# Moderna mRNA Vaccine Plus Keytruda Reduces Melanoma Relapse

Adding a personalized cancer vaccine to a checkpoint inhibitor lowered the risk of recurrence or metastasis by about half.

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With three years of follow-up, a customized messenger RNA (mRNA) vaccine from Moderna and Merck plus the checkpoint inhibitor Keytruda (pembrolizumab) reduced the likelihood that cancer would relapse or spread in people with advanced melanoma, according to a December 14 announcement.

The companies reported that participants who added the vaccine, dubbed mRNA-4157 (V940), to Keytruda in a Phase II clinical trial had a 49% lower risk of melanoma recurrence and a 62% lower risk of distant metastasis compared with the checkpoint inhibitor alone. The data have not yet been presented at a medical conference or published in a peer-reviewed journal.

This study "is the first demonstration of efficacy for an investigational mRNA cancer treatment in a randomized clinical trial and the first combination therapy to show a significant benefit over Keytruda alone in adjuvant melanoma," Kyle Holen, MD, Moderna's senior vice president and head of development for therapeutics and oncology, said in the news release.

The vaccine uses the same mRNA technology as the Moderna and Pfizer-BioNTech COVID-19 vaccines. These vaccines use lipid nanoparticles to deliver snippets of genetic material that carry instructions for specific proteins. While COVID vaccines contain blueprints for the SARS-CoV-2 spike protein, personalized cancer vaccines contain DNA for neoantigens, or abnormal cancer proteins selected by sequencing a patient's tumor biopsy sample.

Thus, the vaccine is designed to teach an individual's immune system to recognize and attack their specific cancer. But some tumors can suppress immune responses. Combining a cancer vaccine with Merck's Keytruda—a monoclonal antibody that restores T-cell activity—could have the effect of releasing the brakes and stepping on the accelerator at the same time.

## Study Results

The Phase IIb KEYNOTE-942 trial (NCT03897881) evaluated mRNA-4157 in 157 people with Stage III or IV cutaneous melanoma. Their tumors were completely removed, but the cancer had spread to their lymph nodes, so they were considered at high risk for recurrence and metastasis. The

participants were randomly assigned to receive either the vaccine (injections every three weeks for nine doses) plus Keytruda (infusions every three weeks for approximately one year) or Keytruda alone.

As previously reported at this year's American Association for Cancer Research annual meeting, the vaccine combination demonstrated "statistically significant and clinically meaningful improvement" over Keytruda alone. Recurrence-free survival rates at 18 months were 79% in the vaccine group versus 62% in the Keytruda monotherapy group, for a 44% reduction in the risk of recurrence or death. Another analysis presented at the American Society of Clinical Oncology annual meeting in June found that the vaccine regimen also reduced the risk of distant metastasis or death by 65%.

Now, the companies are reporting that the vaccine plus Keytruda continues to demonstrate clinically meaningful improvement over a longer period. With a median three years of follow-up, the combination reduced melanoma recurrence or death by 49% and distant metastasis or death by 62% compared with Keytruda alone.

Treatment was generally safe and well tolerated. Side effects were consistent with those observed in previous studies of Keytruda, and adding the vaccine did not substantially increase severe adverse events compared with the checkpoint inhibitor alone (25% versus 20%, respectively). The most common adverse events were fatigue, injection site soreness and chills.

In July, Moderna and Merck launched a larger Phase III clinical trial of mRNA-4157 plus Keytruda after surgery for people with high-risk advanced melanoma (NCT05933577). The companies are also testing the same combination for other tumor types. Earlier this month, they started a Phase III trial for people with non-small-cell lung cancer (NCT06077760). Moderna is also exploring other cancer vaccine candidates, including one that targets tumors with KRAS mutations. In anticipation of Food and Drug Administration approval, the company is building a new vaccine manufacturing facility in Massachusetts.

Moderna's COVID vaccine rival, BioNTech, is also working on cancer vaccines. Researchers recently reported promising results for a vaccine dubbed autogene cevumeran (BNT122) plus Roche's checkpoint inhibitor Tecentriq (atezolizumab) in people with pancreatic cancer.

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