0.3−3.6). Thirty-two patients (63%) underwent allogeneic and 19 (37%) autologous transplantation. Six patients were treated with a total dose of 14.4 Gy/12 fractions, 42 with a total dose of 12 Gy/6 fr, 3 with a total dose of 9.9 Gy/3 fr. Hypothalamic, pituitary, gonadal and thyroid function were routinely assessed before and after HSCT.
Results: The most common observed endocrine dysfunction was hypogonadism, recorded in 24/47 evaluable patients (51%). Five-year and ten-year cumulative risk were 36.5% and 60.1%. In univariate analysis, age at transplantation was the most important risk factor for hypogonadism (cut-off value 8.5 yrs old, median age of the whole patients cohort, $p < 0.01$), with younger patients presenting a lower incidence. T-Student test confirmed this findings ($p = 0.01$). Twelve patients showed severe growth impairment requiring GH replacement therapy (12/50 evaluable patients, 24%). Cumulative incidence of severe growth impairment was 18% at 5 years and 29.9% at 10 years. Non-parametric analysis showed that younger patients had a significant higher incidence of delayed growth velocity ($p \leqslant 0.05$). Hypothyroidism affected 10/47 evaluable patients (21.2%). Cumulative incidence of hypothyroidism was 17% at 5 years and 22% at 10 years.
Conclusions: Long-term survivors treated with TBI-based HSCT in childhood are at significant risk for developing endocrine late toxicity (with age, chemotherapy, status at HSCT and GvHD possibly playing a role), and should be strictly monitored during their follow-up in a multidisciplinary setting.

4116 POSTER

Fusion genes PAX3/7-FKHR as molecular markers of bone marrow micrometastasis in paediatric alveolar rhabdomyosarcoma

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Background: Alveolar rhabdomyosarcoma (aRMS) in children is an aggressive soft tissue tumour. Patients with metastatic aRMS have a very poor prognosis and recurrences are common in advanced localized disease. As known the majority of aRMS have the reciprocal chromosomal translocations t(2;13)(q35;q14) or t(1;13)(p36;q14). The molecular counterpart of these translocations is the generation of the fusion genes PAX3-FKHR and PAX7-FKHR, respectively. Molecular detection of disseminated tumour cells in bone marrow (DTCBM) could contribute to a better staging and treatment stratification in paediatric patients with aRMS.
Material and Methods: Seventeen children with advanced stages aRMS are enrolled in our study. Patients were treated according to the protocols CWS-96 and EpSSG RMS-2005. Sixty-three samples of bone marrow aspirations has been analyzed. Bone marrow samples were collected at diagnosis, after initial chemotherapy before surgery, after completion of therapy and at relapse if present. The presence of DTCBM was analyzed by real-time RT-PCR assay, based on the expression of fusion genes PAX3-FKHR and PAX7-FKHR.
Results: Chimeric transcripts PAX3/7-FKHR has been revealed in bone marrow of 8 patients, in 3 of which DTCBM have not been identified in morphology examination of bone marrow. In 3 patients after protocol therapy DTCBM have not been revealed that evidence on the efficiency of the treatment. These patients are still alive more than 2 years after initial diagnosis. Another 5 patients eventually developed tumour progression and died of the disease 12−14 months after initial diagnosis. It is necessary to emphasize that according to the results of RT-PCR study DTCBM have been revealed in 4 patients with III stage of disease confirmed by complex study. Therefore, these patients can be referred to a high risk group. In the present study of a cohort of children with advanced-stage aRMS, patients with bone marrow involvement had poorer survival than patients without DTCBM.
Conclusion: The detection of micrometastatic disease by real-time RT-PCR, based on the expression of fusion genes PAX3/7-FKHR, yields highly reproducible results. Molecular detection of DTCBM helps specify prognosis, risk group, schedules of therapy and provides its monitoring, allows reliably determine extent of achieved remission.

