

# Personalized Cancer Vaccines Show Promise Against Melanoma

Individually designed vaccines help T cells recognize specific markers on tumor cells.

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Personalized vaccines designed to target an individual's particular type of cancer cells showed good activity in people with melanoma, according to a pair of small, early studies published recently in *Nature*.

Immune-based therapy is a major new approach in oncology that works by helping the immune system fight cancer. The most commonly used immune therapies today, checkpoint inhibitors such as Keytruda (pembrolizumab) and Opdivo (nivolumab), work by taking the brakes off T cells and freeing them to attack cancer cells. A complementary approach is stepping on the accelerator, boosting T cells' ability to recognize and kill off tumor cells.

Personalized cancer vaccines are tailored to recognize the unique set of protein markers,, known as neoantigens, expressed by a tumor. Cancer cells evolve constantly as they grow, and a tumor's specific constellation of mutations determines which neoantigens it will display for recognition by the immune system. These antigens make good targets because they are not expressed on normal, noncancerous cells.

Two research groups, one led by Catherine Wu, MD, of the Dana-Farber Cancer Institute in Boston and the other headed by Ugur Sahin, MD, of the University of Mainz in Germany, reported the first findings showing that this type of vaccine could work in humans.

Both groups used gene sequencing to identify multiple neoantigens on tumors in people with melanoma, selecting those they deemed most likely to elicit an immune response. Melanoma may be especially suited for this approach because it usually develops many mutations. These antigens were used to produce an individualized vaccine for each patient.

Working with Neon Therapeutics, Wu's team developed personalized vaccines that target up to 20 tumor neoantigens. This study enrolled melanoma patients who had their tumors surgically removed but were considered at high risk for cancer recurrence.

The vaccines activated both CD4 (helper) and CD8 (killer) T cells. Four of the six patients were free of cancer recurrence 25 months after vaccination. The other two had recurrent disease and were

treated with Keytruda, after which they experienced complete remission.

The vaccines were well tolerated with few “off-target” effects on healthy cells. The most common side effects were flu-like symptoms, fatigue, rash and mild injection site reactions.

Working with BioNTech, Sahin’s team produced personalized vaccines targeting 10 neoantigens. All 13 vaccinated melanoma patients developed T cell responses, and analysis of surgically removed tumors from two of them showed that these T cells made their way inside the tumors and killed cancer cells.

Eight of these patients had no visible tumors at the time of vaccination and remained cancer-free. The other five had metastatic disease (cancer spread beyond its original site). Two of them experienced tumor shrinkage, although one had a late relapse. A third person added Keytruda and had a complete response.

Although these Phase I studies were small and the effects were modest, they offer proof of concept that this approach can offer clinical benefits. The greatest potential may come from combining personalized cancer vaccines with other types of immunotherapy, in effect releasing the brake and stepping on the accelerator simultaneously.

“Controlled, randomized Phase II clinical trials with more participants are now needed to establish the efficacy of these vaccines in patients with any type of cancer that has enough mutations to provide sufficient antigen targets for this type of approach,” Cornelis Melief, MD, of Leiden University Medical Centre in the Netherlands, wrote in a commentary accompanying the two reports.