

Personalized Vaccines Show Promise for Hard-to-Treat Cancers

Researchers report that vaccines delayed recurrence of pancreatic, head and neck, liver and brain cancers.

May 2, 2024 By [Liz Highleyman](#)

Custom-made vaccines continue to show promise for various types of hard-to-treat cancer, researchers reported at the [American Association for Cancer Research Annual Meeting \(AACR 2024\)](#) this month in San Diego.

One early trial found that pancreatic cancer patients who responded well to a personalized messenger RNA (mRNA) vaccine plus a checkpoint inhibitor continued to have a lower risk for recurrence three years later. Another study showed that people who received a customized vaccine for head and neck cancer did not relapse after more than a year and a half. Adding a DNA plasmid vaccine to a checkpoint inhibitor increased tumor shrinkage for people with liver cancer, and an engineered dendritic cell vaccine may extend survival for people with glioblastoma brain cancer.

Oncology has come a long way with targeted therapies and immunotherapies like checkpoint inhibitors and CAR-T therapies. But some types of cancer do not respond well to existing treatments—or frequently relapse after an initial response—and still have low survival rates. Adding [cancer vaccines](#) to the armamentarium could improve outcomes.

Cancer vaccines are not a new idea, but they fell out of favor after disappointing results in early studies. Now, a better understanding of how cancer develops and how the immune system responds to it, along with better immunotherapy partners, have renewed hope that therapeutic vaccines could halt disease progression, prevent relapse and perhaps even offer a cure.

Pancreatic Cancer

Vinod Balachandran, MD, of Memorial Sloan Kettering Cancer Center [presented the latest results](#) from a Phase I trial ([NCT04161755](#)) of a pancreatic cancer vaccine from BioNTech and Genentech that uses the same nanoparticle [mRNA technology](#) as the Pfizer-BioNTech COVID-19 vaccine. [Pancreatic cancer](#) is among the most deadly malignancies, with a five-year survival rate of around 10%.

Personalized vaccines train the immune system to recognize specific neoantigens (abnormal

proteins) from an individual's tumor. To produce the vaccine, scientists first sequence a sample from a surgically removed tumor and select up to 20 neoantigens that seem most likely to elicit a robust immune response. They then make a customized vaccine for each patient that delivers genetic blueprints for making these proteins.

Sixteen previously untreated patients with pancreatic ductal adenocarcinoma received the vaccine—dubbed autogene cevumeran (also known as BNT122 and RO7198457)—plus Genentech's immune checkpoint inhibitor Tecentriq (atezolizumab) after surgery; all but one also received a standard chemotherapy regimen (mFOLFIRINOX). Participants received seven weekly priming doses and two booster doses administered by intravenous injection.

[As reported last year in Nature](#), eight of the 16 patients developed strong T-cell responses against one or more tumor neoantigens. Participants with good immune responses after vaccination did not experience recurrence over 18 months of follow-up, while nonresponders relapsed after a median of 13.4 months.

This year, Balachandran presented follow-up data showing that activated T cells lasted up to three years in responders. Almost all of these neoantigen-targeting T cells were not detected prior to vaccination, suggesting that they were in fact triggered by the vaccine. Patients with persistent vaccine-induced immune responses continued to be less likely to experience cancer recurrence. Just two of the eight responders relapsed, compared with seven of the eight nonresponders.

"The latest data from the Phase I trial show that we are on the right track. This investigational mRNA vaccine can trigger T cells—the cells that mobilize anti-tumor immune responses—that may recognize pancreatic cancers as foreign," Balachandran said in a [news release](#).

Now, a randomized Phase II trial ([NCT05968326](#)), which aims to enroll 260 newly diagnosed pancreatic cancer patients after surgery, is evaluating the safety and efficacy of autogene cevumeran, Tecentriq and mFOLFIRINOX versus the chemotherapy regimen alone. The vaccine is also being tested for melanoma and colorectal cancer.

