Vaccine shows therapeutic promise against advanced melanoma

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A vaccine for one of the most lethal cancers, advanced melanoma, has shown improved response rates and progression-free survival for patients when combined with the immunotherapy drug, Interleukin-2, according to researchers from The University of Texas M. D. Anderson Cancer Center.

The findings, presented today at the American Society of Clinical Oncology (ASCO), mark the first vaccine study in the disease - and one of the first in cancer overall - to show clinical benefit in a randomized Phase III clinical trial. Patrick Hwu, M.D., professor and chair of M. D. Anderson's Department of Melanoma Medical Oncology, presented the findings on ASCO's press program.

According to the American Cancer Society, melanoma has one of the fastest growing incidence rates of all cancers. In 2009, more than 68,720 people in the U.S. are projected to be diagnosed with melanoma and 8,650 will likely die from the disease. The five-year survival rates for those with regional and metastatic disease are 65 percent and 16 percent, respectively.

"Obviously, this is a disease, in its advanced setting, in need of better therapies for our patients," said Hwu, a co-investigator on the study. "While more follow up is needed, this study serves as a proof-of-principle for vaccines' role in melanoma and in cancer therapy overall. If we can use the body's own defense system to attack tumor cells, we provide a mechanism for ridding the body of cancer without destroying

healthy tissue."

During their tenure at the National Cancer Institute (NCI), Hwu and Douglas Schwartzentruber, M.D., who is currently medical director of the Goshen Center for Cancer Care, were involved in the vaccine's development and early basic and clinical studies. The peptide vaccine, known as gp100:209-217 (200M), works by stimulating patients' T cells, known for controlling immune responses.

"This vaccine activates the body's cytotoxic T cells to recognize antigens on the surface of the tumor. The T cells then secrete enzymes that poke holes in the tumor cell's membrane, causing it to disintegrate," explained Hwu.

After an NCI-led Phase II study combining the vaccine with Interleukin-2 (IL-2) showed response rates of 42 percent in metastatic melanoma patients, a Phase III randomized trial with the two agents opened more than a decade ago.

Conducting a large, multi-institutional trial with IL-2, however, had its own set of unique challenges, explained Hwu, as not all cancer centers and community hospitals are capable of administering the immunotherapy. A highly specialized therapy associated with such significant side effects as low blood pressure and capillary leak syndrome, which poses risks to the heart and lung, IL-2 is often delivered in intensive care units. Just last month, M. D. Anderson opened a special in-patient unit exclusively designed for the drug's delivery; before, the institution was offering the therapy in its ICU.

In the Phase III trial, 185 patients at 21 centers across the country were enrolled in the study. All had advanced metastatic melanoma and were stratified for cutaneous metastasis, a known indicator of response to IL-2. Patients were randomized to receive either high dose IL-2, or IL-2

and vaccine. In the IL-2 arm, 94 patients were enrolled and 93 were treated and evaluated for response; 91 were enrolled and 86 treated and evaluated in the IL-2 and vaccine arm.

The study found that those who received the vaccine had a significant response rate, 22.1 percent, and progression-free survival, 2.9 months, compared to 9.7 percent and 1.6 months respectively in those that did not. While not statistically significant, the median overall survival for those receiving vaccine trended positive, 17.6 months vs. 12.8 months.

"This is one of the first positive, randomized vaccine trials in cancer and the findings represent a significant step forward for treatment of advanced melanoma," said Schwartzentruber, the study's lead author. "However, we've learned a lot over the last decade, and we need to incorporate these new discoveries as we proceed with our validation of this vaccine."

Schwartzentruber, who with Hwu was involved in the earlier trials and the vaccine's development, will present the findings on ASCO's plenary session on May 30.

Hwu agreed that more research with the vaccine is needed, including long-term follow up of the Phase III patients, as well as researching ways to make the study inclusive of more metastatic melanoma patients.

"Right now, the vaccine only can be given to half of those with melanoma because it has to match a patient's tissue type, or HLA. A major priority for us is to figure out ways to broaden our approach and use mixtures of peptides so that more patients are eligible," Hwu said. "We also would like to improve upon it by including other immune-stimulatory agents, such as anti-CTLA4, an antibody that can take the breaks off the immune cells."

Source: University of Texas M. D. Anderson Cancer Center (news : web)