Conclusions: The immunohistochemical expression of p53 protein does not seem to predict tumor response to chemotherapy and does not have any influence in prognosis for children with OS. The most reliable prognostic factors were the presence of metastasis at diagnosis and the tumor necrosis after chemotherapy. There is a need to search for earlier prognostic factor in children with OS.

1233 POSTER

Temozolomide in resistent or relapsed neuroblastoma

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Purpose: We report the results of a feasibility study of a study investigating the role of oral temozolomide (TMZ) in relapsed or resistant neuroblastoma at the dosage of 215 mg/m^2/day × 5 days, or 180 mg/m^2/day × 5 days in pts with prior autologous bone marrow transplantation (ABMT).
Patients and methods: 17 children with resistant or relapsed neuroblastoma were enrolled. 12 had bone marrow involvement and 5 had localized disease. All pts were pre-treated, 106 outpatient courses were administered, with a median of 4.8 courses/pt.
Results: Overall response-rate (CR+PR+MR) in our series was 11.7% (1 CR, 1 MR), SD was observed in 9 patients and PD in 6. The median survival was 7.8 months (range 1–41). Bone marrow responses were 1 VGPR, 1 PR, 5 SD and 5 PD, according to INRC. We have 1 CR and 1 AWD at 37 and 41 months respectively. Haematological toxicity grade 3–4 was observed.
Conclusion: The results obtained in patients with NB, suggest that TMZ might be useful in the setting of minimal residual marrow disease control. Combination therapy with other agents should also be investigated.

1234 POSTER

5 years results of complex treatment high-risk medulloblastoma in children older 3 years with protocol M-2000

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Materials and method: 93 patients with high-risk medulloblastoma 3–15 years of age (median 8 years), 64 boys and 29 girls, were randomized: 46 patients received cyclic polychemotherapy (PCT), 47 – supporting. 19 patients had total removal of the tumor, 74 patients – subtotal. Mts (stages M1-M3) at the time of the diagnosis were found in 52 patients (M1 – 2 patients, M2 – 8 patients, M3 – 22 patients). Radiotherapy (RT) were started at 14–21 days after surgery: craniospinal 35 Gy, posterior fossa – 55 Gy, bust on Mts 10 Gy; with VCR 1.5 mg/m^2 weekly and CCNU 100 mg/m^2 on week 1 of RT. PCT carried out on 4 weeks after RT. Cyclic PCT – 2 alternating cycles each 3 weeks, altogether 4 cycles (1-st cycle: VCR 1.5 mg/m^2 days 1, 8 and Cph 1500 mg/m^2 days 1, 2; 2-nd cycle: VP-16 150 mg/m^2 days 1, 2, 3 and CDDP 70 mg/m^2 day 1). Supporting PCT – 8 cycles each 6 weeks (VCR 1.5 mg/m^2 days 1, 8, 15, CCNU 75 mg/m^2 and CDDP 70 mg/m^2 day 1).
Results: Overall response was seen in 87 patients: CR – 82 (94.3%) patients; PR – 3 (3.4%) patients, 2 (2.3%) patients had PD. Median observation – 19 months. PFS and OS at 5 years – 78±0.07% and 887plusmn;0.04%, respectively. PFS was higher in patients without Mts – 91% vs. with Mts – 53% ($d < 0.05$). PFS was higher in children older 6 years, than under 6 years: 81% and 75%, respectively ($d < 0.05$). Patients who have received the protocol without reduction of RT or/and PCT dozes and in timing according to the protocol had the best PFS: 91% vs. 57% ($d < 0.01$). There was no statistic difference in PFS between patients who received cyclic or supporting PCT (73% vs. 85%, $d < 0.9$). The volume of surgical removal (total or subtotal) had no influence on PFS (60% vs. 83%, $d<0.05$).

