENVIRONMENTAL EXPOSURES AND CHILDHOOD LEUKEMIA: AN EXPLORATORY ANALYSIS IN THE BRAZILIAN POPULATION

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A SPECIAL NUTRICIONAL EVALUATION IN ONCOLOGY PEDIATRICS POPULATION IN QUITO, ECUADOR.

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RIBAVIRIN MONOTHERAPY IN CHILDREN WITH HCV HEPATITIS DURING CHEMOTHERAPY: PRELIMINARY RESULTS

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INCIDENCE OF TUMORS IN AGES FROM NEWBORN TO 12 MONTHS ADMITTED IN PEDIATRIC HEMATOONCOLOGY UNIT DRA. TERESA VANEGAS. UNIVERSITY HOSPITAL DR. ANGEL LARRALDE- PERIOD 1995–2009-VALENCIA-VENEZUELA

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INCIDENCE OF CHILDHOOD LEUKEMIA IN YOGYAKARTA, INDONESIA, 1998–2009

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HEARING LOSS IN PEDIATRIC ONCOLOGY PATIENTS RECEIVING CISPLATIN REGIMENS

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**Q002**

BARRETT'S ESOPHAGUS IN LONG-TERM SURVIVORS OF CHILDHOOD SOLID TUMORS.

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**Q003**

SECOND MALIGNANT NEOPLASMS AFTER CHILDHOOD CANCER IN A PEDIATRIC ONCOLOGY CENTER

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**Q004**

THE DETECTION OF MYOCARDIAL DYSFUNCTION IN LATE CARDIOTOXICITY BY STRAIN ECHOCARDIOGRAPHY IN CHILDHOOD MALIGNANT DISEASE FOR LATE CARDIAC TOXICITY

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**Q005**

NT-PRO-BNP AND TROPONIN T AS MARKERS FOR SUBCLINICAL EARLY-ONSET ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN CHILDREN. A PROSPECTIVE STUDY

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**Q006**

UTILIZATION OF PRESCRIPTION DRUGS AMONG SURVIVORS OF CHILDHOOD AND YOUNG ADULT CANCER IN BRITISH COLUMBIA CANADA

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**Q007**

SECOND MALIGNANT NEOPLASMS IN CHILDHOOD CANCER SURVIVORS

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**Q008**

SECONDARY NEOPLASMS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AS A COMPLICATION AFTER CHEMOTHERAPY AND RADIOTHERAPY.

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**Q009**

LONG TERM SURVIVORS OF LEUKEMIA TREATED WITH PROPHYLACTIC CRANIAL IRRADIATION: LIMITED SUSTAINED ATTENTION CORRELATES WITH DEVIAN'T RESTING STATE BRAIN NETWORKS

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**Q010**

OCURRENCE OF SECOND MALIGNANCIES IN CHILDREN TREATED IN A SINGLE INSTITUTION

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Q011

NEUROTOXICITY IN CHILDREN UNDERGOING VARIOUS SCHEDULE OF RADIOTHERAPY FOR ACUTE LEUKEMIA USING MR IMAGING AND 1 H MR SPECTROSCOPY

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Q012

ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN CHILDREN:RESEARCH VALUE OF QT/QTC INTERVALS DISPERSION AND CARDIAC BIOMARKERS FOR EARLY DETECTION

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Q013

HEALTH RELATED QUALITY OF LIFE FOR YOUNG ADULT SURVIVORS OF EXTRA-CRANIAL CHILDHOOD MALIGNANCIES: A NATIONWIDE SURVEY

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Q014

CARDIAC FUNCTION IN YOUNG ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBlastic LEUKAEMIA: A TISSUE DOPPLER IMAGING STUDY

