Experimental mRNA Vaccine Shows Promise for Pancreatic Cancer

A personalized neoantigen vaccine from BioNTech and Roche/Genentech lowered the risk of relapse after surgery.

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A customized messenger RNA (mRNA) vaccine plus a checkpoint inhibitor and chemotherapy boosted T-cell immune responses in half of people who had received surgery for pancreatic cancer, according to a report this week in Nature. Although the study was small, these findings suggest that the vaccine may help prevent disease recurrence, advancing the growing field of cancer vaccine research.

"It's exciting to see that a personalized vaccine could enlist the immune system to fight pancreatic cancer—which urgently needs better treatments," Vinod Balachandran, MD, of Memorial Sloan Kettering Cancer Center said in an MSKCC news interview.

Pancreatic cancer is often diagnosed late, is difficult to treat and has a low survival rate. It generally does not respond well to immune checkpoint inhibitors, monoclonal antibodies that restore T-cell activity. However, some patients live for many years after diagnosis thanks to especially effective immune responses, which researchers aimed to mimic with a vaccine.

The vaccine, being jointly developed by BioNTech and Roche/Genentech, uses the same mRNA technology as the Pfizer-BioNTech and Moderna COVID-19 vaccines. mRNA vaccines use lipid nanoparticles to deliver bits of genetic material that carry instructions for specific proteins. When the vaccine is administered, human cells produce the proteins, triggering an immune response. The COVID vaccines deliver blueprints for the SARS-CoV-2 spike protein. Personalized cancer vaccines contain instructions for neoantigens, or abnormal proteins on an individual's tumor cells.

To produce the vaccine, dubbed autogene cevumeran (also known as BNT122), researchers sequence a sample from a surgically removed tumor and select neoantigens that seem most likely to elicit a robust immune response. These are then used to create a customized vaccine for each patient, a process that takes several weeks.

"When the mRNA vaccine is injected into a person's bloodstream, it causes immune cells called dendritic cells to make the neoantigen proteins. The dendritic cells also train the rest of the immune system, including T cells, to recognize and attack tumor cells that express these same

proteins," Balachandran explained in the MSKCC interview. "With the T cells on high alert to destroy cells bearing these proteins, the cancer may have a lower chance of returning."

In a Phase I clinical trial (NCT04161755), 16 people with pancreatic cancer had customized vaccines made from their tumors after surgery, containing a maximum of 20 different neoantigens. They were treated sequentially with Roche's PD-L1 checkpoint inhibitor Tecentriq (atezolizumab), the vaccine and a modified four-drug chemotherapy regimen known as mFOLFIRINOX.

As previously reported at last year's American Society of Clinical Oncology annual meeting, Balachandran's team found that eight of the 16 patients developed strong immune responses against one or more tumor neoantigens. According to the Nature report, vaccine-expanded T cells comprised up to 10% of all T cells in the blood, and the number could be further increased with a vaccine booster. These T cells lasted up to two years, Balachandran said.

What's more, participants who mounted good immune responses after vaccination showed no signs of cancer recurrence during 18 months of follow-up. In contrast, patients who did not have good immune responses relapsed after a median of 13.4 months.

"These exciting results indicate we may be able to use vaccines as a therapy against pancreatic cancer," Balachandran said. "The evidence supports our strategy to tailor each vaccine to each patient's tumor."

Treatment was generally safe and feasible, according to the study authors. Adverse events were common, but these were mostly associated with the checkpoint inhibitor and chemotherapy, not the vaccine.

Based on these promising findings, a larger international randomized trial of the vaccine regimen will start this year. Balachandran said his team is working to determine why only half of the study participants had good immune responses after vaccination and to find ways to improve response rates.

"We are encouraged by the 50% response rate observed in the Phase I trial, but additional research and clinical studies will be necessary to determine whether this investigational vaccine-based treatment approach could benefit more patients with pancreatic cancer," the Pancreatic Cancer Action Network said in a statement. "It is important to remember that clinical trials have strict inclusion criteria, so studies like this may not be appropriate for each patient."

Several other companies and academic researchers are also working on vaccines to help the immune system fight cancer. At last month's AACR Annual Meeting, researchers reported that an mRNA vaccine being developed by Moderna and Merck, given with the checkpoint inhibitor Keytruda (pembrolizumab), reduced the risk of recurrence or death in people with advanced melanoma. In February, researchers reported that an off-the-shelf plasmid-based DNA vaccine that trains immune cells to recognize the HER2 protein on tumors showed promising activity in an early study of patients with metastatic breast cancer.

Editor’s note: This article has been updated to include a statement from the Pancreatic Cancer Action Network.

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