4117 POSTER

The extracellular domain of HER-2 as a potential marker for treatment monitoring in osteosarcoma

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Background: The aim of this prospective, diagnostic study was to estimate the predictive value of circulating levels of the extracellular domain of HER-2 (ECD/HER-2) in patients with osteosarcoma.
Methods: Thirty three newly-diagnosed primary osteosarcoma patients treated at the Department of Paediatric Oncological Surgery of the Institute of Mother and Child in Warsaw were included. Median aged 14 years range: 6−18 years. Staging at diagnosis: disease localised (18) and dissemination (15). Patients were treated with standard chemotherapy with ADM and cDDP and/or HD-MTX, and surgery of primary tumour +/− metastasectomy. Follow-up: median 25 months; range 16−38 months. ECD/HER-2 was measured (1) at time of diagnosis, (2) at the end of preoperative chemotherapy, (3) within 30 days after surgery and (4) at the end of treatment. Concentration of ECD/HER-2 was determined by HER-2/neu immunoassay. ECD/HER-2 status was analysed according to clinical and radiological data and percent of viable tumour cells remaining after preoperative chemotherapy.
Results: We analysed the levels of ECD/HER-2 in 33 samples at the time of diagnosis, in 30 samples at the end of preoperative chemotherapy, in 31 samples obtained within 30 days after surgery and in 30 samples at the end of treatment. The cut-off point for ECD/HER-2 levels was assessed as 5.5 ng/mL. The elevation of ECD/HER-2 over time was corresponding with disease progression ($P = 0.003$). The elevated ECD/HER-2 levels had 73% of patients with disease progression and 23% of patients without disease progression. Test sensitivity and specificity were 62% and 85%. The overall survival was lower with ECD/HER-2 levels >5.5 ng/mL compared to ECD/HER-2 levels $\leqslant$5.5 ng/mL: 54% vs 85% ($P = 0.077$). No relationship was found between ECD/HER-2 levels and patients age, disease dissemination at the time of diagnosis, tumour size, or histological response to preoperative treatment.
Conclusions: This pilot study has shown that elevated ECD/HER-2 concentrations over time may correspond with disease progression. Therefore ECD/HER-2 might be considered as a potential marker for monitoring patients with osteosarcoma.

4118 POSTER

Clofarabine: safety and efficacy profile for treatment of pediatric patients with refractory or relapsed acute leukemias

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Background: Despite the considerable progress in the treatment of acute lymphoblastic (ALL) or myeloblastic (AML) leukemia in pediatric patients (pts), the prognosis in case of primary refractory or relapsed disease remains poor. In view of new therapeutic agents, we evaluated the toxicity profile of clofarabine, a novel deoxyadenosine analog. The hybrid of cladribine and fludarabine has been developed to improve the efficacy and minimize the toxicity of its congeners, considering the heavy pretreatment of the population enrolled.
Patients and Methods: 10 pts; 5M and 5F, aged 3−15 years (median 9) with ALL (5) and AML (5), with refractory (4 AML, 1 ALL) or relapsed disease (1 AML, 4 ALL) received 1−3 cycles of clofarabine i.v. over 2 hours on 4 different dose levels between 30 and 52 mg/m^2/day for 5 days (d), as a single agent (2 cycles), or associated with cytosine arabinoside, cyclophosophamide, etoposide and liposomal doxorubicin.
Results: A total of 18 cycles were administered. Three pts received 1 cycle, 6 pts 2 cycles and 1 pt 3 cycles. For every cycle the major toxicity was haematological with 100% of grade 2−3 of anemia, grade 4 of neutropenia and grade 2−4 thrombocytopenia with a median platelet transfusion necessity of 5/cycle. 3 pts remained transfusion-dependent for platelets. Seven out of 10 pts had grade 1−2 headache. Nausea/vomiting of grade 1−3 could be observed in 58% of the performed cycles, despite antiemetic prophylaxis with Ondansetrone ± Dexamethazone and Clorfenamina. Nine out of 10 pts presented grade 1−4 hypertransaminasis. No other major SAE has been registered.
After the first cycle the response rate was 60% of complete remission (CR), 10% of partial remission and 30% of non response (NR). After the second cycle the CR rate was 86% (NR 14%). The only pt who effected a third cycle had NR. All CR have been achieved with Clofarabine associated to

