

Personalized mRNA Vaccine Reduces Risk of Melanoma Spread

Moderna and Merck's customized neoantigen vaccine plus Keytruda lowered the risk for metastasis or death by 65%.

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A customized messenger RNA (mRNA) cancer vaccine being developed by Moderna and Merck plus the checkpoint inhibitor Keytruda (pembrolizumab) reduced the risk for metastasis in people with high-risk advanced melanoma, according to updated study results presented at the [2023 American Society of Clinical Oncology \(ASCO\) Annual Meeting](#).

Researchers reported that the vaccine, which is designed to teach an individual's immune system to recognize and attack their specific cancer, lowered the risk for distant metastasis or death by 65%—exceeding the 44% reduction in disease recurrence [recently reported at another conference](#).

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

The vaccine, dubbed mRNA-4157 (V940), uses the same [mRNA technology](#) as the Moderna and Pfizer-BioNTech COVID-19 vaccines. mRNA vaccines use lipid nanoparticles to deliver bits of genetic material that carry instructions for specific proteins. When administered, human cells produce the proteins, triggering an immune response. The COVID vaccines deliver blueprints for the SARS-CoV-2 spike protein. Personalized cancer vaccines contain DNA for neoantigens—abnormal proteins expressed by tumor cells—selected by sequencing a tumor biopsy sample; mRNA-4157 (V940) contains up to 34 different neoantigens.

Some tumors can suppress natural immune responses meant to keep them in check. Combining a vaccine that helps immune cells recognize cancer with a PD-1 checkpoint inhibitor, such as Keytruda—a monoclonal antibody that restores T-cell activity—could have the effect of letting up on the brakes and stepping on the accelerator at the same time.

The Phase IIb KEYNOTE-942 trial ([NCT03897881](#)) evaluated mRNA-4157 (V940) in 157 people with Stage III or IV cutaneous 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. They 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.

Over about two years of follow-up, adding the vaccine led to “statistically significant and clinically meaningful” improvement compared with Keytruda alone, reducing the risk of distant metastasis or death by 65%, Khattak reported.

Another analysis from the trial, evaluating minimal residual disease using circulating tumor DNA as a biomarker, found that recurrence-free survival was higher with the vaccine plus Keytruda compared with Keytruda alone.

Treatment was generally safe. Side effects were consistent with those observed in previous studies of Keytruda. Adding the vaccine did not substantially increase severe adverse events compared with Keytruda alone (25% versus 18%, respectively). The most common adverse events attributed to the vaccine or the combination were fatigue (61%), injection site pain (56%) and chills (50%).

“Patients who experience metastases at distant sites typically have worse survival outcomes and a poor prognosis, thus these results showing a reduction in the risk of distant recurrence underscore the potential of neoantigen therapy,” Moderna senior vice president Kyle Holen, MD, said in a [news release](#). “These results add to the emerging picture of how individualized neoantigen therapy may advance melanoma treatment and the promise it may hold for other types of cancer.”

A larger Phase III randomized clinical trial of mRNA-4157 (V940) is expected to start this year. Moderna and Merck also plan to expand studies to include other tumor types, including lung cancer. In addition, Moderna is exploring [other cancer vaccine candidates](#), including one that targets tumors with KRAS mutations.

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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