Are New Immune-Based Treatments for Kidney and Pancreatic Cancer on the Horizon?

More information on how well these types of treatments work and their safety should emerge over the next few years.

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New immune-based treatments for kidney and pancreatic cancer have shown promising results in two small clinical trials. In both trials, the treatments appeared to prevent cancer from returning in patients who had successful surgery to remove their tumors.

The treatments are called therapeutic cancer vaccines because they help the immune system eliminate an existing cancer.

In both trials, the treatments were made specifically for each patient based on intensive genetic analyses of their tumor samples collected during surgery. The analyses allowed the research teams to identify mutated proteins, known as neoantigens, on each patient's cancer cells. These rogue proteins can act like an activated security alarm to the immune system, alerting it that the cancer cells are threats that should be killed.

For different reasons, however, this alarm system fails. The neoantigen-based treatments are designed to step into this breach, reinforcing to the immune system that any cells displaying these mutated proteins must be eliminated.

In both studies, patients received multiple doses of their personalized treatments in the months following surgery. Giving the therapy after surgery is intended to kill any remaining cancer cells elsewhere in the body and potentially establish a small band of immune cells that can recognize and kill any cancer cells that pop up in the future.

Of the 16 patients in the pancreatic cancer trial, which was conducted at Memorial Sloan Kettering Cancer Center, 8 had a strong immune response to the treatment and 6 are still cancer-free, some more than 3 years after their initial surgery, the study team reported February 19 in Nature.

The kidney cancer trial, conducted at Dana-Farber Cancer Institute, included nine patients. No patients in the trial have had a recurrence, including four who were still cancer-free more than 3 years after their surgery, according to findings reported February 5 in Nature.

In many participants in both trials, immune cells that could recognize target neoantigens included in their vaccines were still in their blood several years after their last treatment dose. And the treatments appeared to be safe, with only mild side effects reported in both studies.

The research teams that conducted the studies said they are optimistic about the treatments' potential. But they also stressed that larger clinical trials—which have already been launched—are needed to confirm these initial results.

Fewer mutations? How about personalized neoantigen vaccines?

Immunotherapy drugs known as immune checkpoint inhibitors are regularly used to treat people with kidney cancer, primarily patients with cancer that has spread, or metastasized, throughout the body.

For people with pancreatic cancer, however, the immunotherapy revolution has yet to arrive. In clinical trials, immune-based treatments—either alone or in combination with other therapies—have failed to have any impact, including in patients whose tumors can be removed with surgery.

But tumors in people with kidney and pancreatic cancer do share something in common: They usually don't have many genetic mutations. And that's a problem because fewer mutations mean fewer neoantigens on cancer cells to draw the immune system's notice.

However, technological advances have made it easier to find potential neoantigens in any kind of cancer and to predict which neoantigens are most likely to pique the immune system's interest.

Nine people with kidney cancer, no recurrences

In the kidney cancer trial, the research team identified up to 20 neoantigens in each patient's tumor that they felt could generate the strongest immune response. They then chemically synthesized small chunks, or peptides, of the mutated proteins to use in each patient's treatment.

Shortly after surgery, each patient received one treatment dose a week for a month. They also received booster doses approximately 12 and 20 weeks later. Five participants also received a low dose of the immune checkpoint inhibitor ipilimumab (Opdivo) with each treatment dose.

The fact that the cancer has not returned in any trial participants is "encouraging and exciting," said NCI's Mark Ball, M.D., who specializes in treating kidney cancer but was not involved in the trial.

Dr. Ball cautioned, however, that it's not unusual for people with operable kidney cancer to live for several years or longer after surgery without their cancer coming back. So, it's unclear if the immune-based treatment is responsible for the lack of recurrences in the trial.

The “more compelling data” that it is a result of the treatment, he continued, comes from the analysis of patients’ immune system behavior after receiving it.

“They were clearly seeing a very strong immune response” against the neoantigens targeted by the treatment, Dr. Ball said.

Those immune responses occurred within weeks of each dose, the researchers reported, and many patients still had T cells that could recognize the targeted neoantigens several years after receiving the last dose.

“We learned which specific targets in the cancer are most susceptible to immune attack and demonstrated that this approach can generate long-lasting immune responses,” said a lead researcher on the trial, David Braun, M.D., Ph.D., formerly of Dana-Farber and now at Yale Cancer Center, in a press release.

Lasting responses in people with pancreatic cancer

For the pancreatic cancer trial, the Memorial Sloan Kettering researchers partnered with the German company BioNTech. For this trial, the neoantigens were made using mRNA technology.

For each patient’s vaccine, BioNTech constructed mRNAs for up to 20 target neoantigens and manufactured the final treatment, called autogene cevumeran, for each patient.

Patients in the study were given a single dose of the immune checkpoint inhibitor atezolizumab (Tecentriq) at the time of their first autogene cevumeran dose, followed by multiple vaccine doses over several months, and finally a short course of a four-drug chemotherapy regimen.

Eight of the 16 patients in the pancreatic cancer trial responded to the treatment, which the researchers defined as evidence that the immune system had been successfully stimulated to go after cells with the target neoantigens.

Among the eight who did not respond to the treatment, the median time until their cancer returned was about 13 months. Two of the eight responders eventually had a recurrence and the other six are still cancer-free after about 3 years.

Some responders had T cells that could still recognize the target antigens up to 4 years after their last dose.

Larger clinical trials will provide more information about safety, efficacy

In both studies, patients experienced only mild side effects. Particularly in people with kidney cancer that can be removed with surgery, Dr. Ball said, safety is paramount.

People with advanced kidney cancer “are often more willing to tolerate some [side effects] if it

means extending their life," he said. But for those whose tumors can be removed with surgery, there's a different balance to be struck.

"The odds that their cancer will recur are much lower," he said. For an immune-based therapy like this to become part of everyday treatment for these patients, he continued, "we're going to need something that's very well tolerated and safe."

More information on how well these types of treatments work and their safety should emerge over the next few years.

Building on the early results from the Dana-Farber trial, Merck and Moderna are conducting a medium-sized clinical trial testing a personalized neoantigen vaccine as an adjuvant therapy in people with operable kidney cancer.

And Genentech and BioNTech are currently running a trial testing the same mRNA-based therapy used in the Memorial Sloan Kettering trial as an adjuvant treatment in people with pancreatic cancer whose tumors can be surgically removed.

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