other chemiotherapy. Although 7/10 pts died after treatment, none of the deaths were related to drug toxicity.
Conclusions: Clofarabine is a well tolerated novel agent in the treatment of pts with multiple relapsed or refractory leukemia, and its activity is not restricted to a specific leukemia subtype. It did not induce the neurotoxicity know from its analogs, and it has been demonstrated to be safe both in single-agent use and in combination with other drugs. Antiemetic therapy is needed to be adjusted in order to avoid the frequent nausea/vomiting side effects.

4119 POSTER

Hypersensitivity reactions and other complications due to L-asparaginase in the treatment of acute lymphoblastic leukemia according to ALL IC 2002 protocol

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Allergic reaction to all forms of L-asparaginase (ASP) is reported in 5−35% pts of various settings. We have analyzed 277 pts with acute lymphoblastic leukemia (ALL) treated according to ALL IC BFM 2002 protocol in the Czech Republic between 2002 and 2007 with the aim to evaluate the frequency, severity and other details of ASP side effects especially hypersensitivity reactions.
All pts received 8×5000 IU/m^2 of ASP in the treatment induction. Those enrolled to standard (SR) or intermediate (IR) risk group were given additional 4×10000 IU/m^2 in late intensification. High risk (HR) pts obtained 2×25000 IU/m^2 in each of 6 cycles of reinduction chemotherapy. E. coli ASP was switched to PEG ASP in case of hypersensitivity reaction, Erwinia ASP or no other ASP form was given to pts who experienced allergic reaction to PEG ASP. All ASP forms were excluded in pts who manifested reaction to Erwinia ASP.
Allergic reaction occurred in 57 pts (20.5%) treated by E. coli ASP, representing 19.8%, 16.8% and 58.9% in SR, IR and HR group respectively. Abdominal pain, nausea, emesis, dyspnoe and skin rush were the most frequent symptoms. Out of 57 hypersensitivity reactions, 35 (61.4%) appeared during the ninth dose of E. coli ASP following 8 weeks interval from preceding exposition. Hypersensitivity to PEG ASP, Erwinia ASP developed 15 pts (26.3%), 2 pts (30%) respectively. Besides hypersensitivity reactions, we documented various other side effects, out of which pancreas dysfunction/acute pancreatitis appeared in 4 (1.4%) pts. Eleven of 277 pts (3.9%) were not given all protocol listed doses of ASP due to related complications.
Hypersensitivity to all forms of ASP occurred in 20−30% pts, the most frequently in HR group which raise the question of treatment efficacy particularly in this group. Pharmacology studies focused on detection of antibodies and silent inactivation of ASP as well as front line use of PEG ASP may help to decrease frequency of allergic reaction and improve its efficacy.
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4120 POSTER

Childhood cancer pattern: a hospital based cancer registry from a developing country