Head and Neck Cancer

Olivier Lantz, MD, PhD, of Institut Curie in Paris, and colleagues [evaluated another personalized vaccine](#), TG4050, for people with [head and neck cancer](#). This broad category includes various malignancies with different causes. Surgery and radiation for head and neck squamous cell cancer (HNSCC) can be disfiguring, current treatments offer limited effectiveness and patients have a high risk of relapse.

Unlike mRNA vaccines, Transgene's TG4050 employs a nonpathogenic poxvirus (modified vaccinia Ankara) to deliver up to 30 neoantigens unique to each patient's tumor, selected using artificial intelligence tools.

This Phase I trial ([NCT04183166](#)) included 32 patients with Stage III or IV HNSCC of the mouth throat or larynx not caused by human papillomavirus. They had undergone surgery followed by

standard adjuvant radiation and chemotherapy and achieved a complete response. Sixteen participants were randomly assigned to receive TG4050 immediately after standard treatment, while the other 16 received the vaccine if they relapsed. The vaccine was administered by subcutaneous injection once weekly for six weeks, then every three weeks for a total of 20 doses.

None of the evaluable patients in the immediate vaccine group experienced recurrence after a median follow-up of 18.6 months, Lantz reported. In contrast, three people in the deferred vaccine group relapsed at 6.2 months, 8.8 months and 18.5 months. All but one of the vaccine recipients showed evidence of activated neoantigen-specific CD4 helper and/or CD8 killer T cells, most of which were not present prior to vaccination. The number of activated T cells increased rapidly after vaccination and remained stable for up to seven months.

“A therapeutic vaccine tailored to each patient’s unique tumor may lead to strong immune responses, which could eliminate any minimal residual disease that may eventually lead to disease relapse,” Lantz said. “Studies like ours are demonstrating the potential of individualized neoantigen-based therapeutic vaccines to be a part of tomorrow’s standard of care.”

The Phase II part of the trial is expected to begin enrollment within weeks, [according to Transgene](#).

Liver Cancer

Mark Yarchoan, MD, of Sidney Kimmel Comprehensive Cancer Center, presented findings from a Phase I/II trial of a personalized vaccine for hepatocellular carcinoma (HCC), the most common type of primary [liver cancer](#). Often caused by viral hepatitis, fatty liver disease or heavy alcohol use, HCC is typically diagnosed late, and it is one of the leading causes of cancer-related death worldwide.

GNOS-PV02, from Geneos Therapeutics, is a DNA plasmid vaccine that encodes up to 40 selected tumor neoantigens plus the cytokine interleukin 12 as an adjuvant to stimulate a stronger immune response.

The GT-30 study ([NCT04251117](#)) enrolled 36 people with advanced, inoperable HCC who were previously treated with a multityrosine kinase inhibitor such as Nexavar (sorafenib). All participants received the vaccine plus the checkpoint inhibitor Keytruda (pembrolizumab). The vaccine was administered by intradermal injection followed by electroporation, an electric shock that enables it to penetrate cell membranes. They received four doses three weeks apart followed by periodic boosters.

As described in a recent [Nature Medicine report](#), 11 people (31%) experienced tumor shrinkage, about double the overall response rate of HCC patients treated with a checkpoint inhibitor alone in other studies. Three people (8%) had a complete response, eight (22%) had a partial response and nine (25%) had no further disease progression; in one case, a patient’s tumor shrank enough to be surgically removed.

Most evaluable patients (86%) had confirmed neoantigen-specific immune responses, and all 14 patients with paired baseline and on-treatment blood and tumor biopsy samples showed vaccine-

specific CD4 and CD8 effector T cells. Yarchoan presented [additional data at the AACR meeting](#), showing that 41% of evaluable patients had at least a 50% reduction in circulating tumor DNA.

The median progression-free survival time was 4.2 months, the median overall survival time was 19.9 months and the median duration of response was not reached. Treatment was intended to last for two years, but the protocol was extended because patients were still doing well, Geneos CEO Niranjana Sardesai, PhD, [told Fierce Biotech](#). The company next plans to start a randomized controlled Phase II trial comparing the vaccine plus a PD-1 checkpoint inhibitor versus the checkpoint blocker alone.