1235 POSTER

Catheter-related thrombosis in children with solid tumor

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Aim: to determine the prevalence of catheter-related thrombosis in children with cancer.
Patients and methods: children with solid tumor and central venous lines (CVLs), admitted as day care in a period of 3 months, were consecutively enrolled. All the patients (pts) were evaluated by physical examination and biochemical serum analyses including fibrinogen and antithrombin tests. Vessels patency and wall regularity were evaluated by grey scale and eco-color-doppler ultrasonography. Thrombophilia factors were studied in pts with venous thrombosis (VT), both symptomatic and asymptomatic. Thirty-three pts (10 females and 23 males) – mean age 115 months (range 6–252) were enrolled. They were affected by Neuroblastoma (10), Sarcoma (7), Brain tumor (5), Lymphoma (6), Epatoblastoma (1), Langherans' cells histiocytosis (1), Retinoblastoma (1), Malignant Teratoma (1), Wilms' tumor (1). The mean duration of catheter placement was 7 months (range 1–19). Thirty-one pts had Groshong CV 5 Fr or 7 Fr and 2 Broviac 4.2 Fr. No pt received L-asparaginase; 11 pts received corticosteroid therapy.
Results: Four of 33 (12%) pts had VT, 3 of these had asymptomatic and catheter-related VT visualized by sonography, while 1 pt had clinically symptomatic and no catheter-related VT. All these pts received thrombophilia tests that showed: – Abnormal prothrombin gene (prothrombin G20210 A) in 1 pt – Mutation of Plasminogen activator inhibitor-1 (PAI-1): mutation of 4G/5G with hypofibrinolysis in one pt-Hyperhomocysteinemia correlated with MTHFR mutation with T677 and A1298C variants in one pt – Factor V Leiden presence (G1691A) and factor V mutation H1299R) in one pt.
Conclusion: 1) In our series, 12% of pts presented VT. 2) VT was asymptomatic and catheter-related in 10%. 3) In all of these pts thrombophilia genetic risks were found.
CVLs is related to an increasing risk of thrombosis in children with solid tumors. The clinical relevance of genetic risk has to be estabilished. Prospective and multicentric studies are required in order to select patients need prevention strategies.

1236 POSTER

FDG-PET imaging for staging and follow-up of malignant paediatric sarcomas: preliminary results of a prospective multicenter study

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Aim: PET evaluation for staging and therapy control of pediatric sarcomas.
Material and methods: In this study 16 patients (9f, 7m; mean: 12.8y., range 1–17y.) with sarcoma (Osteosarcoma n = 4, Ewing n = 7, Rhabdomyosarcoma n = 5) were enrolled. A total of 41 PET scans for staging (n = 16), therapy monitoring (n = 16) and restaging at least 3 weeks after therapy (n = 9) were performed. Results were compared with conventional imagine modalities (CIM: ultrasound, chest X-ray, CT, MRI) according to EURO Ewing 99, COSS 96 and CWS 02P. Histology (n = 12) and/or clinical and imaging follow-up (n = 15) served as reference endpoint.
Results: For detection of primary tumours PET and CIM were equally effective as all 16 histologically proven primaries were found by either method. 8/16 pts. had initially detected metastases (lung n = 2, regional n = 2, distant and/or multiple n = 6). PET revealed 8 pts. true pos. suffering of metastatic diseases but did not discover two lung metastases. CIM however, detected these lung metastases true pos. and 3 other pts. with multiple lesions, although not as extensively as PET.
PET diagnosed 14 pts. with complete (n = 6) and partial (n = 8) therapy response while primary tumour showed significant ($p<0.001$) reduction of SUV_{max} (initial SUV: 8.2 vs. restaging SUV: 2.7). CIM did not correctly diagnose tumour response during therapy in 4 pts. By final examination PET assumed residual lesions in two pts. which must be considered false pos. presently. By CIM residual disease was suspected in 4/9 pts. So far, clinical follow-up did not show any recurrency in all 9 pts., although a larger observation time (presently mean 218 days) is needed.
In summary, PET caused a change of therapy in 7/16 children. 6 received a more intensive therapy due to initial PET and one pt. underwent a less intensive therapy due to metabolic response in PET.

