Preliminary Breast Cancer Vaccine Study Shows Promise

By Charles Bankhead

A vaccine designed to treat breast cancer has performed surprisingly well in an initial clinical study.

In a phase II trial of 186 patients, the vaccine targeting the HER2/neu E75 peptide reduced the risk of recurrence by 50% in 101 breast cancer patients who were clinically disease free after treatment compared with those who were not treated with the vaccine. Immunized patients also had about a 20% improvement in disease-free survival, according to a presentation at the San Antonio Breast Cancer Symposium in December, though this preliminary finding still needs to be tested in a randomized controlled trial.

“Never did I think that a vaccine that was made up of a single peptide from a single antigen would be sufficient to give us a clinical response or an alteration in clinical recurrence,” said Col. George E. Peoples, M.D., an oncologist at Brooke Army Medical Center in San Antonio.

Because the research is in its early stages, the scientists don’t yet know how long the protective effect of the vaccine might last, he said. Immunized patients appear to need a booster after about 6 months, a hypothesis that an ongoing investigation is evaluating.

The E75 vaccine is just one of several breast cancer vaccines in development, according to Philip Arlen, M.D., from the laboratory of tumor immunology and biology at the National Cancer Institute’s center for clinical research in Bethesda, Md. The research is focused on two different areas. One produces preventive vaccines against viruses that are known to cause certain types of cancer. Probably the best-known example is the human papillomavirus vaccine, which was recently approved for cervical cancer prevention. The other category centers on preventing cancer recurrence after initial treatment, the strategy reflected in the studies of the E75 vaccine, Arlen said.

Those treatment vaccines target a variety of different molecules, proteins, and protein fragments associated with tumor development and growth. The E75 vaccine, for example, targets a specific tissue type through a fraction of the HER2/neu protein. Other vaccines target tumor-associated proteins, like the MUC-1 and CEA proteins in a vaccine Arlen has worked on.

The Future of an E75 Vaccine

According to Peoples, E75 is the most extensively studied HER2/neu peptide. It works in the vaccine by binding to the HLA A2 molecule and stimulating an immune response. In three previous clinical studies involving a total of 24 patients with metastatic breast cancer, the vaccine had shown no clear evidence of activity.

“We felt that vaccines had never been given a fair shot,” Peoples said. “In most cases, vaccines had been tested in patients with metastatic disease.”

Peoples presented combined data from two nonrandomized clinical studies involving a total of 186 patients. One study was designed to assess the vaccine’s safety, and the other the appropriate dose. Both looked at immune response and time to recurrence. The patients had no clinical indication of residual disease after their initial therapy, but they were at risk of recurrence.

The vaccine was a combination of the E75 peptide and 250 µg of granulocyte macrophage–colony-stimulating factor, an immune system stimulant. In the two trials, patients received different combinations of the two agents. The results indicate that the optimal vaccine dose is 1,000 µg.

The two studies comprised a total of 101 vaccinated patients and 85 control patients. In both trials, the vaccine was administered to HLA A2–positive patients, while HLA A2–negative patients served as controls. After a median follow-up of 24 months, the overall recurrence rate was 8.3% in the vaccinated patients and 16% in the control patients, a difference that was not statistically significant. Disease-free survival was 92.5% in the vaccinated group and 77% in the control group.

The vaccine’s investigators “believe the key is to vaccinate patients before a tumor or recurrence can be established. The sooner after completion of therapy, the better,” he said. Vaccination at that point in time gives the immune system a chance to control the small volume of disease.

Subsequent analysis of the data has revealed a distinct difference in recurrence patterns between vaccinated and control patients. Between 40% and 50% of recurrences in control patients were bone only, whereas none of the vaccinated patients had a recurrence in bone.

“We’re not sure what to make of that, but we think that bone metastases probably start from clinically occult disease that resides in the marrow,” Peoples said. “The marrow is already immunologically active, so the vaccine might allow it to clear the disease. We hope to evaluate that in future studies.”

The data also have indicated that the immunity wanes over time, so patients need a booster after about 6 months. Investigators have already begun offer to boosters to patients who completed the trials, and 25 patients have enrolled in the voluntary program.

Much more work still needs to be done. Neither trial was randomized, and few patients received the optimal 1,000-µg dose of the vaccine. The results should be considered preliminary, and these studies often are not confirmed in controlled trials.

Despite the study’s limitations, Peoples said the results provided enough encouragement to warrant considering a randomized phase III clinical trial. Discussions about the trial have begun, but nothing has been finalized.