lates erythropoiesis by the same mechanism as recombinant human EPO (rHuEPO), but has a longer serum t1/2. NESP was shown to be safe and clinically effective in cancer pts when administered every 1, 2, and 3 weeks in phase 1/2 studies. This phase 3 study compared the efficacy of NESP with placebo in lung cancer pts receiving platinum-containing chemotherapy (ctx).

Methods: 320 anemic pts ([Hb] ≤ 11 g/dL) receiving platinum containing ctx (ECOG 0–2, not iron deficient, no rHuEPO therapy within 8 wks or <2 RBC transfusions (tfn) within 4 wks) were randomized to NESP 2.25 μg/kg or placebo (1:1). Study drug was administered SC once weekly (QW) for a maximum of 12 wks (tx phase).

Results: NESP significantly ($p < 0.001$) reduced the Kaplan-Meier proportion (95% CI) of pts transfused during wks 5–12: NESP 21% (15, 28), placebo 51% (43, 60) and during the tx phase (wks 1–12): NESP 26% (20, 33). placebo 60% (52, 68). NESP pts received fewer standard units (mean [SD]) of RBC than placebo pts during wks 5–12: NESP 1.92 (3.27), placebo 0.67 (1.7) and during the tx phase: NESP 2.64 (4.32), placebo 1.14 (2.38). NESP pts were hospitalized fewer mean (SD) days compared with placebo pts (NESP 10.3 [13.5] days, placebo 13.0 [17.7] days). More NESP subjects had a ≥10% increase in the FACT-F scale score than placebo pts ($p = 0.023$) suggesting that NESP decreases fatigue. The safety profile of NESP was similar to placebo and as expected for this population.

Conclusions: NESP 2.25 μg/kg administered QW significantly reduced the proportion of subjects with RBC tfns and was well tolerated. The clinical benefit of NESP was sooner than previously reported for rHuEPO (Abels, 1991) where RBC tfn only reached statistical significance only if the first month of treatment was excluded.

982 POSTER DISCUSSION

Oncologic acute toxicity unit: development of a new tool in the oncologic clinical practice

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Introduction: We have developed an oncologic acute toxicity unit (OATU) in order to attend promptly the specific acute symptoms related to chemotherapy.

Objectives: To analyse the characteristics of patients that contact with the OATU and their outcome.

Patients and methods: Our data set included all the patients receiving chemotherapy in our hospital and the symptoms related to this treatment.

In the first chemotherapy cycle each patient receive an information booklet with the contact phone of the OATU. When patients called, a specialised nurse attended them and she consulted to the medical oncologist if it was necessary. The unit provides access to complementary exams, ambulatory treatment and hospitalisation if it is indicated.

Results: 829 patients established 1465 contacts to the OATU from February 1999 to February 2001. Most common tumours were breast 216 (26%), colorectal 172 (21%) and lung 165 (20%). Most contacts were done by phone (86.5%) and 38.6% were considered inappropriate. From 899 appropriate contacts, the most frequent chemotherapy schedule were 5-FU-Folinic Acid (12.6%) and CMF (11.6%) and the most frequent complaints were fever (35.3%), diarrhoeas (20%), mucositis (15.8%) and emesis (14.5%). 488/899 (54.3%) required attendance to the OATU and 191/488 required hospitalisation (21.2% of the initial appropriated contacts). Grade III/IV neutropenic fever was the most frequent cause of hospital admission (58.1%).

Conclusions: The development of an OATU provides a quick and easy access for patients who suffer acute toxicity related to chemotherapy treatment. In our experience it guaranties a prompt and specialised treatment and avoids unnecessary consults in the Emergency Room. Hospital admission, which was required in 21.2% of appropriate contacts, is therefore optimised.

Paediatric oncology

983 POSTER DISCUSSION

Impact of radiotherapy on survival in supratentorial PNET of childhood: results of the German prospective HIT-trials

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Purpose: To evaluate dose, volume, and sequence of radiotherapy (RX) with respect to progression free survival and pattern of relapse.

Methods: Since 1988 in Germany and Austria children with newly diagnosed malignant brain tumors were enrolled in the multicenter brain tumor trials. In the pilot trial HIT'88/'89 all pts. received immediate postoperative chemotherapy (CX) consisting of 2 cycles of Ifo/VP-16, hdMTX, DDP/Ara-C followed by RX (prescription: 35.2 Gy craniospinal + 20 Gy tumor boost). In the HIT'91 trial pts. were randomized after surgery either to undergo preirradiation CX, or immediate RX followed by maintenance CX (8 x CCNU/VCR/Cis).

Results: 63 children (age 2.9-17.7 months) were eligible. 23 children received maintenance CX, 40 received preirradiation CX. 48 children underwent irradiation according to the guidelines. 7 children were irradiated only locally, in 2 children no RX at all was administered. In 6 children dose was less than 54 Gy to the tumor site, or less than 35 Gy to the neuraxis. Follow-up was 31 months. Overall survival at 3 yrs. was 48.4%. Progression occurred in 38 children with local recurrences in 27 pts. Median time to progression was 10 months. 9 progressions occurred during preirradiation treatment. Dose and volume of RX had significant impact on survival; PFS after 3 years was 49.3% with correct dose and volume of RX as compared to 6.7% for 15 pts. with violations of RX guidelines ($p=0.0001$).