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Q015

QUALITY OF LIFE IN SURVIVORS OF CHILDHOOD CANCER: A LIFE SPAN DEVELOPMENT PERSPECTIVE

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Q016

HEALTH STATUS OF CHILDREN WITH HEMOBLASTOSIS IN COMPLETE REMISSION

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Q017

CHILDBIRTH OF FEMALE CHILDHOOD CANCER SURVIVORS IN SLOVENIA

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Q018

EVALUATION OF A NEW METHOD OF CLASSIFYING PEDIATRIC OTOTOXICITY INCORPORATING THE CONCEPT OF “EAR AGE” 1D

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Q019

EVALUATION OF CARDIAC FUNCTIONS BY TISSUE DOPPLER ECHOCARDIOGRAPHY IN LONG-TERM SURVIVORS OF HODGKIN'S LYMPHOMA

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Q020

MORBIDITY PROFILE IN CHILDHOOD CANCER SURVIVORS IN A TERTIARY CARE HOSPITAL

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R001

REVIEW OF THE JAPANESE SCHOOL RE-ENTRY SUPPORT SYSTEM FOR CHILDREN WITH CANCER

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PALLIATIVE AND PAIN MEDICINE PROJECT IN CHILDREN HOSPITAL ZAGREB (CROATIA)
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HOW ANIMALS HELP HEAL THOSE WHO ARE SICK BY PROVIDING COMPANY, SUPPORT AND LOVE
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R004
PEDIATRIC PALLIATIVE CARE: A BEST PRACTICE MODEL FOR INDIA
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R005
PALLIATIVE CARE FOR CHILDREN WITH CANCER IN RUSSIA: WHERE WE ARE TODAY
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R007
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R008
PREVENTION AND ASSESSMENT OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN CHILDREN AND ADOLESCENTS WITH CANCER
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R009
PROCEDURAL SEDATION AND ANALGESIA USING MIDAZOLAM AND KETAMINE IN PEDIATRIC HEMATOLOGY ONCOLOGY PATIENTS
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R010
IMMUNIZATION PRACTICE AMONG PEDIATRIC ONCOLOGISTS IN RUSSIAN FEDERATION
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R011
CASPOFUNGIN TREATMENT IN CHILDREN: EXPERIENCE OF A SINGLE HEMATOLOGY-ONCOLOGY CENTER
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R012
COMPARISON OF CONTINUOUS INFUSION GRANISTRON+DEXAMETHASONE WITH FOUR-DRUG ANTIEMETIC COMBINATION FOR ANTIEMETIC EFFICACY IN CHILDREN RECEIVING CHEMOTHERAPY
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R013
POTENTIAL BENEFITS OF PROPHYLACTIC INTRAVENOUS IMMUNOGLOBULIN IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN
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R014
INVASIVE PULMONARY FUNGAL INFECTION IN CHILDREN WITH CANCER UNDERGOING CHEMOTHERAPY
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R022

HOSPITALS ARE KNOCKING AT PATIENT’S DOORS. THE FUTURE OF HEALTH CARE CAN BE RESPECTFUL OF PATIENT’S QUALITY OF LIFE

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S003

COGNITIVE FUNCTIONING AND ADAPTIVE BEHAVIOR ASSOCIATED WITH PEDIATRIC BONE MARROW TRANSPLANT

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S004

LONG-TERM TREATMENT OF BRAIN TUMORS: SUFFERING EXPERIENCED BY PATIENTS AND THEIR FAMILIES

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S005

SOCIAL AND PROFESSIONAL REHABILITATION OF TEENAGERS AND ADULTS TREATED FOR CANCER DURING THEIR CHILDHOOD

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S006

CHILDREN’S ONCOLOGY CAMPING ASSOCIATION INTERNATIONAL (COCA-I): TREATING CLINIC AND CAMP LIAISON SURVEY FOR QUALITY IMPROVEMENT OF ONCOLOGY CAMPS

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S007

TREATMENT NON-ADHERENCE IN TEENAGE AND YOUNG ADULT CANCER PATIENTS. WHAT DO WE KNOW?

