correlation with the appearance of acute hepatoxicity. It is important to monitore drug pharmacokinetics to be able to use intensive supportive care if it is necessary to avoid serious adverse effects.

4114 POSTER

Monitoring of Bone Marrow Clearing by an Automated Imaging Device (Immunofluorescence Plus Genetics) Identifies Different Risk Groups in Neuroblastoma Patients Over 18 Months

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Background: Reliable response criteria are still lacking in stage 4 neuroblastomas. We hypothesized that the dynamics of BM clearing mirrors the response to cytotoxic treatment and is thus able to identify prognostically differing subgroups of stage 4 patients.
Patients and Methods: BM samples from 81 stage 4 patients registered in two neuroblastoma Trials were tested with a fully automatic fluorescence based device combining GD2 based immunocytology and molecular-cytogenetic analyses of identical cells (automatic immunofluorescence plus FISH, AIPF). 44 patients (age 0 to 239 months, 219 BM specimens, median observation time 8.2 years) met the inclusion criteria (BM specimens at diagnosis and given time points during treatment and genomic information on the primary tumour) with a complete data set.
Results: BM clearing after 2 to 4 chemotherapy cycles was achieved by 28 patients (63.6%) and was significantly associated with overall survival (OS) in patients above 18 months at diagnosis ($p < 0.0002$, Logrank test) but not in the younger age group. Stage 4 patients below 18 months had a good prognosis irrespective of BM clearing and tumour genetics. In younger patients, none of the genetic markers showed a correlation with OS. MNA was associated and intact 11q showed a trend towards association with BM clearing ($p < 0.3$ and $p = 0.0735$, both Fisher's Exact Test).
Conclusion: The determination of BM clearance reaches the so far highest prognostic impact in stage 4 neuroblastoma patients over 18 months of age making accurate BM monitoring an important tool for risk assessment in this patient group.

4115 POSTER

Thiopurine-S-Methyl-Transferase Gene Polymorphisms and Antimetabolite Drug Toxicity in Children Treated for Acute Leukemia and Non-Hodgkin's Lymphoma

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Background: Thiopurine-S-Methyl-Transferase (TPSMT) enzyme activity may be changed due to different mutations in its allelles. Heterozygous or homozygos TPSMT mutations may result in more drug toxicity. Major adverse effects of 6-mercaptopurine and 6-thioguanine are hematologic and hepatic toxicities in the treatment of acute leukemia and non-Hodgkin's lymphoma (NHL).
We aimed to study TPSMT polymorphisms in a pediatric population who are treated for acute leukemia and NHL, and to relate this polymorphisms with hematologic and hepatic toxicity observed during maintenance treatment.
Materials and Methods: The study included 49 patients with median age 8 years (2−17) (30 male, 19 female). 40 patients had ALL, 3 AML, and 6 lymphoblastic lymphoma. The control group consisted of 84 children with median age 9.5 years (34 male and 50 female).
Eight polymorphisms of TPSMT gene were examined by RT-PCR method in the extracted DNA from peripheral blood of the study and the control groups. Grade III or IV hematologic (Hb, WBC, platelet counts) and hepatic toxicity (serum ALT, AST, bilirubin levels) data were recorded using patients charts. Chi-square test was used in statistical analysis.
Results: We have found that the patients to have generally wild-type TPMT (*1) in 87.3%, TPMT*2 (G238C) in 2%, and TPMT*3B polymorphisms (G460A) in 20.4%. The other polymorphisms including TPMT*3A, TPMT*3C (A719G), TPMT*3D, TPMT*4 (G−A), TPMT*5 (T146C), TPMT*6 (A539T) and TPMT*7 (T681G). In the control group, wild-type TPMT (*1) was in 98.8%, TPMT*3B in 1.2%. Other polymorphisms were not detected. In comparison, the patients were found to have less wild- type TPSMT, but more TPMT*3B polymorphism ($p = 0.0001$ and 0.0001). We did not find any relationship between hematologic and hepatic toxicity and TPSMT gene polymorphisms.
Conclusions: We conclude that severe hematologic or hepatic toxicity in the maintenance treatment of acute leukemia and NHL is not related with TPSMT gene polymorphisms.

