

## *Risk and Safety*

Antineoplastons A10 and AS2-1 are basically nontoxic in animal tests. Phase I studies of A10 and AS2-1 began in April 1980 and proved lack of significant toxicity.<sup>1,2</sup> The incidence of adverse drug reactions is arrived from data on 1216 patients with various types of malignancies treated under IND #43,742. Most patients who participated in the clinical studies or were treated under Special Exceptions had advanced cancer with short life expectancies. In many patients it was difficult to identify whether the side effects were due to the advanced stage of the disease or to antineoplastons. The most important adverse reaction was serious hypernatremia, which occurred in 0.8% of patients.

Additional side effects were usually mild and included increased diuresis and slight thirst, hypochloremia, hypocalcemia, hypomagnesemia, hypokalemia, nausea and vomiting, anemia, leucopenia, thrombocytopenia, allergic reaction, febrile reaction, peripheral neuropathy, somnolence, confusion, headaches, vertigo, slurred speech, tinnitus and decreased hearing, and decreased and blurred vision.

## *Efficacy*

The initial Phase II studies in astrocytoma and high-grade glioma began in 1988 and 1990 and were conducted outside IND process. Astrocytoma study included 20 patients and most of them (15) were diagnosed with Grade 3 astrocytoma. The complete and partial responses occurred in 30% of patients; stable disease, 50%; and progressive disease, 20%.<sup>6</sup> The study in high-grade glioma involved 12 patients diagnosed with glioblastoma multiforme and anaplastic astrocytoma. Thirty-three percent of patients obtained complete and partial responses. Stable disease and progressive disease were determined in 33% of patients.<sup>7</sup>

The first FDA-supervised Phase II study included 36 evaluable patients diagnosed with glioblastoma multiforme (39% of patients), anaplastic glioma (36%), low-grade glioma (14%), PNET (8%) and malignant meningioma (3%). Complete responses were documented in 25%; partial responses, 19.5%; stable disease, 33.3%; and progressive disease, 22.2%. The median survival time from the first day of treatment is approximately 3 years.

In FDA-controlled Phase II studies in astrocytoma in 80 evaluable patients complete and partial responses have been documented in 31%; stable disease, 41%; and progressive disease, 28%.

In a group of 37 evaluable patients with brain stem glioma, 30% obtained complete and partial responses; 40%, stable disease; and 30%, progressive disease. The responses were categorized as defined by the National Cancer Institute and required complete disappearance of all contrast-enhanced tumors on imaging studies for 4 weeks or longer for designation of complete response. More than 50% reduction was required in the sum of the products of the greatest perpendicular diameters of contrast-enhanced tumors for at least 4 weeks and no appearance of new lesions for designation of partial response. Stable disease was defined as less than 50% change (either greater or smaller) in the sum of the products of the greatest perpendicular diameters of the contrast-enhanced tumors for a minimum of 12 weeks. Progressive disease was defined as a greater than 50% increase in the sum of the products of the greatest perpendicular diameters of the contrast-enhanced tumors compared with the nadir evaluation or appearance of new lesions.