

Official Journal of the Society for Neuro-Oncology since 1997

NEURO-ONCOLOGY

Volume 9

Issue 2

April 2007

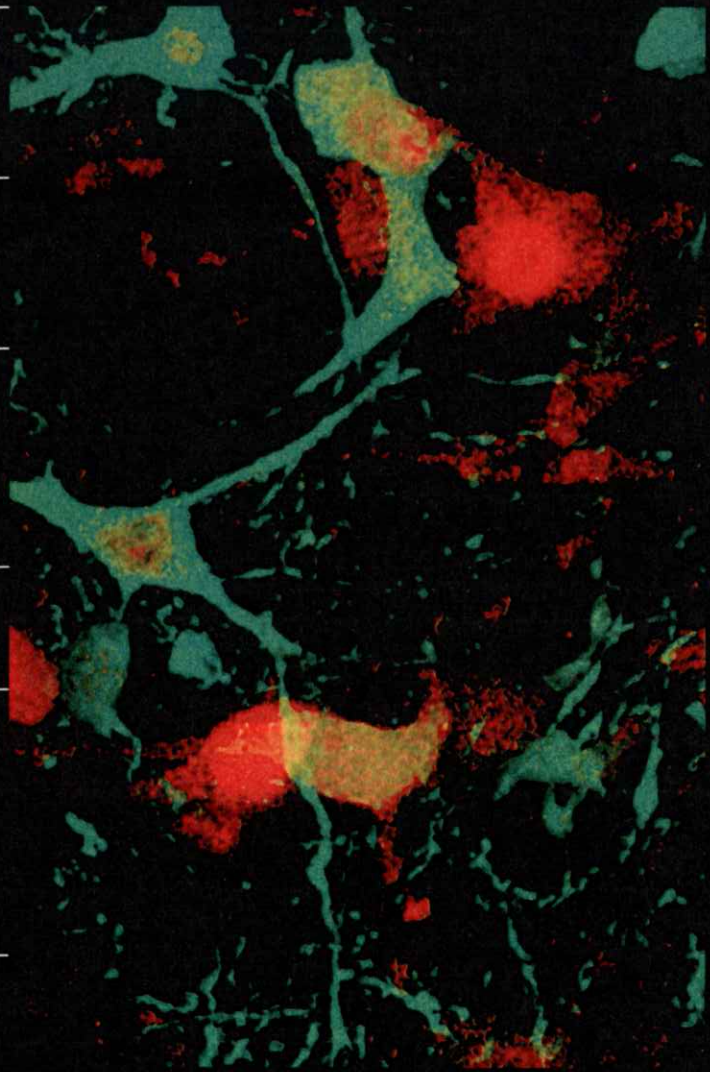
Rapid Report: In vivo efficacy of combined HDACI-radiotherapy against glioma • page 82

High-dose methotrexate in parenchymal brain masses of uncertain origin • page 96

Imaging of brain and brain tumor specimens by time-resolved multiphoton excitation microscopy • page 103

Special Focus Section: Pediatric Neuro-Oncology • page 113

Abstracts from the Twelfth International Symposium on Pediatric Neuro-Oncology (ISPNO), June 6–9, 2006, Nara, Japan • page 169



determined the pattern of expression of oligodendroglial differentiation markers (ODMs) in PA and correlated their expression with PI.

Methods: Sixty-nine patients with PA from TCH records (January 1995 to February 2005) were reviewed. Representative sections were selected for immunostaining for Ki-67 (PI) and ODMs, including MBP, platelet-derived growth factor receptor alpha, Olig-1, and Olig-2. Sections were graded semiquantitatively for intensity and extent of staining. PI was expressed as a percentage of positively stained cells out of 1000 tumor cells from the most mitotically active areas. Linear regression and Spearman rank-order correlation analysis were done. P values $< .05$ were considered statistically significant.

Results: The patients ranged in age from 8 months to 19 years (mean, 6.5 years). Cases were distributed as follows: 49 cerebellum, 7 brainstem/spinal cord, 8 hypothalamus/chiasm, 4 cerebral hemisphere, and 1 pineal gland. PI ranged from 0% to 9.5% (mean 1.4%). No significant differences in gender or tumor locations were observed. There was a significant inverse correlation between MBP expression and PI (Spearman's $P = 0.0305$, $r^2 = 0.696$, $P = 0.014$, respectively). A positive correlation was observed between PI and PDGFRalpha ($r^2 = 0.727$, $P = 0.011$).

Conclusion: An inverse relationship between MBP expression and PI is confirmed. We suggest that expression of ODMs and PI may identify clinical subsets of PA.

176. A PHASE I TRIAL OF STI571 (IMATINIB MESYLATE) IN CHILDREN WITH NEWLY DIAGNOSED POOR-PROGNOSIS BRAINSTEM GLIOMAS AND RECURRENT INTRACRANIAL MALIGNANT GLIOMAS: A PEDIATRIC BRAIN TUMOR CONSORTIUM (PBTC) REPORT

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Purpose: The objectives of this study were to define the maximal tolerated dose (MTD) of imatinib with irradiation in children with newly diagnosed brainstem gliomas, and those with recurrent malignant intracranial gliomas, stratified according to use of enzyme-inducing anticonvulsants (EIACDs).