4116 POSTER

Glioblastoma Multoforme as a Second Malignant Neoplasm After Radio-chemotherapy for Pediatric Malignancies

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Background and Purpose: Reports of secondary high-grade glioma (HGG) in survivors of childhood cancer are limited.
Patients and Methods: We performed retrospective study in the group of patients with paediatric glioblastoma multiforme (42 patients) 6 children developed glioblastoma as a second malignancy (age 7−15 years, median 12 yrs). We report on 6 patients (2 males, 4 females) treated in childhood for a primary cancer. All patients previously had received radiation and chemotherapy for either acute lymphoblastic leukaemia (n = 5) or medulloblastoma (n = 1). Children developed glioblastoma 5−10 years thereafter (median 6 yrs). Median of dose of primary cranial irradiation was 18 Gy. Tumours were localized supratentorialy in 5 cases and was infratentorial (cerebellum) in one patient. Patients underwent surgery resection (2 − total, 3 − subtotal, 1- partial) followed by standard fractionated local radiation and chemotherapy. The dose of irradiation was 55−60 Gy (median 55 Gy). One patient progressed after subtotal resection and irradiation (2 mo after surgery). Five children received temozolomide (TMZ) as single-agent 150–200 mg/m^2 administered on 5 consecutive days every 28 days (number of courses 2−8, median 3).
Results: In 3 cases chemotherapy was stopped because severe myelotoxicity after 2−4 courses. Four patients have died and the median overall survival time was 16 months. Overall survival rate was 62.5±21.3% and 20.8±18.4% at 1 and 2 years after diagnosis respectively with follow up 4–24 mo with median 11 mo. Two patients are alive, but the only one without signs of disease progression.
Conclusions: Prognosis in secondary malignant gliomas in children is poor despite intense therapy. The risk of a severe myelotoxicity is high. ALL and medulloblastoma survivors must undergo systematic, long-term surveillance for early detection of intracranial neoplasms.

4117 POSTER

Intensive Chemotherapy and Temozolomide in Children With Newly Diagnosed Anaplastic Astrocytoma

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Background: To evaluate the efficacy of temozolomide and poly-chemotherapy in a retrospective nonrandomized study among newly diagnosed children with anaplastic astrocytoma.
Patients and Methods: We analyzed 39 patients (age 4 mo to 17 years, median 9 years) from pediatric oncology departments in three institutions between January 1996 and April 2010 (at median follow-up of 13 mo, range 4–108 mo) in order to identify influence of different chemotherapy modalities in newly diagnosed paediatric anaplastic astrocytoma. All patients (pts) underwent resection (34pts) or biopsy (5 pts), followed by standard fractionated local radiation and chemotherapy. Two children were not irradiated because of the young age. Patients were divided into 3 groups according to treatment modalities. Eighteen pts received temozolomide (TMZ) as single-agent 150–200 mg/m^2 administered on 5 consecutive days every 28 days (number of courses 2−12, median 6), 12 children of the group also received concurrent chemotherapy during radiation with TMZ (75 mg/m^2/day). Second group of patients (18 pts) received polychemotherapy − one of two chemotherapy regimens: cyclophosphamide, etoposide, cisplatin and vincristine or ifosfamide, etoposide, carboplatin and vincristine (number of courses 2−26, median 8). Third group (3 pts) received polychemotherapy and TMZ sequentially because of the residual tumour after 4−8 courses of polychemotherapy (total number of courses 11−16).
Results: Overall survival rates in group of temozolomide were 51.6±12.5% and 43.0±13.0 (with a median of 20.0 mo) at 1 and 5 years after diagnosis, respectively. Overall survival rates in the group of polychemotherapy at 1 and 5 years were 77.8±9.8% and 61.1±11.5% (median undefined). Survival rates in both groups since 2 years after diagnosis were constant stable; nobody died or relapsed after two years of follow up. The log-rank test in OS between the two groups was not statistically significant ($P = 0.14$).

