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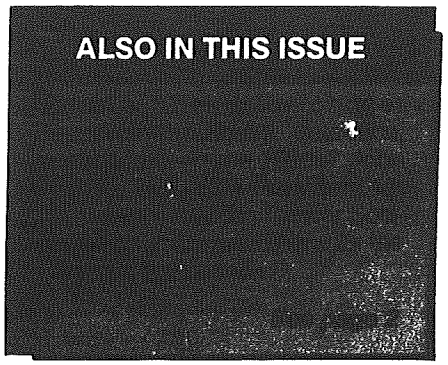
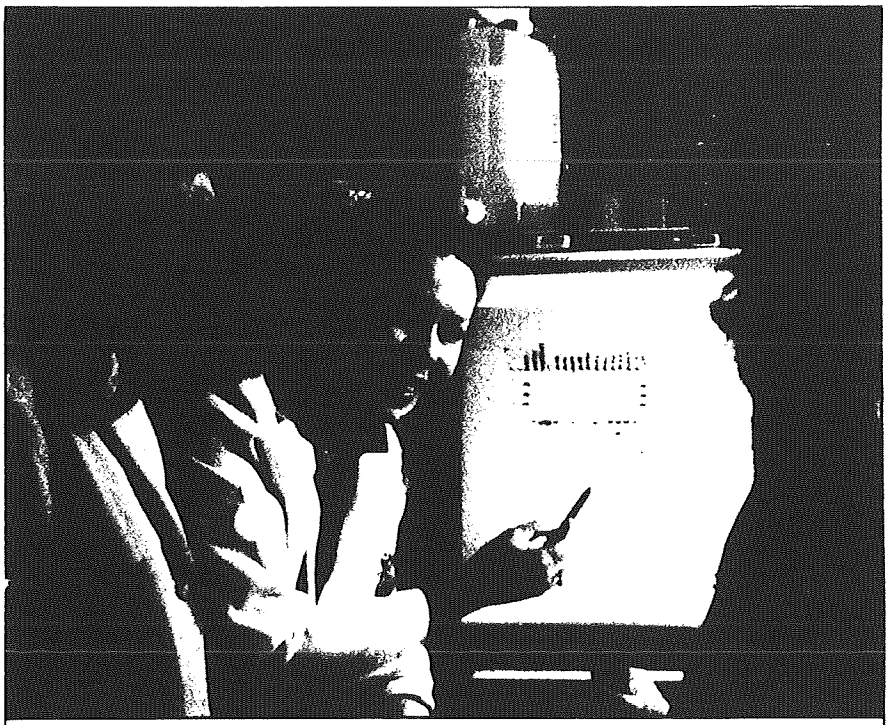


Trials Underway at Several Research Centers

Antineoplastons: New Antitumor Agents Stir High Expectations

GENEVA, Switzerland—A completely new type of antitumor agent that is nontoxic and seems to make malignant cells revert to normal is capturing the interest of cancer clinical investigators.

The agents, known as antineoplastons, are naturally occurring peptides and amino acid derivatives. They were first isolated from human urine and are now undergoing trials in several parts of the world. Preclinical and preliminary clinical results were presented here at the 9th International Symposium on Future Trends in Chemotherapy.



'Because they are natural compounds... we minimize...adverse effects.'
Dr Samid

Studies by Dvorit Samid, PhD, and her colleagues at the Uniformed Services University of Health Sciences, Bethesda, have shown that antineoplaston AS2-1 (a mixture of the sodium salts of phenylacetylglutamine and phenylacetic acid) can prevent neoplastic transformation and suppress the growth of malignant cells carrying the *ras* or *myc* oncogenes. AS2-1 profoundly inhibits oncogene expression and the proliferation of malignant cells without exhibiting any toxicity toward normal cells, reported Dr Samid.

Terminal Differentiation

The antineoplaston can actually induce terminal differentiation, she continued. It restores collagen expression in fibrosarcoma cells, induces hemoglobin production in an erythroleukemia line, and turns embryonic mesenchymal cells into fat cells.

"Such a dramatic phenomenon is seldom seen," Dr Samid noted. "One other chemotherapeutic drug—azacytidine—also induces terminal differentiation; however, it also causes tumor progression. AS2-1, in all our systems tested, induced differentiation and did not induce tumor progression. I am very excited about these findings.

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Antineoplastons Stir High Expectations (Continued from page 1)

There are a lot of questions to be answered, but I think that what we see is rather striking."

Dr Samid stressed that AS2-1 does not kill cancer cells.

"It has a direct antitumor activity, inducing phenotypic reversion, reprogramming the biology of the tumor cell—not killing it but making it behave more normally."

Other speakers at the same session presented the results of the use of antineoplastons in patients with cancer refractory to other forms of therapy. Hideaki Tsuda, MD, from Kurume University, Japan, has been studying antineoplaston A-10. His group administered cisplatin intraperitoneally followed by an A-10 infusion of 20 g/d and later 10 g/d orally to an elderly woman with inoperable metastatic

Dr Stanislaw R. Burzynski

ovarian carcinoma with massive ascites.

At the second-look operation following this therapy, the ovarian tumor could be removed easily, Dr Tsuda reported. The patient received a further 30 mg of intraperitoneal cisplatin. She no longer has ascites; her tumor marker CA 125 has dropped from 24000 to 45. "She is now enjoying her life very much without any side effects," he added. "By this kind of combination, we will be able to augment the anticancer effect and reduce the miserable side effects of anticancer agents and keep up the patient's quality of life."

Further encouraging results come from a phase 2 trial of AS2-1 and diethylstilbestrol (DES) in 14 patients with prostatic cancer refractory to hormonal therapy. The results were presented by Stanislaw R. Burzynski, MD, who was the first to isolate antineoplastons.

Both agents were administered orally in divided doses: 100 to 130 mg/kg/d of AS2-1 and 0.01 to 0.02 mg/kg/day of DES. "The treatment was tolerated well without any appreciable side effects from antineoplaston AS2-1. The only side effect was the smell of the medicine. But some patients have shown some mild side effects typical of DES.

Complete Remissions

"By the end of the study we were able to identify two cases of complete remission, three partial remissions, seven objective stabilizations, and two cases of progressive disease." Clinical improvement was accompanied by a drop in prostate cancer markers and by improvements in bone scans.

Dr Tsuda

"Currently, approximately 2 years after the beginning of the study, two patients are in complete remission. Two partial remission cases are now approaching complete remission...Two patients in the stabilization group are now approaching partial remission."

Dr Burzynski suggested some mechanisms by which the antineoplastons may exert their effects. By forcing the malignant cells to differentiate and enter a normal cell cycle, they hasten cell death. Ultimately, all the malignant cells will become more normal and die.

A further explanation is that the phenylacetic acid in the antineoplaston formulation conjugates with the l-glutamine in the cell to form phenylacetylglutamine. This reduces glutamine levels. The phenylacetylglutamine also inhibits protein synthesis by competing with the glutamine that remains. Dr Burzynski explained that cancer cells require more glutamine than normal cells.

In her summation, Dr Samid, who co-chaired the session, said that antineoplaston therapy restored to the body "those natural compounds that have anticancer activity. Because they are natural compounds, the body tolerates them well, and therefore, we minimize the problem of adverse effects." Antineoplastons, she concluded, "could be a very valuable, effective, and safe approach to cancer therapy."