

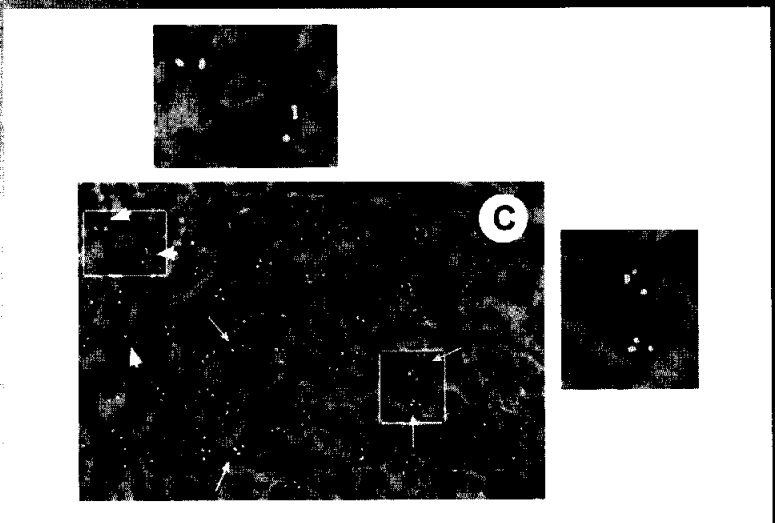
# Neuro-Oncology

## Editorial

### Basic and Translational Investigations

Abstracts from the Ninth Annual Meeting of the Society for Neuro-Oncology  
Toronto, Ontario,  
November 18–21, 2004

Abstracts from the Eleventh International Symposium on Pediatric Neuro-Oncology  
Boston, Massachusetts  
June 13–16, 2004



Official Journal of the International Association of Neuro-Oncology since 1997



Official Journal of the Japan Society for Neuro-Oncology since 2000



Official Journal of the European Association for Neuro-Oncology since 2002



Official Journal of the World Federation of Neuro-Oncology Societies since 2002

## TP-02. LONG-TERM SURVIVALS IN PHASE II STUDIES OF ANTINEOPLASTONS A10 AND AS2-1 (ANP) IN PATIENTS WITH DIFFUSE INTRINSIC BRAIN STEM GLIOMA

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Patients with diffuse intrinsic brain stem gliomas (DBSG) have poor survival, which has not substantially changed despite various new treatments. ANP consists of three active ingredients including sodium salts of phenylacetylglutamine (PG), phenylacetylisoglutamine (isoPG), and phenylacetic acid (PN). Preclinical data support that the mechanism of antineoplastic activity in DSBG involves interruption of signal transmission in the *RAS*, (PN) *AKT2*, and *TGF $\beta$ 1* (PG) pathways, activation of *p53* and *p21* tumor suppressor genes (PN) and apoptosis (PG and isoPG). The objective of this study is to determine the long-term survival of assessable patients who participated in Phase II studies with ANP and to identify which patient characteristics would predict their survival. A total of 60 patients received ANP; 46 were diagnosed with recurrent tumor after previous therapy and 14 with progressive DSBG, without prior treatment. A group of 31 patients did not meet admission criteria to the study because of a Karnofsky Performance Status (KPS) of 30 to 50; therefore, these patients were treated under Special Exceptions (SE). The overall survival for 29 patients who were admitted to the study at 2 years was 45% and at 5 years was 24%. The maximum survival is over 15.5 years (high-grade DSBG recurrent after radiation and chemotherapy). Corresponding data for SE patients are as follows: survival at 2 years, 32%; at 5 years, 16%; and maximum survival of 11 years (high-grade DSBG recurrent after radiation and chemotherapy). The progression-free survival (PFS) at one year was 41% for study patients and 29% for SE. Patient PFS is measured from the start date of study drugs to the date of progressive disease (PD), death, or the last contact with the patient. In study patients, a complete response (CR) occurred in 24%, partial response (PR) in 21%, stable disease (SD) in 21%, and PD in 34%. In the SE group, the corresponding results were as follows: CR 16%, PR 6%, SD 52%, and PD 26%. ANP was well tolerated. There were no grade 4 toxicities, and reversible grade 3 toxicities included single cases of allergic skin rash, hypertension, neutropenia, hypokalemia, and anemia. Patients in the ANP study group who were in better clinical condition and had higher KPS (60 or higher) than patients in the SE group had substantially longer overall survival and PFS and higher CR and PR rates. In conclusion, the use of ANP for DSBG compares favorably with standard radiation therapy, which offers less than a 10% survival at 2 years for newly diagnosed DSBG.