

Antineoplastons A10 and AS2-1 are synthetic analogues of naturally occurring amino acid derivatives and phenylacetate.^[1] These compounds have been examined in humans and animals for toxicity and have been shown to have antineoplastic activity in studies in cell cultures and animal models.^[2] In addition, they have been employed to treat a wide variety of neoplastic diseases since the 1970s.^[3]

An independent review of seven patients with brain tumours concluded that an association exists between antineoplon administration and objective tumour regressions.^[4] After this review, four prospective and one retrospective phase II clinical studies were authorised by the US Food and Drug Administration (FDA). In accordance with FDA guidelines, the retrospective study (CAN-1) involved patients with a diagnosis of refractory malignancy who had received previous treatment with antineoplastons. In addition, in agreement with FDA guidelines, patients enrolled in this retrospective study had to agree to participate as a condition for continuation of antineoplon therapy. The CAN-1 study divided the patients into six cohorts according to type of disease. Of all patients treated with antineoplastons for primary brain tumours, 65% enrolled in the study.

This report objectively describes the brain tumour cohort in terms of the course of the disease before and after antineoplon therapy. Antineoplon efficacy is quantified in terms of both survival and the magnitude and duration of reduction in tumour size.

Patients and Methods

Study Participants

All patients were initially evaluated and treated in Houston at the Burzynski Clinic. Follow-up of patients was performed by the clinic and also by co-investigators in the USA and Australia.

The total population of cases of primary brain tumours treated at the clinic at the beginning of the study, on 23 February 1996, was 66 patients. Of

these 66 patients, 43 were admitted to the study, but only 36 were evaluable.

The eligibility and self-selection criteria of this study did not result in an enrolled population markedly different from the initial pool of patients in terms of age, gender, diagnosis and outcome. The percentage of nonevaluable patients was higher in the group not admitted to the protocol of CAN-1. This could be explained by the lack of evaluation of patients who did not wish to participate in the study and who refused the pre-admission evaluation. However, the reason for the non-evaluability of most patients in this study was too small a tumour size or too short an interval from previous therapy.

All 36 patients enrolled in this study were diagnosed with primary brain tumours, with diagnoses being confirmed histologically. Multiple tumours were found in 14% of patients. All patients had undergone previous surgery. Disease progression or recurrent tumour before admission to the study was documented in 92% and stable tumour size in 8% of patients.

To be considered evaluable, patients must have completely recovered from surgery and have had an intertherapy interval of more than 6 weeks for radiation therapy and more than 4 weeks for chemotherapy (6 weeks for nitrosoureas). Pretreatment characteristics are listed in table I.

All patients or legal guardians signed an informed consent form approved by the FDA and the Institutional Review Board (IRB).

Treatment

Antineoplon A10 injection is a sterile solution of sodium phenylacetylglutamate (PG) and phenylacetylisoglutamate (isoPG). Each millilitre of the injection contains from 230 to 250mg of PG and from 55 to 65mg of isoPG. The combined concentration of the active ingredients PG and isoPG is $300 \text{ g/L} \pm 15 \text{ g/L}$.

Antineoplon AS2-1 injection is a sterile solution of sodium phenylacetate (PN) and PG in water that is pH-adjusted to 7.0. Each millilitre of the injection contains from 62 to 66mg of PN and from