

Four-week vaccination regimen knocks out early breast cancer tumors, researchers find

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Researchers at the Perelman School of Medicine at the University of Pennsylvania report that a short course of vaccination with an anti-HER2 dendritic cell vaccine made partly from the patient's own cells triggers a complete tumor eradication in nearly 20 percent of women with ductal carcinoma in situ (DCIS), an early breast cancer. More than 85 percent of patients appear to have a sustained immune response after vaccination, which may reduce their risk of developing a more invasive cancer in the future. The results of the study were published online this month of Cancer and in the January issue of the *Journal of Immunotherapy*.

The researchers say the results provide new evidence that therapeutic breast cancer vaccines may be most effective for early, localized disease, and when the treatment goes after a protein critical to cancer [cell survival](#).

"I think these data more than prove that vaccination works in situations where the target is right," says the study's leader, Brian Czerniecki, MD, PhD, surgical director of the Rena Rowan [Breast Center](#) at the University of Pennsylvania and Surgical Director of the Immunotherapy Program for the Abramson Cancer Center. "Previous vaccines targeted tissue antigens that were expressed on the [cancer cells](#), but were not necessary for [tumor](#) survival. So a vaccine response would cause the tumor to just stop expressing the antigen and the tumor would be fine. Here we're going after HER2/neu, which is critical for survival of early breast cancers. If we knock it out with the immune response, we cripple

the tumor cells."

Czerniecki and colleagues enrolled 27 women with HER2-positive DCIS. They isolated specialized white cells from the patients' blood using standard apheresis techniques similar to the blood donation process. Once isolated, the researchers activated the [dendritic cells](#), which are key regulators of the immune system, and primed them with small pieces of the HER2/neu protein. Each patient then received four shots, one week apart, of their personalized anti-HER2 vaccine. And two weeks later patients had surgery to remove any remaining disease, which is standard care for DCIS patients.

The new approach has several critical advantages, compared to testing a vaccine in patients with more advanced disease. First, the activated immune cells have fewer [tumor cells](#) to kill. Second, patients' immune systems are still responsive, unlike advanced cancer patients whose immune systems have been suppressed by their disease. Third, the investigators are able to see results quickly, by looking at serum and tumor biomarkers.

In fact, when the team compared pre-vaccination biopsy samples with post-vaccination surgical samples, they saw dramatic changes: Five patients had no disease visible at the time of surgery, indicating that their immune system had wiped out the tumor. Of the remaining 22 patients, HER2 expression was eliminated in half (11 patients), and reduced by 20 percent or more in another two. "We are continuing to see this pattern in our second, ongoing trial," Czerniecki says.

When the team looked at immune responses, they found that 85 percent of patients had HER2-reactive CD4 and CD8 T cells, suggesting that the patients developed a robust and relatively complete immune response after vaccination. Importantly, some patients maintained their immune responses as long as 52 months, which means that they continue to have

some protection from recurrence of HER2-positive disease – a key insurance policy for patients, since doctors currently are unable to accurately predict which women are likely to develop invasive breast cancer following a DCIS diagnosis.

The results of the study show the vaccine is safe and relatively easy for the women, with only low-grade side effects. The most common side effects were malaise (72 percent), injection site soreness (59 percent), chills or rigors (38 percent), fever (28 percent) and headaches (24 percent).

While the numbers of patients treated in the trial are relatively small, Czerniecki thinks they will have some idea whether the vaccination reduces the risk of disease recurrence within the next two years. In the meantime, the team continues enrolling patients in a larger study, is designing another study to test the approach in women with early invasive breast cancer, and also plans to test vaccination with additional antigens, including HER3 and HER1.

"I think if we target several of the HER2 family members, we'll drive the tumor to a place where it has nowhere to go," Czerniecki says.

"Basically, we'll push it over a cliff because those pathways are critical for tumor survival."

Czerniecki notes that what the team is learning in DCIS is applicable to invasive [breast cancer](#), and to other solid tumors that rely on the HER family of signaling proteins, including melanoma, lung, brain, and colon cancers.

Provided by University of Pennsylvania School of Medicine

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