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SYNTHETIC VERSION OF SCORPION VENOM DELIVERS RADIOACTIVE IODINE TO MALIGNANT BRAIN TUMORS

LOS ANGELES (EMBARGOED UNTIL JULY 28, 2006 AT 6:00 P.M. EDT) – A new method of delivering a dose of radioactive iodine – using a man-made version of scorpion venom as a carrier – targets deadly brain tumors called gliomas without affecting neighboring tissue or body organs. After a Phase I clinical trial conducted in 18 patients showed the approach to be safe, a larger Phase II trial is underway to assess the effectiveness of multiple doses.

Adam N. Mamelak, M.D., a neurosurgeon at Cedars-Sinai Medical Center’s Maxine Dunitz Neurosurgical Institute, led the Phase I trial and is first author of an article in the August issue of the *Journal of Clinical Oncology*.

The key ingredient is TM-601, a synthetic version of a peptide, or protein particle, that naturally occurs in the venom of the Giant Yellow Israeli scorpion. TM-601 binds to glioma cells and has an unusual ability to pass through the blood-brain barrier that blocks most substances from reaching brain tissue from the bloodstream.

“We’re using the TM-601 primarily as a carrier to transport radioactive iodine to glioma cells, although there are data to suggest that it may also slow down the growth of tumor cells. If studies continue to confirm this, we may be able to use it in conjunction with other treatments, such as chemotherapy, because there may be a synergistic effect. In other words, TM-601’s ability to impede cancer growth could allow us to reduce the dose of chemotherapy to achieve a therapeutic effect,” said Mamelak, who serves as co-director of the Pituitary Center at Cedars-Sinai.

About 17,000 Americans are diagnosed with gliomas each year. The tumors are extremely aggressive and deadly, with only eight percent of patients surviving two years and three percent surviving five years from time of diagnosis. Even when surgery is performed to remove a glioma, some cancer cells invariably remain behind and proliferate.

“Despite advances in surgical technology, radiation therapy and cancer-killing drugs, length of survival has remained virtually unchanged for patients with gliomas,” said Keith L. Black, M.D., director of the Maxine Dunitz Neurosurgical Institute and interim chair of Cedars-Sinai’s Department of Neurosurgery. “Only in the recent past have we begun to discover some of the molecular, genetic and immunologic mechanisms that enable these deadly cancer cells to evade or defy our treatments, and we are developing innovative approaches, such as this one, that capitalize on these revelations.”

Patients who consented to participate in the Phase I study first underwent tumor-removal surgery. Fourteen to 28 days later, a single, low dose of radioactive iodine (¹³¹I) attached to TM-601 was injected through a small tube into the cavity from which the tumor had been removed.

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Although TM-601 had been tested in earlier laboratory and animal experiments, it had never been given to humans. Therefore, the primary objective of this study was to document that ¹³¹I-TM-601 could be administered to humans safely. In addition, the researchers sought to begin to assess the drug's anti-tumor effect and dosing standards. Six patients agreed to receive additional doses at one of three different levels (.25 mg. of TM-601, .5 mg. of TM-601, and 1 mg. of TM-601, each carrying the same amount of iodine).

“In this first human trial, treatment of patients with recurrent high-grade glioma with a single intracavitary dose of ¹³¹I-TM-601 was well tolerated to the maximum dose Very few adverse side effects occurred during the initial 22-day observation period, suggesting the dosing level of peptide used in this study is safe and well-tolerated in humans,” the article states.

While median length of survival for all patients was 27 weeks, two patients, women in their early 40s, had a “complete radiographic response,” meaning there was no evidence of residual tumor according to magnetic resonance imaging scans. The patients were still alive beyond 33 and 35 months after surgery, despite the low dose of TM-601 and radiation levels that were below expected therapeutic levels.

Analyses also showed that most of the radioactivity delivered by the drug left the region within 24 hours of administration. That which lingered was “tightly localized to the tumor cavity and surrounding regions, suggesting discrete binding to the tumor.” The drug was eliminated primarily through the urine, with radiation doses to the thyroid and other vital organs remaining extremely low and harmless.

Mamelak said TM-601 binds to tumors other than gliomas, and this therapy will be studied in a variety of tumor types. He conducted this study with colleagues from City of Hope Cancer Center in Duarte, the University of Alabama at Birmingham, St. Louis University in Missouri, and TransMolecular, Inc., of Birmingham. TransMolecular also provided funding for the study.

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Citation: *Journal of Clinical Oncology*, August, 2006, “Phase I Single-Dose Study of Intracavitary Administered ¹³¹I-TM-601 in Adults with Recurrent High-Grade Gliomas”

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