Conclusion: In this study, PET caused a change of therapy in 44%. FDG-PET has great potential in the assessment of tumour response to combined radio-/chemotherapy and is superior to CIM for this purpose.

1237 POSTER

High-dose chemotherapy with autologous stem-cell rescue in children with high-risk medulloblastoma/PNET.

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Purpose: To determine the efficacy of treatment of high-risk medulloblastoma/PNET Children with high-dose chemotherapy (HDCT) and PBSC.
Patients and methods: 44 patients with high-risk medulloblastoma/PNET (unresectable tumor, brain stem involved, CNS metastasis, age less 3 years) were treated with four sequential courses of chemotherapy (cis-platinum or carboplatinum, cyclophosphamide, etoposide and vincristine). PBSC harvesting was performed after last course of chemotherapy. Then children were randomized to receive or not HDCT consisting of thiotepa 150 mg/m^2 – 8-7-6-5, carboplatinum 500 mg/m^2 – 8-7-6-5, etoposide 250 mg/m – 8-7-6-5. Craniospinal radiotherapy was performed after cessation chemotherapy to all children more than 3 years old.
Results: 4-year PFS for all patients was 56%. PFS for children received HDCT was 61+0.15 in compare of 45+0.09 for those who did not. There were no transplanted related deaths.
Conclusion: Patients with high-risk medulloblastoma/PNET may benefit from treatment approach including HDCT with condition thiotepa, carbo-platinum, etoposide. The toxicity of this regimen was tolerable.

1238 POSTER

Clinical characteristics of large cell lymphomas in childhood

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Background: Large cell lymphoma (LCL) represents 15–30% of childhood non-Hodgkin lymphomas. Like other childhood lymphomas, LCLs are highly chemosensitive tumors. We aimed to determine clinical characteristics and treatment results of our cases with LCL.
Patients and methods: We reviewed the records of 24 children with LCL treated and followed at Hacettepe University Institute of Oncology, Department of Pediatric Oncology between January 1993 and December 2004. Data regarding age, gender, presenting features, results of radiological and other laboratory studies, histopathology, disease stages, treatment modalities, and outcome of patients were recorded from hospital charts. Patients were staged according to Murphy's system and treated depending on disease stage with modified 'lymphoma malign B' (LMB-89) and 'lymphoma malign T' (LMT-89) chemotherapy regimens.
Results: In this 12-year period, among 314 non-Hodgkin lymphoma cases, 24 were diagnosed as LCL (7.6%); 14 were boys and 10 girls. The median age for all cases was 8.5 years (range, 1.25–17) and 7 were younger than 5 years. Eight patients (33%) had anaplastic large cell lymphoma (ALCL). Eighteen cases (75%) had advanced disease (stages III and IV) and 6 had localized disease. Nodal disease was present in 17 patients (70.8%), extra-nodal disease in 15/24 (62.5%). Common extra-nodal sites were soft tissues (6/24), skin (4/24), kidneys (4/24), central nervous system (3/24) and ovaries (2/24). In 3 patients, bone marrow involvement was detected. Five of 8 patients with ALCL had T-cell lineage disease and 8 other patients had disease of B-cell lineage. For all patients, overall survival (OS) and event-free survival rates were 66.6% and 55.3%, respectively. Overall survival rates for ALCL and other LCLs were 66.3% and 61.3%, respectively. Four patients with LDH levels <500 IU/L are alive with no disease at a median follow-up of 32.4 months. Overall survival rate of the patients with higher LDH levels (>500 IU/L) was 60.7%. In localized and advanced disease, OS rates were 83.3% and 60.4% ($p = 0.48$), respectively. The OS rates for cases $\leqslant$5 years and older cases were 28.5% and 81.4% ($p = 0.07$), respectively.
Conclusions: Compared to other common NHLs in childhood, LCLs frequently present with nodal disease. Although not significant, survival rates were better in cases older than 5 years and in those with LDH <500 IU/L. We need more novel treatment approaches such as immunotherapy with more intensive chemotherapy to improve survival rates, especially in younger cases with advanced disease and LDH >500 IU/L.