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S008

PSYCHOLOGICAL SUPPORT GROUPS FOR SIBLINGS OF CHILDREN WITH CANCER: A PILOT EXPERIENCE

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S009

ETHICAL CONSIDERATIONS FOR SIBLING DONORS OF BONE MARROW: A CASE ILLUSTRATION

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S010

YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER: SUBJECTIVE PERCEPTION OF QUALITY OF LIFE

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S011

RADIOTherapy: RELATIONSHIP BETWEEN MOTHER AND CHILD WITH CANCER AND TREATMENT ADHERENCE

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T001

INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH CANCERS – SINGLE INSTITUTION EXPERIENCE

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T002

ETHICAL ISSUES IN THE CARE OF ONCOLOGY PAEDIATRIC PATIENTS: DEVELOPMENT AND EVALUATION OF PRACTICAL WORKSHOPS FOR MEDICAL AND NURSING STAFF

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T003

ASSESSING THE IMPACT OF PAEDIATRIC ONCOLOGY PUBLICATIONS USING THREE CITATION DATABASES - WEB OF SCIENCE, SCOPUS AND GOOGLE SCHOLAR

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T004

QUALIFYING PAEDIATRIC ONCOLOGY RESEARCH IN INDIA

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T005

PROGESTERONE AND ESTROGEN RECEPTORS IN NEUROFIBROMAS OF PATIENTS WITH NEUROFIBROMATOSIS TYPE 1

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T006 SUCCESSFUL COLLABORATION BETWEEN PAEDIATRIC HEMATO-ONCOLOGY CENTER IN MONZA, ITALY AND PAEDIATRIC HEMATO-ONCOLOGY CENTERS IN SERBIA

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T007 IS PROCALCITONIN A RELIABLE STAND ALONE MARKER OF BACTERIAL INFECTION IN CHILDREN WITH FEBRILE NEUTROPENIA?

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T008 PLASMA AND SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR IN CHILDHOOD SOLID TUMORS

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T009 MULTIDISCIPLINARY APPROACH TO EWING’S SARCOMA FAMILY TUMORS: A SINGLE-INSTITUTION EXPERIENCE

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T010 QUALITY OF LIFE OF SURVIVORS OF PEDIATRIC CANCER: A CROSS-SECTIONAL STUDY USING THE FERTIGKEITENSKALA MÜNSTER/HEIDELBERG INDEX AND PEDQL QUESTIONNAIRE

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T011 VALUE OF PET SCANNING IN SARCOMA OF CHILDHOOD

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T012 RECREATIONAL ACTIVITY AS THERAPEUTIC PROGRAMME IN CHILDREN WITH CANCER: FIRST SUCCESSFUL EXPERIENCE IN ITALY

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T013 INFORMATIVE SIGNIFICANCE OF COMPUTED TOMOGRAPHY IN CHILDREN WITH MALIGNANCIES AND SUSPECTED INFECTION.

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T014 INCIDENCE OF RESPIRATORY VIRUSES IN CHILDREN WITH MALIGNANCES AND SUSPECTED INFECTION.

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T015

BIOCHEMICAL MARKERS WITH PROGNOSTIC VALUE IN PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA

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T016

AUDIT OF DENTAL REFERRAL PATHWAY IN A CHILDHOOD CANCER LEUKAEMIA GROUP CENTRE (CCLG)

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T017

NEUTROPENIC SEPSIS ON A CHILDREN’S ONCOLOGY UNIT: TRENDS IN PATHOGENS AND RESISTANCE OVER A SIX-YEAR PERIOD

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T018

IMPACT OF MODERN CHEMOTHERAPY PROTOCOLS (COSS/EURAMOS) ON SURVIVAL IN CHILDREN’S AND ADOLESCENTS’ OSTEOSARCOMA

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T019

A NATIONAL APPROACH TO INTERNATIONAL COLLABORATION: DEVELOPING THE C17 COUNCIL TO PROMOTE AND FACILITATE INTERNATIONAL CLINICAL TRIALS IN CANADA

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