MedicalXpress

Researchers to provide update on Phase II trial of vaccine for malignant brain tumors

June 2 2014

A multicenter team of investigators, led by researchers from the Cedars-Sinai Department of Neurosurgery, the Cedars-Sinai Maxine Dunitz Neurosurgical Institute and Dana-Farber Cancer Institute in Boston, have found in a Phase II clinical trial that an immune system-boosting therapy slowed the recurrence of glioblastoma multiforme, or GBM, the most common and deadly malignant brain tumor.

They will present their findings in an oral presentation June 1 at the annual meeting of the American Society of Clinical Oncology in Chicago.

The study included 124 newly diagnosed patients at 25 clinical trial sites in the U.S. Two-thirds of the patients were treated with ICT-107, an experimental vaccine based on immune system cells called dendritic cells that were exposed to six synthetic proteins, or antigens, known to be involved in GBM development. Immunization is intended to stimulate the immune system to detect and fight cancer cells. The remaining one-third of patients, composing a control group, received injections of their own dendritic cells that were not exposed to tumor antigens. All patients also were given standard care, including surgical tumor removal, chemotherapy and radiation therapy.

Of the 124 patients, 117 were able to participate according to study protocol, which included four initial treatments with ICT-107 followed by periodic maintenance doses. The trial was designed to evaluate overall survival statistics and progression-free survival – the period of time

between initial treatment and tumor recurrence. Glioblastomas are so aggressive and resistant to treatment, they usually return within months of surgical removal, despite standard treatments.

In the most recent results of the trial, treatment increased median overall survival by two months in patients treated according to protocol. This did not reach statistical significance, in part, researchers believe, because follow-up time has been relatively short; 45 patients remain alive for further assessment. Median progression-free survival, which increased by three months in patients receiving therapy, was statistically significant.

"This trial had two major findings. First, the time until a patient's tumor progressed was significantly extended in patients that received the vaccine therapy. The quality of life of these patients was maintained longer as well as their performance score, and they needed steroids less frequently than non-vaccinated patients. Second, we believe the vaccine may be particularly beneficial for a group of patients with the HLA-A2 type, which suggests that as we move forward, there may be advantages in targeting this population," said John Yu, MD, vice chair of the Department of Neurosurgery, director of surgical neuro-oncology, medical director of the Brain Tumor Center and neurosurgical director of the Gamma Knife Program at Cedars-Sinai. He is the abstract's senior author.

Among subgroup analyses, the study evaluated patients' human lymphocyte antigen type, whether HLA-A1 or HLA-A2. HLA categorization is used to designate genetics related to immune cells. About 60 percent of those in the trial, as in the general population, were identified as HLA-A2 patients. The researchers said HLA-A2 patients treated with ICT-107 appeared to have increased overall survival, compared to those with HLA-A1.

Among key subgroup analysis focused on variations of a gene – O-6-methylguanine-DNA methyltransferase, or MGMT – that can affect a patient's response to treatment. Glioblastoma cells with "unmethylated" MGMT tend to be less responsive to chemotherapy and radiation than those that are "methylated."

In patients with HLA-A2 and unmethylated MGMT, those in the control group had a median overall survival of about 12 months, compared with about 16 months in the treatment group. Median progression-free survival improved by 4.5 months, from about six months in the control group to about 10.5 months among those treated.

In patients with HLA-A2 and methylated MGMT, neither the control group nor the treatment group has reached a median survival point to date. However, median progression-free survival is statistically significant, with the control group at about 8.6 months and the treatment group at 24.5 months – a 16-month advantage for the ICT-107 group.

"This is the first placebo-controlled, randomized study of a vaccine for glioblastoma to show a significant benefit in a clinically meaningful endpoint, progression-free survival. In addition, the subgroup of patients with unmethylated MGMT promoter and HLA-A2 appear to particularly benefit," said Patrick Y. Wen, MD, director of the Center for Neuro-Oncology at Dana-Farber Cancer Institute and professor of Neurology, Harvard Medical School, who will present the data at the conference. He is the abstract's first author.

ICT-107 is a product of the biotechnology company ImmunoCellular Therapeutics Ltd. John S. Yu, MD, vice chair of the Department of Neurosurgery, director of the Brain Tumor Center, director of Surgical Neuro-Oncology and surgical director of the Gamma Knife Center at Cedars-Sinai, is founder, chief scientific officer and chairman of the board. Yu is a salaried employee of the company and owns stock in it.

Dendritic cell immunotherapy for GBM was first used in experimental treatment at Cedars-Sinai in 1998. Certain rights in the vaccine technology and corresponding intellectual property have been exclusively licensed by Cedars-Sinai to ImmunoCellular Therapeutics, including subsequently developed versions of the vaccine investigated in this clinical study. Cedars-Sinai also owns stock in the company.

Twenty authors, including Surasak Phuphanich, director of Cedar-Sinai's Neuro-Oncology Program, contributed to this study. One author is affiliated with ImmunoCellular Therapeutics as a consultant or adviser; one receives research funding from the company; one receives honoraria and serves in an advisory or consultant role to a company called Stemline Therapeutics; one receives honoraria from Merck. No other authors report disclosures or potential conflicts of interest.

More information: Oral presentation June 1 at American Society of Clinical Oncology annual meeting: "A randomized, double-blind, placebo-controlled phase 2 trial of dendritic cell (DC) vaccination with ICT-107 in newly diagnosed glioblastoma patients."

Provided by Cedars-Sinai Medical Center