Experimental design: In the brainstem glioma stratum, imatinib was initially administered twice daily during irradiation, but because of possible association with intratumoral hemorrhage, was subsequently started two weeks after irradiation. The protocol was also amended to exclude children with prior hemorrhage.

Results: Twenty-four evaluable patients received therapy before the amendment, and 3/6 with a brainstem tumor experienced dose-limiting toxicity (DLT), one asymptomatic intratumoral hemorrhage, one grade 4 neutropenia, and one renal insufficiency; 0/18 with recurrent glioma experienced DLT. After protocol amendment, 2/16 brainstem glioma patients and 2/11 recurrent glioma patients not receiving EIACDs experienced new hemorrhages, three symptomatic. In addition to the five hemorrhages during the DLT monitoring period, 14 patients experienced hemorrhages (eight symptomatic) thereafter. The recommended phase II dose for brainstem gliomas was 265 mg/m². Three of 27 patients with brainstem gliomas with imaging before and after irradiation, prior to receiving imatinib, had new hemorrhage, excluding their receiving imatinib. The MTD for recurrent high-grade gliomas without EIACDs was 465 mg/m² but the MTD was not established with EIACDs, with no DLTs at 800 mg/m².

Conclusion: Recommended phase II imatinib doses were determined for children with newly diagnosed brainstem glioma and recurrent high-grade glioma not receiving EIACDs. Imatinib may increase the risk of ITH although the incidence of spontaneous hemorrhages in brainstem glioma is sufficiently high that this should be considered in studies of agents in which hemorrhage is a concern.

177. NIMOTUZUMAB, A HUMANIZED H-R3 MONOCLONAL ANTI-EGFR ANTIBODY, IN THE TREATMENT OF ADVANCED HIGH-GRADE GLIOMAS IN CHILDREN AND ADOLESCENTS

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In children with refractory high-grade gliomas (HGGs) there are only a few therapeutic options and the expected life span is only several weeks. Recently novel therapeutic approaches are investigated in order to improve the survival of these patients while preserve a good quality of life. This phase II trial was designed to explore the feasibility and efficacy of nimotuzumab, a humanized h-R3 monoclonal anti-EGFR antibody, in advanced HGGs. Pediatric patients with glioblastoma multiforme, anaplastic astrocytoma, or intrinsic pontine glioma (PG) with radiologically proven progressive disease following primary or relapse treatment were eligible to the study. The treatment consisted of an induction therapy including a weekly infusion of 150 mg/m² nimotuzumab for six weeks, and in case of non-PD, a subsequent consolidation therapy of four infusions in a three-week interval. Between June 2004 and January 2006, 40 patients (median age, 11.4 years; range, 5.0 to 17.4 years) were enrolled. In the MRI of week 8, 12 of 37 evaluable patients showed response according to RECIST (PR, n = 1 and SD, n = 11) accompanied by clinical deterioration in four patients and marked clinical improvement in three. Surprisingly, nine PR/SD were observed in 18 patients with PG. Eight patients continued with the consolidation therapy and showed three PR, one SD, and four PD in week 21. No severe side effects of the antibody were observed. Repeated application of nimotuzumab is well tolerated and safe. It has cytotoxic efficacy especially in intrinsic PG. A phase III study in patients with newly diagnosed PG is planned.

178. PHASE II STUDIES OF ANTINEOPLASTONS A10 AND AS2-1 (ANP) IN CHILDREN WITH NEWLY DIAGNOSED DIFFUSE, INTRINSIC BRAINSTEM GLIOMAS

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The purpose of the studies is to evaluate the outcome of newly diagnosed diffuse, intrinsic brainstem glioma (NDBSG) in children treated with ANP in FDA-monitored phase II trials. Twenty assessable children were involved in the studies. Five patients had high-grade gliomas. Age ranged from three months to 20 years. ANP was administered intravenously daily through a subclavian venous catheter via a double-channel infusion pump. The median duration of the treatment was eight months and the average dosage of A10 was 10.0 g/kg/day and AS2-1 0.36 g/kg/day. NCI CTC were used for evaluation of toxicity and responses based on MRI and PET scans. Complete response (CR) was achieved in 30%, partial were response (PR) in 10%, stable disease in 20%, and progressive disease in 40% of patients. The overall survival (OS) at two years was 40% and five years 30%; median survival (MST) 16.4 months and the maximum survival is over 12 years. Serious toxicities included five cases of anemia and single cases of skin rash, hypokalemia, and elevation of transaminases. There were no chronic toxicities. The results compare favorably with the outcome of standard radiation therapy in combination with chemotherapy (RAT) which produced 2% CR, 31% PR, 7% two-year and 0% five-year OS, and MST 8.5 months (Mandell et al., 1999). In conclusion, ANP is well tolerated and provides encouraging results in the treatment of NDBSG. The results should be confirmed in randomized phase III trial comparing RAT and ANP scheduled to begin soon.

179. A PILOT STUDY OF HIGH-DOSE FOCAL RADIOTHERAPY AND CONCURRENT IRINOTECAN (CPT-11) FOLLOWED BY INTRAVENOUS BCNU PLUS CPT-11 FOR CHILDREN WITH DIFFUSE INTRINSIC BRAINSTEM GLIOMAS

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Purpose: To determine the feasibility and toxicity of concurrent twice-daily RT and CPT-11 followed by maintenance BCNU + CPT-11(MC) in patients (pts) with newly diagnosed brainstem glioma (BSG).