



CEDARS-SINAI MEDICAL CENTER®

NEWS

8700 Beverly Blvd., Room 2429A ■ Los Angeles, CA 90048-1865
Office (310) 423-4767 ■ Fax (310) 423-0435

Media Contact: Sandra Van
Telephone: 1-800-880-2397
E-mail: sandy@vancommunications.com

FOR IMMEDIATE RELEASE – AUG. 15, 2004

Citation: *Clinical Cancer Research*, August 15, 2004

HIGHLIGHTS:

A type of malignant, incurable brain cancer called glioblastoma multiforme grows quickly, spreads rapidly and usually takes the lives of its victims within months of diagnosis. Although it has been the target of both conventional and experimental treatments, it has remained virtually unstoppable. Now a combination of two therapies appears to slow its progress and significantly lengthen patient survival.

IMMUNE VACCINE FOLLOWED BY CHEMOTHERAPY SLOWS INCURABLE BRAIN TUMORS, LENGTHENS SURVIVAL

LOS ANGELES (Aug. 15, 2004) – Researchers at Cedars-Sinai’s Maxine Dunitz Neurosurgical Institute have found that the combination of immunotherapy and chemotherapy significantly slowed tumor progression and extended survival of patients with glioblastoma multiforme (GBM), extremely aggressive and incurable brain tumors.

Although the exact mechanism is yet to be identified, the research team theorizes that like a one-two punch, the anti-tumor vaccine delivers an initial blow to the tumor cells which increases their vulnerability to tumor-killing drugs.

In an article published in the August 15, 2004 *Clinical Cancer Research*, the scientists say these “results suggest that chemotherapy synergizes with previous therapeutic vaccination to generate a uniquely effective treatment that slows GBM progression and significantly extends patient survival relative to individual therapies.”

The average length of survival was extended to about 26 months when patients received the combined therapies, compared to 18 months for those who received vaccine alone and 16 months for those undergoing chemotherapy alone.

Five of 12 patients (41.7 percent) who received vaccine and chemotherapy survived past the two-year point, compared with only one of 12 (8.3 percent) who received the vaccine alone and one of 12 who received chemotherapy alone. Also, two patients who underwent combined therapy lived past the three-year mark while no patients receiving either single therapy survived this long.

“We’re very excited about the results. Obviously they need to be confirmed in a randomized trial, but assuming these outcomes are reproducible, it would be extremely gratifying to see this kind of increase in

(more)

survival for such a devastating disease,” said Keith L. Black, MD, Institute director and one of five Institute researchers who authored the paper.

Patients ranged in age from 32 to 78 years, with an average of 55 years. All of those whose cases were reviewed had first undergone tumor-removal surgery and radiation therapy. One group then received chemotherapy alone, another received vaccine alone and a third group was treated with vaccine followed by chemotherapy. Those who received vaccine, either alone or in combination, were participants in dendritic-cell vaccine studies conducted between 1998 and 2001 at the Institute.

Pioneered at Cedars-Sinai in the treatment of GBM, dendritic cell immunotherapy introduces foreign proteins from surgically removed tumors to “dendritic” cells taken from a patient’s blood. Dendritic cells, also called antigen-presenting cells, are elements of the immune system that “present” foreign material to cell-killing T lymphocytes.

In the laboratory, the tumor cells are cultured with the dendritic cells to enable the immune cells to recognize cancer cells as targets for attack. When the “new,” specialized dendritic cells are injected back into the patient, they seek out remaining tumor cells and signal for T lymphocytes to destroy them.

In this study, all patients in the immunotherapy groups received three vaccines at two-week intervals. Patients in one of the clinical trials received a fourth injection six weeks later. All patients underwent magnetic resonance imaging to monitor their progress every two to three months.

Although several studies in the laboratory and in human tissue have documented the cancer-tracking and attacking abilities of dendritic cells and T lymphocytes, actual patient survival rates have remained virtually unchanged, perhaps because the tumor-killing action of T lymphocytes cannot keep pace with tumor cells that rapidly multiply and mutate.

“We know from our ongoing studies that the vaccine is able to elicit a strong anti-tumor response, but it appears that these extremely malignant tumors are inherently resistant to vaccine-elicited immune destruction alone,” explained Christopher J. Wheeler, PhD, research scientist who is the paper’s first author.

“The fact that tumors treated with dendritic cell therapy are highly sensitive to subsequent chemotherapy suggests that the vaccine either ‘primes’ the cell-death machinery or fundamentally alters the genetic or structural makeup of the tumor cells. Based on these results, it appears that this weakness can be exploited by the follow-up administration of drugs that attack the tumor’s DNA.”

Asha Das, MD, who directs the Institute’s Neuro-oncology Program and has extensive clinical and research experience, said the benefits of combined therapy appear to markedly surpass those seen in previous vaccine studies and even the most optimistic analyses of chemotherapy in the treatment of GBM. “This is the first demonstration that a vaccine-based therapy followed by chemotherapy can provide clinical improvement to a majority of treated cancer patients,” she said.

The authors went on to show that chemotherapeutic responsiveness in all vaccinated GBM patients was most strongly correlated with the size of a particular population of newly produced immune cells thought to be especially important for anti-GBM immune responses.

“Despite the limitations associated with a non-randomized study, this constitutes evidence favoring the hypothesis that anti-tumor immunity impacts GBM chemosensitivity. Based on these results, we are developing a randomized Phase III trial with other institutions to confirm whether dendritic cell vaccination followed by chemotherapy will prolong survival in patients with glioblastoma,” said John S. Yu, MD, who directs the Institute’s Stereotactic Radiosurgery Program, oversees clinical vaccine administration, and serves

as co-director of the Comprehensive Brain Tumor Program. He and Gentao Liu, PhD, contributed immune cytotoxicity analysis for the report.

Seeing such positive results against a cancer as virulent as GBM, the Cedars-Sinai researchers anticipate that similar vaccine-drug combinations may prove to be at least as effective against other types of cancers. Assuming that follow-up studies support these early findings, the dendritic vaccine-chemotherapy approach may quickly become the treatment of choice for GBM patients while the search continues for even more effective treatments.

“Until now, there has been very little in terms of therapy that makes a difference for this type of disease. What we’re seeing here for the first time is what appears to be a significant increase in survival,” said Dr. Black, who founded the Maxine Dunitz Neurosurgical Institute in 1997, directs Cedars-Sinai’s Division of Neurosurgery and the Comprehensive Brain Tumor Program, and holds the Ruth and Lawrence Harvey Chair in Neuroscience.

The study was supported by a grant from the Joseph Drown Foundation to Dr. Wheeler.

Cedars-Sinai is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, it has been named Southern California's gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities.

###

If you have received this news release in error and do not wish to receive future advisories, or if they should be directed to someone else in your organization, please call 1-800-396-1002, so we can update our records. Alternatively, you may fax your updated information or your request for removal from our list to 808-263-3364 or e-mail it to sandy@vancommunications.com.