In the 3 group 2 pts died 24 and 18 months after diagnosis from disease progression, 1 pt is in complete remission with 59 mnth of follow up.
Conclusions: TMZ did not result in a better outcome when compared with polychemotherapy in pts with newly diagnosed paediatric anaplastic astrocytoma. Although aggressive treatment seems to provide sustained remissions in some patients, the optimal management is still to be defined.

4118 POSTER

Prospective Randomized Trial of Hypofractionated Conformal Radiotherapy for Pediatric Diffuse Pontine Glioma

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Background: Children with diffuse pontine glioma has dismal outcome even with addition of chemotherapy, radiosensitized or using hyperfractionated radiotherapy.
Patients and Methods: Fifty four children, ages 3−15, were prospectively randomized either to receive: 1. Hypofractionated radiotherapy (Hypo) 39 Gy/13 fractions/2.5 weeks or, 2. Standard conventional 55.8 Gy/31 fractions/6 weeks. Patients' demographic and radiologic data were not significantly different in the two groups.
Results: Tolerance to radiotherapy was similar in the two groups. Time to symptoms and signs alleviation and the need to restart CNS dehydration were also not significantly different in both groups. The median survival were 7.3 months (95% CI: 3.5–10.7) and 9.5 months (7.9–11.2) for Hypo and conventional group respectively. Median time to progression was 6.4 months (2.0–10.8) and 7.3 months (5.8−8.5) for Hypo and conventional group respectively. The one-year overall (OS) was 35.8±10.8% and 26.9±10.1%, while the 2-year OS was 22.4±10.2% and 21.5±9.4% for hypo and conventional group, respectively. The one-year progression-free survival (PFS) rate was 22.7±9.9% and 21.4±9.0%, while the 2-year PFS was 11.1±9.1% and 21.4±9.0% for the hypo and conventional group, respectively. None of these differences was statistically significant.
Conclusion: Hypofractionated radiotherapy is as tolerable and effective as conventional fractionation with nearly similar OS and PFS rates. It has the advantage of being rapid with less burden on the patient, his family and on the treatment machines.

4119 POSTER

Hematopoietic Stem Cell Transplantation With Total Body Irradiation Conditioning in Childhood Acute Lymphoblastic Leukemia Patients With Relapsed or High Risk Group

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Background: This study retrospectively analyzed the patient characteristics and treatment outcomes of childhood acute lymphoblastic leukemia (ALL) patients treated with total body irradiation (TBI) conditioning followed by hematopoietic stem cell transplantation (HSCT).
Material and Methods: Between 1994 and 2008, 119 childhood ALL patients were treated with HSCT using TBI conditioning regimen. Patients were at high or very high risk group (73.1%) or relapsed after first complete remission by chemotherapy (51.3%). The dose of TBI was 200 cGy per fraction, twice a day up to 1200 cGy for 3 consecutive days. The type of HSCT was allogeneic (81.8%) or autologous (1.7%). The donors of allogeneic HSCT were human leukocyte antigen (HLA)-identical siblings (44.5%) or unrelated matched persons (35.3%). The cell source was bone marrow (66.4%), peripheral blood (16.8%) and cord blood (16%). Disease free survival (DFS) and overall survival (OS) were estimated by the Kaplan–Meier method, and late complications were assessed including the development of second malignancy.
Result: Patients were aged from 1 to 14 years (median 6). Median follow-up was 8 years (range, 2−14). Successful engraftment was achieved in 87.4% of patients. Acute and chronic GVHD developed in 68.9% and 21.8% of patients, respectively. Recurrence rate was 10.1% at bone marrow, 5% at central nervous system (CNS), and 5% at other extramedullary site. 5-year CNS relapse rate was 8.3%, and there was no significant benefit of prophylactic cranial irradiation (PCI) ($p = 0.789$). The 5-year DFS and OS rate were 77.2% and 53.9%, respectively. Age at diagnosis and the experience of an engraftment failure were significant prognostic factors for unfavorable DFS. Relapse after chemotherapy, umbilical cord blood stem cell source, unrelated matched donor, the presence of HLA mismatch and the experience of engraftment failure significantly decreased OS. Multivariate analyses showed that age at diagnosis and the experience of engraftment failure were significant predictors for OS ($p = 0.025$ and $p = 0.004$, respectively). Late complications were cataracts in 9 patients, endocrine disorders in 37 patients and bone related problems in 9 patients. No secondary malignancy was observed.
Conclusion: Our study showed that HSCT with TBI-based conditioning is a still good option for pediatric ALL patients who were at high risk group or experienced a relapse. The results achieved relatively high rate of engraftment and survival on long term follow up.

