

cept for tamoxifen, in which case the complete response rate was 3.1%. This rate was substantially lower than the 25% in the CAN-1 study. Although the percentage of stable disease (46.5%) was higher in the study with 13-*cis*-retinoic acid than in that with antineoplastons (33.3%), the progressive disease rate was higher with 13-*cis*-retinoic acid (56.2%) than with antineoplastons (22.2%). The percentage of patients with stable disease in the CAN-1 study surpassed the other studies.^[24,25]

The highest partial response rates were reported by Jeremic et al. (21%) with combination chemotherapy and by Couldwell et al. (21.9%) with tamoxifen. These rates were slightly higher than the 19.5% rate obtained with antineoplastons.^[24-27] The total response rate (complete response + partial response + stable disease) of 77.8% with antineoplastons was markedly higher compared with every study listed here.

Median time to progression (MTP) and median survival time (MST) were estimated using the Kaplan-Meier method (table II).^[27]

As shown in table II, MTP in the CAN-1 study was markedly higher compared with all the other studies. The MST was more than double compared with all the other studies. The results of this study indicated that 42% of evaluable patients are alive, and 31% are alive and showing complete or partial response. In addition to a decrease and disappearance of tumours, patients have marked improvement in their physical condition. Karnofsky performance status (KPS) increased in 47% of all 36 cases. Stable KPS was determined in 23%, and improvement of KPS followed by worsening in 19%. Continued decline of KPS was documented in 4%.

Except for GBM, the population of patients in the remaining diagnostic groupings was too small for statistical analysis. Such analysis was attempted in GBM. The efficacy of antineoplastons in GBM was compared with the results of most recent studies in recurrent GBM with prior radiation therapy (table III). In addition to CAN-1 patients, the data are also presented for the entire population of evaluable GBM, from which CAN-1 patients were selected. The comparison showed

markedly higher complete and partial response rates, MTP and MST for patients treated with antineoplastons.

Most patients tolerated daily administration of antineoplastons A10 and AS2-1 very well, even for as long as 10 years in one patient. The dose-limiting factor for A10 seems to be the volume of intravenous fluid, and for AS2-1, it is increased sleepiness and weakness. It was determined that no relationship exists between dosage and other toxicities. A number of patients developed electrolyte abnormalities, despite normal baseline levels in all patients. In most cases these abnormalities were only laboratory values, without any change in the patient's physical condition. Electrolyte changes were intermittent in most cases. It is important to note that the ADEs were mild and did not result in prolonged interruption or discontinuation of the treatment programme. The ADEs did not persist after discontinuation of treatment. No grade 3 or 4 ADEs were reported.

Conclusion

Antineoplaston therapy produced complete or partial responses in 16 of 36 (44.5%) patients with brain tumours. Compared with standard treatment, antineoplaston therapy was associated with prolonged survival time and prolonged time to disease progression.

The described cohort study, requested by the FDA, provided a preliminary mechanism to identify the types of brain tumours that may respond to antineoplastons A10 and AS2-1. The weaknesses of the study included its retrospective nature, a heterogeneous patient population according to histology, pretreatment modalities, times and sites of relapse. This clinical trial was not a controlled prospective study. From the entire population of 66 patients, only 36 evaluable patients were selected. It is understandable that the statistical value of these results is inferior to prospective trials. However, the authors decided to publish the results of this trial based on a substantial number of objective responses with long-term survival, which may be of interest to physicians treating brain tumours.