1239 POSTER

An analysis of prognostic factors and the five year survival rate in childhood acute lymphoblastic leukaemia

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Background: Acute Lymphoblastic Leukaemia (ALL) is the most common malignancy in childhood. With newer drug protocols the five year survival rate is now close to 80%. Various factors have been reported to be important for prognosis and should be considered at the time of planning treatment. A prospective study was designed to evaluate the prognostic factors and response to treatment in newly diagnosed paediatric acute lymphoblastic leukaemia patients. This study was started in 1998 and preliminary results complied in 2004.
Materials and methods: A total of 105 patients were recruited into the study. The patients were stratified prognostically into good risk, poor risk and intermediate risk on the basis of age, sex white cell blood count at presentation and disease bulk. All patients received standard treatment consisting of induction (vincristine, prednisolone, daunorubicin, IT Methotrxate, L-Asparginase), consolidation on week five (vincristine, prednisolone, daunorubicin, cytosine arabinoside, thioguanone, prednisolone, IT methotrxate) CNS radiation followed by maintainance therapy with monthly vincristine, daily mercapopurine, weekly oral methotrexate, prednisolone 5 days a month All patients received late intensification (same drugs as consolidation)on month five of induction.
Results: By December 2003, 34.3% of the patients were alive in remission, 23% of the patients died due to relapse or infection during follow up. Forty five patients failed to comply with the treatment protocol and lost to follow up. Among all the variables a worse prognosis was associated ($p < 0.05$) with WBC counts greater than 50,000/ml at presentation and relapse in the bone marrow. The high number of drop outs and factors that might have account for a poorer prognosis included the difficult access to medical care, poor nutrition, decreased compliance of families due to exhausted economic and psychological reserves and inadequate knowledge about the disease course and treatment.
Conclusion: We conclude that most of our patients present late for treatment and have bulky disease at presentation. The above treatment was effective in our patients. Treatment related morbidity and mortality is predictable and controllable. However, further diagnostic risk group stratification is required like immunophenotyping, cytogenetics and molecular studies to classify these patients. This will help to achieve a stratified treatment approach for various risk groups based on known clinical and genetic features that play a critical role in directing therapy for ALL.

1240 POSTER

Treatment results for B-cell non-Hodgkin's Lymphoma and leukemia using BFM protocols with reduced MTX to 2 g/m^2: a single institution experience

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Objective: To evaluate the results achieved in children with B-cell non-Hodgkin's lymphoma and leukemia (B-NHL and B-ALL) treated according to protocols Berlin-Frankfurt-Munster-90 and 95 (BFM-90 and BFM-95).
Methods: Forty fourth children (41 with B-NHL and 3 with B-ALL) admitted to our hospital between January 1993 and January 2005. were evaluated. Patients were staged according to the BFM protocol. Due to inability to determine plasma MTX levels, HD-MTX was reduced from 5 to 2 g/m^2.
Results: There were 33 boys and 11 girls median age 8 years (range 3–17). Primary site for children with B-NHL was the abdomen (30), head and neck (11) and other (3). Three had B-ALL. Based on BFM therapy group staging classification at diagnosis: therapy group R1 (1), R2 (13), R3 (16) and R4 (14). None of the patients had cerebrospinal fluid involvement. Treatment protocols where BFM-90 (10) and BFM-95 (34). All patients entered complete remission. No toxic death was seen. Two patients relapsed and died. One was HIV positive and showed aggressive behaviour after relapse. Second relapsed three months after therapy in bone marrow, after four months of second line therapy did not achieve remission and stop therapy. Forty two patients (95.45%) are alive and disease free, with median follow up 47 months.
Conclusions: These results of our group of B-NHL/B-ALL can be considered satisfactory despite reduction of MTX dosage from 5 to 2 g/m^2.