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 ($P = 0.14$).