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Background: More than 80% of world children live in developing countries where adequate medical care is limited. A very few studies have been done in the epidemiology of childhood cancer in the developing countries. Whatever studies have been done in Asia, the incidence of child hood cancer is 3−5% of all cancers. The aim of our study is to see the incidence of childhood cancer and their disease pattern from the hospital based cancer registry.
Material & Methods: During period from January 2002 to December 2008 we analyzed our hospital based Cancer Registry data in Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata a tertiary cancer center in Eastern India. There were total 20568 patients who attended in our institution as Outpatients and Inpatients. Among them 1859 were the childhood age groups (<18 yrs).
Results: In our hospital based cancer registry the patients of childhood age (<18 yrs) group were 9%. The distribution of patient according to the age group (1−5 yrs), (6−10 yrs) and (11−18 yrs) were 365 (19.6%), 901 (48.46%) and 593 (31.89%) respectively. Most frequently childhood cancer were Acute Lymphatic Leukemia 471 (25.33%), Lymphomas 466 (25.06%) (Hodgkin's disease 25%, Non Hodgkin's disease 75%), Round Cell Tumours 279 (15%) (Ewing's Sarcoma 33.33%, Primitive Neuro Endocrine Tumour 26.66%, Rhabdomyosarcoma 22.22%, Neuroblastoma 12.44%), Brain Tumour 183 (9.86%) (Meduloblastoma 91.21%, Astrocytoma 8.78%), Wilm's Tumour 967 (5.2%), Acute Myeloid Leukemia 82 (4.4%), Germ Cell Tumour 77 (4.13%), Osteosarcoma 68 (3.66%), Chronic Myeloid Leukemia 52 (2.8 %), Retinoblastoma 36 (1.93%), Soft tissue sarcomas and other malignancies 48 (2.58%).
Conclusion: The incidence of paediatric cancer in our study was higher as compared to other studies. Children in Indian subcontinent showed a different pattern of cancers with excess of Lymphomas (especially Hodgkin's Lymphoma) and Round cell tumours as compared to those reported in Western Literature.

4121 POSTER

DNA ploidy and proliferative activity in common round cell tumors in children and their value as prognostic indicators

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Background and Aim: Traditional clinico-pathologic criteria are often inadequate to accurately identify, children with small round cell tumors who will have poor response to therapy. Abnormal cellular DNA content (aneuploidy), has been linked to the rate of cell proliferation, and ultimately to prognosis. Flowcytometry (FCM), is a relatively rapid and precise technique, allowing quantitative detection of DNA content and measurement of S phase fraction (SPF), which can be used to classify cases into prognostically different subgroups. This may help in choosing the suitable chemotherapeutic regimens.
The aim of this study, was to evaluate the ploidy status and cells in SPF of common round cell tumors of Egyptian children, using FCM, correlating these parameters with the clinical and biological features and showing their effect on treatment and survival.
Material and Methods: The study included 50 children with round cell tumors, presenting to the National Cancer Institute (NCI), Cairo University. Only patients with complete follow up, full data were included in the study. Patients in each tumor type received the same treatment, and response to treatment was assessed according to the World Health Organization (WHO) criteria. Survival was calculated from the first day of diagnosis until the last date of follow up or death. Nuclear suspension was prepared for each sample, stained with propidium iodide. Measurements were performed using a FACScan flow cytometer and 10.000 cells were acquired for each sample. Results presented as frequency distribution histograms.
Results: In 20 neuroblastoma cases, DNA ploidy and index correlated significantly with progression free survival (PFS) and overall survival (OS). Diploid tumors fare worse than aneuploid ones. Response to treatment significantly correlated to ploidy ($p = 0.019$) and status of patient ($p = 0.006$). SPF correlated significantly to ploidy ($p = 0.03$) and to DNA index. In 15 rhabdomyosarcoma cases, only ploidy significantly correlated with PFS and to OS. DNA index significantly correlated with OS. In 15 Non Hodgkin's lymphoma (NHL) cases, only SPF correlated significantly to PFS.
Conclusion: DNA analysis by FCM is a valuable prognostic factor of great benefit in treatment of neuroblastoma, and can be used to confirm biological entity of tumors. Ploidy is prognostic in rhabdomyosarcoma, identifying high risk patients for treatment failure even with favourable standard criteria. In NHL, SPF may be a useful prognostic marker, only to response to treatment but not to survival.

4122 POSTER

The effect of self care on quality of life of children with acutelymphocytic leukemia

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Introduction: Acute Lymphocytic Leukemia (ALL) is the most common childhood cancer that with current treatment 80% of children survive more than 5 years. But treatment is long term, painful and invasive, So prevention of adverse effects and their effects on Quality Of Life (QOL) is an important problem that confirm need of self care. The purpose of this study was to determine the effect of self care on QOL of children with ALL in Medical centers of Isfahan in 2008.