Conclusion: Craniospinal RX is needed to achieve reasonable treatment results in supratentorial PNET in childhood. At least doses of 54 Gy to the tumor, and 35 Gy to the neuraxis are required. The delay of RX seems to increase risk of early progression. Relapses mainly occur at the primary tumor region, but also within the CNS.

984 POSTER DISCUSSION

Dose intensive therapy and myeloablative chemotherapy with haematopoietic stem cell rescue in childhood poor prognosis Ewing's sarcoma

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Purpose: To improve the prognosis of paediatric patients (pts) with high risk Ewing's Sarcoma (HR-ES).

Methods: Previously untreated pts, aged less than 18 years at diagnosis, with newly diagnosed HR-ES of bone because metastatic or localised but with tumour volume more than 100 cm3. Treatment consisted of: induction therapy with two courses of Vincristine (Vcr) 2 mg/m2, Cyclophosphamide (C) 2200 mg/m2 and Adriamicina (Adr) 90 mg/m2 in two days (Hyper-VAdC), alternated to two courses of Etoposide (VP16) 600 mg/m2 in three days plus C 4000 mg/m2 (CE); G-CSF supports each cycle of chemotherapy in order to improve dose intensity and enhance peripheral blood stem cell mobilisation after CE; Surgery and/or Radiotherapy for local control of primary and/or metastatic sites of disease; Maintenance chemotherapy consisting of two courses of Vcr 1,5 mg/m2, C 1200 mg/m2 and Adr 80 mg/m2 in two days (VAdC) alternated with two courses of VP16 500 mg/m2 plus Ifosfamide 9000 mg/m2 in five days (IE). At the end of this phase pts who were not in progression of disease were eligible for consolidation therapy and received Busulfan (Bu) 4 mg/kg/die for 4 days, VP16 800 mg/m2/die for 3 days and Thiotepa (TT) 300 mg/m2 followed by peripheral blood stem cell rescue.

Results: From April 1993 to May 1999, 43 pts 10 with localised and 33 with metastatic disease were enrolled in this protocol. Four pts progressed during the maintenance phase and 34/39 pts eligible were grafted. At time of graft 12 pts were in CR. The median number of CD34+ infused was 6.9 (2.5-40.1)x106/kg. Despite 10 patients received both Bu and total lung irradiation, nor pulmonary toxicity and toxic death related to consolidation procedure were registered. After a median follow up from the diagnosis of 47 (23-89) months, 20/43 patients are in CR, and 2 are alive with disease. The 6 years OS (SE) and PFS (SE) were 48.6% (9.6) and 42.3% (8.3) respectively. Patients with metastasis at diagnosis fared substantially worse than pts with localised disease (6 years PFS 35.8% vs 64.0%, p=.066), moreover pts with bone metastasis (PFS = 14.4%) have a poorer outcome.

Conclusion: The results if compared with other national and international experience, demonstrate an increment in terms of 6 years OS. Only extension of disease at diagnosis, site of metastasis and surgery on primary site of disease seems to influence the outcome in terms of PFS.

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985 POSTER DISCUSSION

Potential role of MLL cleavage as a biomarker for treatment-related leukaemogenesis associated with topo 2 inhibitor therapy in children

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Purpose: Treatment-related leukaemia (TRL) is the most serious complication of effective topoisomerase 2 (topo 2) inhibitors in paediatric cancer therapy. Most TRLs are associated with rearrangement of the Mixed Lineage Leukaemia (MLL) gene, following drug-induced gene cleavage, and with a very poor outcome. Analysis of MLL cleavage may therefore be useful in assessing individual susceptibility to the genotoxic effects of topo 2 inhibitor therapy and, in predicting the risk of TRL.

Methods: 400 serial blood and marrow samples, obtained from 71 children receiving topo 2 inhibitors for primary malignancies and haemophygocytic lymphohistiocytosis (HLH), were studied. Cleavage in the breakpoint cluster region (BCR) of the MLL gene was detected using a hybridisation assay with a MLL cDNA probe and quantified by real time autoradiography. The results were correlated with clinical outcome and the adverse effects of treatment, and compared with those of 71 cord blood controls.

Results: MLL cleavage fragments (6.7 & 1.5kb) were detected in 6 bone marrow samples from 4 children with acute lymphoblastic leukaemia (ALL) and one with HLH. Only the 8.3kb germ-line MLL BCR product was found in the controls. MLL cleavage was identified at different time points after etoposide and anthracycline therapy in the 4 ALL patients, and following the last course of etoposide in the child with HLH. Cleavage fragments comprised 23-50% of the total MLL BCR signals. All 5 children experienced serious treatment related toxicity. Of these, one with T-cell ALL relapsed and died during treatment and the patient with HLH developed a TRL with MLL rearrangement post therapy.

