Hybrid vaccine demonstrates potential to prevent breast cancer recurrence

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A breast cancer vaccine already shown to elicit a powerful immune response in women with varying levels of HER2 expression has the ability to improve recurrence rates and is well tolerated in an adjuvant setting, according to new research from a clinical trial led by researchers at The University of Texas MD Anderson Cancer Center.

The findings, released today, will be presented on Monday, June 4 in an oral presentation at the 2012 Annual Meeting of the American Society of Clinical Oncology (ASCO). It builds on previous research showing the vaccine, known as AE37, to safely and effectively raise immunity against human epidermal growth factor receptor 2 (HER2) – an oncoprotein that promotes tumor growth and is expressed to some extent in 75-80% of breast cancer tumors.

The researchers found that patients who received the vaccination had an estimated recurrence rate of 10.3% compared to 18% in the control group at a median follow up of 22 months. This represented a 43% reduction in the risk of recurrence.

"The vaccine educates the immune system to recognize HER2 as an invader," said Elizabeth Mittendorf, M.D., assistant professor in the Department of Surgical Oncology at MD Anderson and the trial's national principal investigator. "By introducing it into women who have had breast cancer, our goal is to instruct the immune system to immediately recognize any recurring cancer cells and orchestrate an attack."

Building a Powerful Vaccine

The AE37 peptide vaccine used in this study is a hybrid modified to increase its potency in generating an immune response specific to cancer cells expressing HER2. It consists of a fragment of the HER2 protein (AE36), a MHC Class II epitope, linked to an Ii-Key peptide. Together, they work to stimulate a robust CD4+ T cell response, prompting the components of the immune system to seek and destroy tumor cells.

To help T cells better recognize AE37, researchers also paired the vaccine with an immune stimulant known as granulocyte/macrophage colony stimulating factor (GM-CSF). The vaccine is injected under the skin similar to a tetanus shot. The initial series consists of inoculations given monthly for six months followed by four cycles of boosters every six months.

Preventing Breast Cancer Relapse

Most experimental drugs are first evaluated in patients with metastatic disease, when tumors have undergone drastic changes, including immunoescape – a mechanism that allows tumor cells to evade elimination by the immune system. "There's very little chance a single peptide vaccine like AE37 will overcome a tumor at this stage of disease," said Mittendorf. "For this reason, it's more realistic to use the vaccine to prevent recurrence rather than to treat a large mass of already present cancer cells."

In the Phase II randomized clinical trial of 201 disease-free breast cancer patients, 103 women received the AE37 peptide plus GM-CSF adjuvantly; a control group of 98 patients received GM-CSF alone. All patients had varying levels of HER2 expression.

Results showed that the vaccine was well tolerated in the patients and toxicity was minimal; short-term side effects included redness at the injection site, flu like symptoms and bone pain. In addition to being consistent with earlier data which showed a significant immune response to the vaccine, the study also revealed how the vaccine affects recurrence rates.

The vaccine appears to prevent recurrence and work in women with any level of HER2 expression. Further, the findings draw parallels to other vaccines we now have advanced to later phase trials, Mittendorf said. MD Anderson currently has three different types of HER2-based peptide vaccines in various stages of testing and development. AE37 is the only one that targets CD4+ T cells.

"Off the Shelf" Capability

Among the benefits of a peptide-based vaccine are that it's simple to produce and administer, and that it can be easily exported to the community compared to other available vaccines. Mittendorf noted whereas dendritic cell vaccines require patients to go to the hospital for a large blood draw that is shipped to a processing center – a complicated and expensive process – peptide vaccines can be administered to patients "off the shelf."

The vaccine possibly offers advantages to today's adjuvant therapies as well. "Adjuvant therapies currently used for breast cancer are taken ongoing. Otherwise, their effect to block cancer development is diminished," said Mittendorf. "In theory, once a response is generated with immunotherapy, we can expect a longer lasting therapeutic effect without repeated dosing.

"This is an exciting time for immunotherapy as we transfer knowledge from the lab to clinic. There's a renewed enthusiasm to manipulate the

immune system therapeutically – from vaccines and antibodies to combining these modalities and improving response rates."

The findings will be presented at ASCO by Timothy J. Vreeland, M.D., resident at Brooke Army Medical Center. The trial is funded in part by Antigen Express, the company that licenses the vaccine technology. Based on this study, Antigen Express plans to apply for a special protocol assessment from the US Food and Drug Administration to continue Phase III research needed on the vaccine.

Provided by University of Texas M. D. Anderson Cancer Center