“Other recent industry trials have tested personalized cancer vaccines in patients with highly immune-sensitive tumor phenotypes and no measurable disease. In marked contrast, the GT-30 trial assesses personalized therapeutic cancer vaccines in HCC, a cancer with very low tumor mutational burden and an immune-excluded phenotype, and in patients with significant late-stage unresectable and metastatic disease,” Sardesai said in a [news release](#). “Despite the small size of this study, our results are important for the advancement of the field.”

Glioblastoma

Researcher also presented early data on a [personalized dendritic cell vaccine for glioblastoma](#), an aggressive type of [brain cancer](#) that has a median five-year survival rate of about 10%.

Joseph Georges, DO, PhD, of Banner University Medical Center Phoenix, and colleagues conducted a Phase I trial ([NCT04552886](#)) of Diakonon Oncology’s dendritic cell vaccine, dubbed DOC1021, for people with newly diagnosed or recurrent glioblastoma multiforme.

To make the vaccine, scientists collect a sample of dendritic cells from a patient, train them in a lab to recognize antigens from that individual’s tumor and inject the altered cells near cervical lymph nodes in the neck. [According to Diakonon](#), this “tricks the body into perceiving cancer cells as virally infected cells, mirroring the natural detection and elimination process for viral infections.” Study participants received the dendritic cell vaccine at one of four dose levels after standard-of-care chemotherapy and radiation.

Analysis of tumors removed during a second surgery after vaccination showed enhanced CD8 T-cell infiltration, and analysis of circulating blood cells revealed an expansion of both CD4 and CD8 memory T cells in all four patients analyzed.

After about a year of follow-up, 12 of 16 patients (88%) were still alive—well beyond the 12-month survival rate of about 50% for people treated with standard care in prior studies. The median overall survival has not yet been reached, exceeding the median survival time of 12.7 months with standard care. The first patient enrolled in October 2021 survived more than two years, the next four patients survived more than 15 months and two people remain alive at 17.5 and 20.3 months, according to a [Diakonon news release](#).

“These very encouraging results support our confidence in the potential for our dendritic cell

vaccines to significantly improve the lives of patients with the most deadly cancers,” said Diakonos CEO Mike Wicks.

A Phase II trial is expected to begin within the next year, and Diakonos is also studying the dendritic cell immunotherapy approach for pancreatic cancer and angiosarcoma.

Moving Forward

One benefit of cancer vaccines is that they are well tolerated. In these trials, adverse events were typically mild to moderate, including injection site reactions, and generally did not add much to the side effect burden of the checkpoint inhibitors or other therapies used with them.

“We are at an exciting time in new therapy development,” Elizabeth Jaffee, MD, of Johns Hopkins Kimmel Cancer Center, said in a [news release](#) about the liver cancer study. “Personalized vaccines are the next generation of vaccines that are showing promise in treating difficult cancers when given with immune checkpoint therapy.”

In addition to personalized vaccines that train the immune system to recognize an individual’s tumor, researchers are also studying off-the-shelf vaccines that use antigens, such as HER2, that are shared by people with the same type of cancer.

A caveat is that vaccines appear to work better for keeping residual cancer in check after tumors have been removed or other types of treatment have brought about remission, rather than eliminating large established tumors.

As cancer vaccines move into mid- and late-stage trials, the Food and Drug Administration (FDA) stands ready to consider them for approval. This is a new challenge because customized vaccines are based on antigens from a patient’s tumor, so each individual receives a slightly different product. Reviewing cancer vaccines will include evaluating the AI algorithms used to select neoantigens, [Fierce Biotech reports](#).

“We are ready to review—we’re open for business,” Peter Marks, MD, PhD of the FDA’s Center for Biologics Evaluation and Research said at the 2024 World Vaccine Congress in early April. “I think we would review them very much like we could review potentially a CAR-T cell or other therapeutic products.”

Click here to read a Cancer Health feature about [cancer vaccines](#).

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