was given on an outpatient basis and without any side effects correlated with the use of nimotuzumab. Two/37 children were alive without tumour progression 21 and 29 months after their diagnosis.
Materials and Methods: In a subsequent mono-institutional experience, with a view to exploring add-on strategies, we began a pilot protocol on a compassionate case-by-case basis using nimotuzumab together with vinorelbine, combined with radiation, and adopting consolidation courses with the same timing as in the previous international radiation plus nimotuzumab protocol. Vinorelbine was adopted at a dose of 20 mg/sqm/weekly together with nimotuzumab at the standard dose of 150 mg/sqm during the 6 weeks when radiotherapy was delivered, and 25 mg/sqm in any other week, with the same dose of nimotuzumab during the consolidation courses, planned until tumour progression or for a total of two years.
Results: We have so far treated 13 children, 7 males and 6 females, with an age range of 2−13 years, enrolled according to the standard MRI inclusion criteria. After a median follow-up of 10 months (range 3- 20), 11/13 were alive, their PFS at 9 months was 47±15% and their OS at 12 months was 92±7%. Median PFS was 9 months and median OS has not been reached. According to MRI evaluation, in 12/13 children evaluable for response, 9 had partial remission and 3 stable disease, 100% had symptom amelioration.
Conclusions: The nimotuzumab/vinorelbine combination was very well tolerated, with no acute side-effects. As in the case of nimotuzumab alone, all children were treated on an outpatient basis. The observation time for this new series is long enough to give the impression that this combination has promise, with statistically significant differences with previous reported experiences as far as OS.

4126 POSTER

Hsp70 Stress Protein is a Promising Tool in the Treatment of Brain Tumours in Children

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Background: Primary malignant brain tumours are the second common malignancies, after leukemia, and represent 20% of all children's cancers. In the majority of cases the therapy includes surgery followed by radiotherapy and concomitant chemotherapy. Despite this aggressive multimodal approach, the prognosis for patients is poor. As such, investigative therapies could be based on immunomodulatory activity of molecular chaperons, particularly Hsp70.
Material and Methods: To define *in vivo* response we used a model of intracranial C6 glioma in rats, which were intratumorally injected with Hsp70. To characterize immune effect we used cytotoxicity assay of spleen lymphocytes (CTL-test), immunohistochemistry of brain sections for CD3+, CD4+, CD8+ cell infiltration, tumour volume assessment by magnetic resonance imaging, MRI. All animals were followed for survival.
Patients (n = 10) with diagnosis of malignant brain tumour following operation were treated by intratumoral administration of five doses of Hsp70 (at 500 μg for one injection) − totally 2.5 mg of protein. Immunological assays including lymphocyte subpopulations measurement, cytokine levels (INFgamma, TNFa, IL-4, IL-6, IL-10), cytotoxic activity of NK-cells before and after treatment were made. The courses were performed on the base of informal agreement and the resolution of the Ethical Committee of the Russian Neurosurgical Institute by A.L.Polenov MHSD RF.
Results: *In vivo* intracranial delivery of Hsp70 increased survival rate of rats from 18.5±2 till 35±3 Days ($P > 0.001$) depending on a mode of the chaperone injection. The delay was accompanied by C6-specific CTL response, infiltration with CD3+, CD4+ and CD8+ cells both in the area of injection and in tumour Itself. The hindrance of tumour volume growth according to MRI in Hsp70 treated group was also observed.
Intracranial delivery of Hsp70 in patients was not associated with any evidence of toxicity or serious adverse effects. One patient had an objective clinical response as revealed by MRI. After treatment we observed the elevated levels of INFgamma, TNFa, T-cell lymphocytes (CD3+CD4+, CD3+CD8+, CD3+HLA DR+). Cytotoxic activity of NK-cells was not significantly changed.
Conclusions: Our data provide the evidence of the feasibility, safety, and *in vivo* immunomodulatory activity of Hsp70 in patients. The results suggest that the target delivery of the chaperone Hsp70 can become a useful therapeutic strategy against malignant brain tumours.

