Pancreatic Cancer Vaccine Shows Promise in Small Trial

Using mRNA tailored to each patient's tumor, the vaccine may have staved off the return of one of the deadliest forms of cancer in half of those who received it.



A colored scanning electron microscope image of pancreatic cancer cells. Credit...Anne Weston/Francis Crick Institute, via Science Source

By <u>Benjamin Mueller</u>, for the New York Times

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Five years ago, a small group of cancer scientists meeting at a restaurant in a deconsecrated church hospital in Mainz, Germany, drew up an audacious plan: They would test their novel cancer vaccine against one of the most virulent forms of the disease, a cancer notorious for roaring back even in patients whose tumors had been removed.

The vaccine might not stop those relapses, some of the scientists figured. But patients were desperate. And the speed with which the disease, pancreatic cancer, often recurred could work to

the scientists' advantage: For better or worse, they would find out soon whether the vaccine helped.

On Wednesday, the scientists <u>reported results</u> that defied the long odds. The vaccine provoked an immune response in half of the patients treated, and those people showed no relapse of their cancer during the course of the study, a finding that outside experts described as extremely promising.

The study, published in Nature, was a landmark in the yearslong movement to make cancer vaccines tailored to the tumors of individual patients.

Researchers at Memorial Sloan Kettering Cancer Center in New York, led by Dr. Vinod Balachandran, extracted patients' tumors and shipped samples of them to Germany. There, scientists at BioNTech, the company that made a highly successful Covid vaccine with Pfizer, analyzed the genetic makeup of certain proteins on the surface of the cancer cells.

Using that genetic data, BioNTech scientists then produced personalized vaccines designed to teach each patient's immune system to attack the tumors. Like BioNTech's Covid shots, the cancer vaccines relied on messenger RNA. In this case, the vaccines instructed patients' cells to make some of the same proteins found on their excised tumors, potentially provoking an immune response that would come in handy against actual cancer cells.

"This is the first demonstrable success — and I will call it a success, despite the preliminary nature of the study — of an mRNA vaccine in pancreatic cancer," said Dr. Anirban Maitra, a specialist in the disease at the University of Texas MD Anderson Cancer Center, who was not involved in the study. "By that standard, it's a milestone."

The study was small: Only 16 patients, all of them white, were given the vaccine, part of a treatment regimen that also included chemotherapy and a drug intended to keep tumors from evading people's immune responses. And the study could not entirely rule out factors other than the vaccine having contributed to better outcomes in some patients.

"It's relatively early days," said Dr. Patrick Ott of the Dana-Farber Cancer Institute.

Beyond that, "cost is a major barrier for these types of vaccines to be more broadly utilized," said Dr. Neeha Zaidi, a pancreatic cancer specialist at the Johns Hopkins University School of Medicine. That could potentially create disparities in access.

But the simple fact that scientists could create, quality-check and deliver personalized cancer vaccines so quickly — patients began receiving the vaccines intravenously roughly nine weeks after having their tumors removed — was a promising sign, experts said.

Since the beginning of the study, in December 2019, BioNTech has shortened the process to under six weeks, said Dr. Ugur Sahin, a co-founder of the company, who worked on the study. Eventually, the company intends to be able to make cancer vaccines in four weeks.

And since it first began testing the vaccines about a decade ago, BioNTech has lowered the cost from roughly \$350,000 per dose to less than \$100,000 by automating parts of production, Dr. Sahin said.

A personalized mRNA cancer vaccine developed by Moderna and Merck reduced the risk of relapse in patients who had surgery for melanoma, a type of skin cancer, the companies announced last month. But the latest study set the bar higher by targeting pancreatic cancer, which is thought to have fewer of the genetic changes that would make it ripe for vaccine treatments.

In patients who did not appear to respond to the vaccine, the cancer tended to return around 13 months after surgery. Patients who did respond, though, showed no signs of relapse during the roughly 18 months they were tracked.

Intriguingly, one patient showed evidence of a vaccine-activated immune response in the liver after an unusual growth developed there. The growth later disappeared in imaging tests.

"It's anecdotal, but it's nice confirmatory data that the vaccine can get into these other tumor regions," said Dr. Nina Bhardwaj, who studies cancer vaccines at the Icahn School of Medicine at Mount Sinai.

Scientists have struggled for decades to create cancer vaccines, in part because they trained the immune system on proteins found on tumors and normal cells alike.

Tailoring vaccines to mutated proteins found only on cancer cells, though, potentially helped provoke stronger immune responses and opened new avenues for treating any cancer patient, said Ira Mellman, vice president of cancer immunology at Genentech, which developed the pancreatic cancer vaccine with BioNTech.

"Just establishing the proof of concept that vaccines in cancer can actually do something after, I don't know, thirty years of failure is probably not a bad thing," Dr. Mellman said. "We'll start with that."

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