Democracy Dies in Darkness

A melanoma vaccine was hailed as a breakthrough. Which cancers are next?

Trials investigating mRNA vaccines for lung cancer, pancreatic cancer and other diseases are already underway.

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By Daniel Wu

The reported success of an experimental drug that uses messenger RNA to deliver personalized skin cancer vaccines could herald a wave of new treatments that harness the potent technology for a range of cancers, researchers say.

Drugmakers Moderna and Merck this summer announced that a cancer vaccine, intismeran autogene, had succeeded in a Phase 3 clinical trial in preventing the recurrence of melanoma, a result experts celebrated as a breakthrough for mRNA-based cancer treatments.

Trials investigating mRNA vaccines for lung cancer, pancreatic cancer and other diseases are already underway. They use the same approach as intismeran that might once have seemed like science fiction: analyzing a tumor sample to create a vaccine customized to target its specific mutations, so each patient receives a unique drug for their cancer.

Some of these treatments are still years or decades from fruition, if they prove to be effective, but researchers said the still-nascent field of mRNA vaccines could eventually transform our approach to cancer care.

“It is not too far-fetched to consider that in the future, when one is diagnosed with cancer, part of your specimen is going to go to the pathologist, who’s going to confirm the cancer [diagnosis],” said Dan Costin, director of the White Plains Hospital Center for Cancer Care in New York and a lead investigator in an mRNA lung cancer vaccine trial. “And the other part will be going to a laboratory where they will be preparing a special vaccine.”

How do mRNA cancer vaccines work?

mRNA-based treatments gained prominence as the platform that allowed drugmakers to speedily develop coronavirus vaccines during the pandemic.

The cancer vaccines being developed now are generally therapeutic — they treat a disease a patient already has — rather than preventive. They work in the same way other vaccines do: A patient is injected with a substance that helps the body develop immunity to it. A flu shot, for example, usually contains inactive or dead proteins from the surface of the influenza virus.

This is easier to do for pathogens, which the immune system is already hardwired to recognize as foreign to the body and attack. Vaccinating against cancer represents a different challenge, experts said.

“For cancers, these are not foreign [but] derived from our own tissues,” said Vinod Balachandran, director of the Olayan Center for Cancer Vaccines at Memorial Sloan Kettering Cancer Center. “So to develop a vaccine or a strategy to teach our immune system to recognize a specific component of our cancers as foreign, and through that, the entire cancer as foreign, is a major scientific hurdle.”

Many of the cancer vaccines currently being developed use mRNA to do this. mRNA is naturally produced by cells and tells the body how to make proteins, which perform most of the body's functions. The mRNA in cancer vaccines teaches the body to produce antigens that instruct the immune system to recognize and attack a cancer.

"We're teaching the human body a new recipe," said Jeff Coller, a professor of RNA biology and therapeutics at Johns Hopkins University.

mRNA-based vaccines are much faster to produce than those using microorganisms like a virus, which must be grown over weeks or months.

That allows researchers to quickly produce mRNA vaccines tailored to a patient's specific cancer. In trials for intismeran, experts analyzed tumor samples to identify the specific mutations in a patient's cancer, then produced and delivered a customized vaccine targeting those mutations in weeks.

As they boost the immune system, many cancer vaccines are designed to be given alongside existing immunotherapy treatments, which also spur the body's defenses to attack cancer.

Which cancers could they treat?

Lung cancer

Several trials are underway testing vaccines for other cancers, including a Phase 3 clinical trial that is investigating intismeran's effectiveness in treating early-stage lung cancer. Lung cancer is the biggest cause of cancer deaths in the United States.

Earlier-stage trials have shown some promising results in intismeran's ability to prevent recurrence of lung cancer, which can be a fatal risk for some patients, said Costin, who is a lead investigator in the trial.

"Our standard of care for most patients with early stage lung cancer is to surgically remove the cancers and then to observe the patients," Costin wrote. "But many patients with early stage lung cancer have high risk features that can portend a risk of recurrence and death as high as 30% if surgery is the only treatment."

Pancreatic cancer

Researchers recently began a Phase 2 clinical trial testing another mRNA cancer vaccine, autogene cevumeran, for pancreatic cancer. In a Phase 1 trial, the drug prompted an immune system response from eight out of 16 participants. Of those eight, seven were still alive four to six years after surgery. (The five-year survival rate for pancreatic cancer is 13 percent.)

Despite the small trial size, the results were encouraging, said Balachandran, the principal investigator for the Phase 1 trial. While lung and skin cancer are treatable with immunotherapies, around 80 percent of cancers currently cannot be treated with immunotherapy, according to Balachandran.

Pancreatic cancer, with a few exceptions for a small subset of patients, is one of them. It was “sort of thought to be the last cancer where an immunotherapy would work,” he said. If an mRNA vaccine for pancreatic cancer proved successful, it would break new ground.

Pancreatic cancer is one of the deadliest when it comes to survivability.

“If we can get an immunotherapy to work in pancreas cancer, perhaps this can enable the learnings to be extended to other cancer types,” Balachandran said. “Crack the toughest, maybe you can crack the rest.”

Early experiments for other cancers

Other cancer vaccines being evaluated in clinical trials include treatments for breast cancer and glioblastoma, a brain tumor. They also use mRNA or similar technologies to produce personalized vaccines for a patient’s cancer.

Researchers cautioned that vaccines in early-phase clinical trials could still be years away from fruition and must still be proven safe and effective on a larger scale. Moderna and Merck have also not yet released full results from the Phase 3 intismeran trial for skin cancer.

Coller of Johns Hopkins University also echoed warnings from experts across the field that the Trump administration's disparaging of mRNA vaccines, and the termination of contracts to develop mRNA vaccines, could threaten future development.

"The news of Moderna and Merck's melanoma trial is really significant because it changes the narrative," Coller said. "... You shouldn't play politics with science."

Director Jay Bhattacharya of the National Institutes of Health has said that the public lost trust in mRNA vaccines for the coronavirus. But at a December event at the Council on Foreign Relations, he said: "At NIH we have a lot of investments in mRNA technology, for instance, in cancer vaccines I think are very promising. We're still investing in those. We're going to continue to invest in those."

What readers are saying

The comments reflect a mix of skepticism and hope regarding advancements in mRNA technology for cancer treatment. Many express concern over political figures like RFK Jr. and Donald Trump, who are perceived as opposing scientific progress, particularly in mRNA research. There is... Show more

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