4127 POSTER

Myocardial Performance Index − an Early Indicator of Subclinical Functional Anthracycline-induced Alteration in Children With Acute Lymphoblastic Leukemia

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Background: The risk of anthracycline-induced cardiovascular disease remains a major concern in children with acute lymphoblastic leukemia (ALL), giving the growing number of survivors. We investigated on the role of serum concentrations of biomarkers (cTnT and NT-pro-BNP) and myocardial performance index (MPI), as predictors of subclinical functional anthracycline-induced alterations.
Methods: All children admitted to our Pediatric Oncology Department from January 2007 to October 2008 with the diagnosis of ALL receiving anthracyclines as part of their therapy were enrolled in this study. Following informed consent, cTnT and NT-pro-BNP were evaluated in all patients at diagnosis, before the anthracycline therapy, 2 and 24 hours following every anthracycline administration. Physical examination, ECG and detailed echocardiography were performed at diagnosis, 24 hours after every anthracycline course and 12 months after the end of the chemotherapy.
Results: 19 children with standard-risk ALL were evaluated. The mean age was 6 years (range 10 months-14 years). The cumulative doxorubicin dosage was 240 mg/m^2, according to the AIEOP ALL 2000 protocol. None of 19 patients developed clinical signs or symptoms of congestive heart failure. With increasing cumulative dosages of anthracyclines a significant increase was seen in MPI (p 0.014). This increase was statistically significant both at a cumulative dosage of 240 mg/m^2 (p 0.018) and at the follow-up (p 0.05), compared to baseline, while the median NT-pro-BNP did not changed significantly during the treatment. In all patients the cTnT levels remained negative in all samples.
Conclusion: A proportional increase of MPI was observed with increasing anthracycline doses, while cTnT and NT-pro-BNP levels did not change significantly during the therapy.
MPI is a sensitive and reliable parameter, able to detect subclinical cardiac dysfunction in children receiving anthracycline-based treatment. More prolonged follow-up is required to establish the impact of MPI on the prediction of possible cardiac dysfunction.

4128 POSTER

Procedural Analgo-sedation Role in Reducing the Incidence of Traumatic Lumbar Puncture in Children With Acute Lymphoblastic Leukemia

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Background: Invasive procedures, such as the lumbar puncture (LP), can cause anxiety and pain in children undergoing treatment for acute lymphoblastic leukaemia (ALL), often leading to traumatic lumbar punctures (TLPs). TLP increases the risk of central nervous system (CNS) relapse. The objective of the study is to evaluate the safety and efficacy of procedural analgo-sedation and its role in reducing risk of TLP in children with ALL.
Patients and Methods: From September 2007 to November 2008 we performed a total of 225 LPs in 25 children with ALL, treated according to AIEOP ALL 2000 protocol. Thirteen males and 12 females were included, with a median age at diagnosis of 5.7 years (age range, 2 months to 14 years). All the procedures were performed under deep sedation, using Propofol and Ketamine. Vital parameters were monitored thought procedures and possible side effects were recorded. The efficacy of deep sedation was evaluated using Ramsay and CHEOPS scales. Cerebrospinal fluid (CSF) was collected for chemical and cytologic examinations. LP was defined as traumatic if 10 or more erythrocytes per cubic millimeter were found in CSF.
Results: In all patients a satisfactory sedation and analgesia were achieved. The mean awakening time was 25±10 minutes. The evaluation of vital parameters didn't show any significant variation compared to baseline values. No apnoea episode was recorded and O2 Saturation ranged between 94% and 99%. No side effects related to the drugs utilized were recorded. The mean Ramsay and CHEOPS scores were 6.15±1 and 5.5±0.5 respectively. Out of 225 LPs performed under analgo-sedation only 3 (1.3%) resulted traumatic.
Conclusion: Procedural analgo-sedation was safe and efficacious, improving comfort and quality of life of children with ALL. Moreover, deep sedation reduce the risk of TLP that, especially at diagnosis, increases the risk of CNS relapse, negatively influencing the patient outcome.