

mRNA Cancer Vaccines Advance to Next Stage of Clinical Trials

A personalized melanoma vaccine enters a Phase III study, while a pancreatic cancer vaccine moves on to Phase II.

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Two personalized messenger RNA (mRNA) [cancer vaccines](#), using the same technology as COVID-19 vaccines, are moving forward to the next stage of clinical trials after researchers reported promising results in earlier studies.

Modern and Merck [recently announced](#) the start of a Phase III trial testing an experimental melanoma vaccine dubbed V940 (mRNA-4157), while BioNTech's pancreatic cancer vaccine, autogene cevumeran (BNT122), is entering a Phase II trial.

To create personalized cancer vaccines, scientists genetically sequence a sample from a patient's tumor and identify neoantigens (abnormal proteins) that are most likely to trigger an immune response. mRNA vaccines use lipid nanoparticles to deliver bits of genetic material that carry instructions for specific proteins. While COVID vaccines deliver genetic blueprints for the SARS-CoV-2 spike protein, cancer vaccines contain DNA for the selected neoantigens.

Both vaccines are being tested in combination with immune checkpoint inhibitors, monoclonal antibodies that are already approved for many types of cancer. Some tumors can suppress natural immune responses; PD-1 and PD-L1 checkpoint inhibitors release the brakes and restore T-cell activity. Combining a vaccine that helps immune cells recognize cancer with a checkpoint inhibitor could have the effect of letting up on the brakes and stepping on the accelerator at the same time.

Melanoma Vaccine

V940 was tested in a Phase II trial that enrolled 157 people with Stage III or IV melanoma. Their tumors had been completely removed, but the cancer had spread to a lymph node, so they were considered at high risk for recurrence and metastasis.

At this year's American Association for Cancer Research conference in April, [researchers reported](#) that people who received the vaccine plus Merck's checkpoint inhibitor Keytruda (pembrolizumab) after surgery had a 44% lower likelihood of disease recurrence or death compared with those who received Keytruda alone. And at the American Society of Clinical Oncology (ASCO) annual meeting

June, [they reported](#) that patients treated with the vaccine plus Keytruda had a 65% lower risk of metastasis or death. The vaccine was generally safe and well tolerated; the most common side effects were injection site pain and flu-like symptoms.

“These results provide further evidence that a personalized neoantigen approach is potentially beneficial for cancer patients,” investigator Adnan Khattak, MD, of One Clinical Research and Edith Cowan University in Australia, and colleagues concluded.

V940 is the first vaccine to be tested in a late-stage trial. The pivotal Phase III study (V940-001) will enroll people with high-risk Stage IIB to Stage IV cutaneous melanoma who have not received prior systemic therapy. After surgery, they will be randomly assigned to receive V940 or a placebo injection plus Keytruda. The primary endpoint is recurrence-free survival. The study will enroll more than 1,000 people in over 25 countries. For more information, including inclusion and exclusion criteria and study sites, see [ClinicalTrials.gov study NCT05933577](#).

Pancreatic Cancer Vaccine

BioNTech—Pfizer’s COVID vaccine partner—tested its vaccine candidate in a Phase I trial in which 16 people received Roche/Genentech’s checkpoint inhibitor Tecentriq (atezolizumab), autogene cevumeran and a chemotherapy regimen known as mFOLFIRINOX after surgery for pancreatic cancer.

At last year’s ASCO annual meeting, researchers reported that half of the participants had strong T-cell responses against tumor neoantigens. Further results, [reported in the journal Nature](#), showed these responders had no signs of cancer recurrence during 18 months of follow-up. Here, too, the vaccine was generally safe and well tolerated.

“It’s exciting to see that a personalized vaccine could enlist the immune system to fight pancreatic cancer—which urgently needs better treatments,” said senior investigator Vinod Balachandran, MD, of Memorial Sloan Kettering Cancer Center (MSKCC). Balachandran describes the discovery and development of the vaccine in a [recent MSKCC news article](#).

The Phase II trial will enroll people with newly diagnosed pancreatic ductal adenocarcinoma who have not received prior systemic therapy. After complete surgical removal of the tumor, they will be randomly assigned to receive autogene cevumeran, Tecentriq and mFOLFIRINOX chemotherapy or standard treatment using mFOLFIRINOX alone. The primary endpoint is disease-free survival. The study aims to enroll 260 people at MSKCC in New York City and nearly 80 other sites around the world. For more information, see [ClinicalTrials.gov study NCT05968326](#).

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