Conclusion: MLL cleavage may provide a useful biomarker for the risk of TRL associated with topo 2 inhibitor therapy in children and warrants further investigation.

986 POSTER DISCUSSION

Paediatric Fine Needle Aspiration Cytology (FNAC) of NHL. An eleven-years study

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Introduction: Fine needle aspiration cytology (FNAC) is performed in IPOFG, for the initial diagnosis of paediatric lesions since 1987. It is particularly useful for the rapid diagnosis of non-Hodgkin lymphomas (NHL), and a final diagnosis can be achieved by using flow cytometry as a complement. In this study we reviewed the cases of NHL diagnosed by FNAC and compared its accuracy in NHL.

Materials and Methods: From a total of 1300 FNAC performed on paediatric patients between 1990 and 2000 in IPOFG, Lisboa, 387 corresponded to lymphoid lesions. FNAC diagnosis of NHL was done in 78. The other diagnoses were: reactive-188, Hodgkin's lymphoma-50, metastasis-21, inflammation-9, suspicious for malignancy-8, non-conclusive-18, unsatisfactory for diagnosis-17. In 71 of the 78 NHL smears were available for review and were reclassified using the REAL classification. Ancillary studies were performed in 59 cases: immunocytochemistry (34), flow citometry (25) and cytogenetics (5). Subsequent histology was performed in 28 cases. For the analysis we divided our cases in Burkitt's lymphoma (BL) and other types of NHL. Clinical records were available in 60 cases.

Results: NHL represented 60,9% of the lymphomas diagnosed by FNAC. The diagnosis of BL was done in 42 cases (59,1%). The other NHL were Lymphoblastic lymphoma-18, Diffuse large B cell lymphoma-7, Anaplastic large cell lymphoma, ALK+-2 and high grade NHL, NOS-2. Clinically, there was a male predominance. The median age was 6,3 yrs for BL and 7,5 yrs for the other NHL. BL cases were abdominal (31/42), nodal 8, facial 2 and 1 from the palatine tonsil. The other NHL were predominantly from superficial lymph nodes (13/29) and mediastinum (10/29). The median follow-up time was 48,6 months(1-126)for BL and 49,3 months (1-120)for other NHL. 40/60 patients are alive without disease (BL-73%;other NHL-56,5%),10 are alive with the disease (BL-16,2%; other NHL-17,4%), and 10 dead of the disease (BL-10,8%; other NHL-26,1%). FNAC morphology in conjunction with ancillary techniques rendered a final diagnosis in 85,7% and 75,9% of the BL and other NHL, respectively. The global diagnostic accuracy of NHL by FNAC was 81,7%.

Conclusion: FNAC is an accurate method to diagnose and classify paediatric NHL. The clinico-patologic features are identical to other published series from Western countries except for the higher frequency of BL. Its distinct morphologic features make BL the most accurately lymphoma diagnosed by FNAC.

987 POSTER DISCUSSION

Does pregnancy elicit clinical heart failure in anthracycline treated female survivors of childhood cancer?

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Purpose: Anthracyclines (AC) are well known for their ability to induce late clinical heart failure (CHF). In view of patient care we wished to establish guidelines allowing for safe peripartum management in AC treated survivors (ATS) of childhood cancer. Only two case reports about peripartum heart failure in ATS were found in the literature. In order to develop a strategy for additional clinical research it was decided to analyse the pregnancy histories of ATS registered in the database (PLEKsys) of our late effects outpatient clinic.

Methods: Female survivors were identified on the use of AC and on data entry on pregnancies. Data collected included treatment dates, cumulative AC doses, date of delivery, and cardiac problems before and/or after the pregnancies.

Results: Out of 35 pregnancies in 20 ATS 26 children were born. Seven abortions/miscarriages were found and the outcome of two pregnancies was unknown. The deliveries took place on average (± SD) 14 years (± 4) after AC treatment. Average dose of AC was 250 mg/m2 (± 154). Nine women received a dose of > or = 300 mg/m2 and 11 women received a dose of < 300 mg/m2. Eight out of the group of 9 women treated with a dose > or = 300 mg/m2 delivered in total 12 children. At last follow-up 1 of the 8 had developed a dilatation of the left ventricle more than three years after her second and last delivery and approximately 12 years after chemotherapy. In ATS treated with lower doses, one woman reported cardiac symptoms on several control visits both before and after the birth of her daughter. None developed peripartum cardiac problems.

Conclusions: No peripartum cardiac problems were found in ATS known at our late effects outpatient clinic. However, the numbers of ATS, pregnancies and deliveries are small. Up to 5% of AC treated patients will develop CHF 15 years after treatment (Kremer et al., JCO, 2001). The number studied in this series therefore is too small to be conclusive. Four of the women identified for this study have a wish to become pregnant at least once more. A further 67 ATS with this wish could be traced in the PLEKsys database, of which approximately 50% are using oral anticonceptive drugs. These observations and the lack of clinical evidence thus far, serve to illustrate both the urgency and the possibility for a well-developed clinical study to answer the question posed in the title