4120 POSTER

Low Bone Mineral Apparent Density in Childhood Survivors of Medulloblastoma

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Background: To detect the difference in bone mineral apparent density (BMAD) of the lumbar spine in childhood survivors of medulloblastoma (MB) and healthy peers.
Material and Methods: 47 childhood survivors of MB and 56 healthy peers were included in the study. Treatment protocol for MB included surgical treatment, chemotherapy and craniospinal irradiation. Bone mineral content (BMC, g) and bone mineral density (BMD, g/cm^2) of the L_1-L_4 spine region were measured with the densitometry device Lunar Prodigy GE. To minimize the effect of bone size on BMD value, we calculated BMAD for each lumbar vertebral body by dividing BMC per vertebrae volume. For analysis, arithmetical mean of the BMAD of the L_1-L_4 was used (BMAD L_1-L_4, g/cm^3). To detect the difference in BMAD L_1-L_4 in healthy and survivor's groups, regression analysis and estimation of the Fisher's criterion were used, with p value <0.05 considered significant.
Results: The mean (SD) follow-up at study was 4.8(2.2) years for boys and median (range) 4.6 (2.5−7.1) years for girls.

	Girls		Boys	
	Healthy, n = 22	Survivors, n = 20	Healthy, n = 34	Survivors, n = 27
Age at study, years	13.0 (5.0)	13.8 (4.5)	15.0 (6.0)	14.1 (6.0)
BMAD L_1-L_4, g/cm^3	0.415 (0.087)	0.398 (0.061)	0.392 (0.059)	0.357 (0.057)

Correlation coefficients (r) of the BMAD L_1-L_4 with chronological age were the following: healthy girls, r = 0.847; survivors girls, r = 0.325; healthy boys, r = 0.673; survivors boys, r = 0.458. There was a significant difference in BMAD L_1-L_4 both in the group of survivors girls and healthy girls (F = 6.294, p = 0.004) and in the group of survivors boys and healthy boys (F = 3.471, p = 0.04).
Conclusion: Obtained results denote that during long-term follow-up the decreased BMAD of the L_1-L_4 spine region is observed both in boys and girls survivors of medulloblastoma.

4121 POSTER

Carcinomas in Adolescents − Single Centre Experience

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According to U.S. SEER epidemiology data, the incidence of cancer is approximately 40% higher among patients aged 15−19 years than in younger children. Types of cancer in adolescents differ from the ones in children under 15 years of age, however epithelial tumours (carcinomas) are still very rare.
Between 2005–2009, 248 adolescents and young adults aged 15−19 years were treated at our department: 190 pts with solid tumour (1 tumour duplicity) and 58 pts with acute leukemia. Following diagnoses were documented: 20× NHL, 42× MH, 37× CNS tumour, 19× MMT, 22× bone sarcoma, 23× GCT, 12× other rare cancer, 47× ALL and 11× AML. In 16 pts, carcinoma (ca) was diagnosed: 3× thyroid ca, 2× ca of tongue, 2× nasopharyngeal ca, 1× hepatocellular ca, 1× adrenal cortical ca, 1× renal cell ca and 1× tubal ca. Carcinomas including thyroid cancer represent 8.3% of all solid tumours and 6.4% of all cancer in adolescents. In the same 5-year period, 8 pts in the age of 0−14 were treated for carcinoma at our department. Therefore epithelial cancer in adolescents represents 67% (16/24) of total carcinomas in our pts. Thyroid cancer was documented in only 1.2% (3/248) adolescents compared to SEER data presenting 8%