

Authors and Disclosures

Journalist

Daniel M Keller, PhD

Daniel M. Keller is a freelance writer for Medscape.

Daniel M. Keller has no disclosures.

From Medscape Medical News Vaccine Made of Glioblastoma Lysate Prolongs Survival



Daniel M. Keller, PhD

April 21, 2011 (Denver, Colorado) — A vaccine of dendritic cells (DCs) pulsed with a lysate of autologous glioblastoma tumor cells was associated with improved patient survival compared with a vaccine of DCs pulsed with 4 glioma-associated antigens. At this time, the median survival of patients who receive the standard of care is 12 to 14 months, prompting researchers to look for better therapies. The glioblastoma lysate vaccine approach resulted in significantly longer survival times in phase 1 studies.

Speaking here at the American Association of Neurological Surgeons (AANS) 79th Annual Meeting, lead author Isaac Yang, MD, assistant professor of neurosurgery at the University of California–Los Angeles, presented the results of 2 simultaneous, prospective phase 1 clinical trials in which 34 patients with histopathologically confirmed malignant gliomas received either of the 2 forms of vaccine between 2003 and 2010.

Dr. Yang explained that DCs incorporate antigens, and "subsequently, this antigen-presenting cell interacts with the immune system to activate the immune system...to come back to recognize, to target, and to potentially destroy the brain cancer cell."

In these phase 1 studies, tumors were resected, and patients received radiation therapy and temozolomide, and then 7 weeks after surgery, DCs were collected via leukapheresis and were pulsed either with autologous whole tumor lysate or with the glioma-associated peptide antigens gp100, TRP2, her2, and survivin. Dr. Yang noted that "all 4 of these [antigens] have been reported in the literature to be overexpressed in glioblastoma."

Patients received the vaccines by injection 8 weeks after surgery (day 0) and on days 14 and 28, and then had booster injections every 3 months thereafter.

The 9 women and 25 men in the trial ranged in age from 25 to 70 years (mean, 49.3 years). The age difference between the whole-tumor lysate and glioma-associated antigen cohorts was not statistically different (50.9 vs 43.0 years, respectively; $P = .145$). All participants had to have Karnofsky performance status scores greater than 60 and tumors amenable to resection, to have tissue from which to make the vaccine.

Presenting the trial results, Dr. Yang said, "In the glioblastoma grade 4 group...overall survival in the whole tumor–pulsed lysate group is significantly improved compared to the [DCs] pulsed with peptide, and this difference was statistically significant, with a P value of .0357." Earlier results on 26 of the patients showed an overall survival of 35.5 months vs 17.5 months in favor of the whole-tumor lysate vaccine group.

Considering the entire group of 34 patients, survival at 1, 2, and 3 years for the whole-tumor lysate group was 91%, 55%, and 47% vs 50%, 33%, and 0% for the peptide antigen-pulsed DC group, respectively. Survivals of University of California–Los Angeles glioblastoma control patients receiving the current standard of care for the respective time points were 69%, 34%, and 21%. The time to progression of the 2 trial cohorts did not differ ($P = .082$).

"In summary, this suggests that...whole-tumor lysate-pulsed [DC] therapy is associated with improved overall survival compared...with specific peptide-pulsed [DC] therapy, and that the time to progression was not significantly different in these 2 groups," Dr. Yang told the audience.

He also monitored peripheral blood immune cells in the patients and found that the patients who received the whole-tumor lysate DC vaccine and who had the longest survival had decreased CD4+/CD25+ regulatory T cells ($P = .029$), which are immunosuppressors. Conversely, in the peptide-pulsed DC group, the investigators saw no change in the regulatory T cells. "This may potentially suggest a mechanism for this difference in overall survival," Dr. Yang said.

Limitations of the study are the small sample size and that it was performed in a single institution. Dr. Yang said the findings demonstrate correlation, but not causality. Furthermore, the peptides chosen for pulsing the DCs may not have been optimal antigens. Validation of the results will require multicenter phase 2/3 studies. Strengths of the study are that all data were collected prospectively, there is long-term follow-up, and the investigators monitored immune function.

Andrew Parsa, MD, PhD, associate professor in residence of neurological surgery and principal investigator of the Brain Tumor Research Center at the University of California—San Francisco, commented on Dr. Yang's study. Dr. Parsa has research experience in the development of a brain tumor vaccine, but was not involved in this study.

He said, "The key focus of immunotherapy is to identify T cells that can clonally expand and target specific antigens on the glioma target." He added that Dr. Yang and colleagues "have elegantly demonstrated to us the possibility of that by looking at specific T cell subsets.

"The importance of the study is that it's the first to endeavor to try to dissect out which of these particular vaccine strategies may be more or less effective. In essence, what Dr. Yang showed — which is what we've expected all along — is that if you have a more wide repertoire of tumor cell lysates, more wide repertoire of antigens, you're going to get a better response in terms of overall survival and T cell specificity," Dr. Parsa concluded. These results should help guide the field toward an approach of using multiple antigens to target glioblastoma, he added. Remaining questions are the optimal dosing schedule to use, and how the immune response can be amplified to improve efficacy.

Dr. Yang and Dr. Parsa have disclosed no relevant financial relationships.

American Association of Neurological Surgeons (AANS) 79th Annual Meeting: Plenary Session I. Presented April 11, 2011.

Medscape Medical News © 2011 WebMD, LLC
Send comments and news tips to news@medscape.net.