Adding new vaccine type to leading immunotherapy dramatically reduced melanoma recurrence

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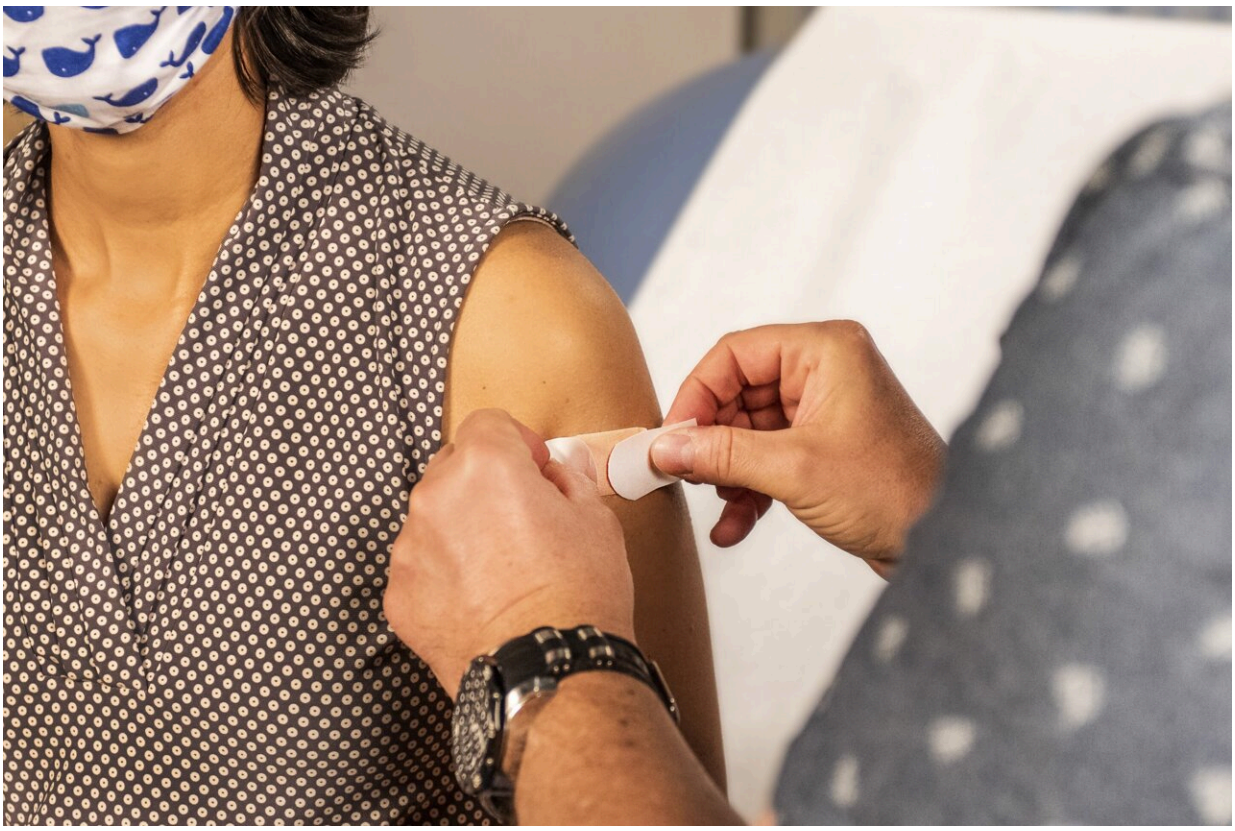

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The combination of an experimental mRNA vaccine with an immunotherapy reduced the likelihood of melanoma recurring or

causing death by 44% when compared to immunotherapy alone, a new clinical trial shows.

Led by researchers at NYU Langone Health and its Perlmutter Cancer Center, the randomized phase 2b trial involved men and women who had surgery to remove melanoma from lymph nodes or other organs and were at high risk of the disease returning in sites distant from the original cancer.

Among 107 study subjects who were injected with both the experimental vaccine, called mRNA-4157/V940, and the immunotherapy pembrolizumab, the cancer returned in 24 subjects (22.4%) within two years of follow-up, compared with 20 out of 50 (40%) who received only pembrolizumab.

"Our phase 2b study shows that a neoantigen mRNA vaccine, when used in combination with pembrolizumab, resulted in prolonged time without recurrence or death compared with pembrolizumab alone," said study senior investigator Jeffrey Weber, MD, Ph.D., the deputy director of the Perlmutter Cancer Center.

The phase 2b trial results are to be presented at the annual meeting of the American Association for Cancer Research on April 16 in Orlando, Fla.

While randomized phase 3 trials test whether a treatment is superior to current standard therapies, phase 2 trials like the current study provide preliminary reassurance that one treatment is likely to be better than another, and lead to larger studies to confirm those results. Phase 3 trials of the combination of the mRNA-4157/V940 vaccine with pembrolizumab versus pembrolizumab alone are already planned at NYU Langone and a number of other medical centers globally, said Weber, the Laura and Isaac Perlmutter Professor of Oncology in the Department of Medicine at NYU Grossman School of Medicine.

Study results so far led the United States Food and Drug Administration in February to grant Breakthrough Therapy Designation to mRNA-4157/V940 in combination with pembrolizumab, a designation designed to speed government reviews of trial results.

The current results highlight the role of immune system T cells capable of attacking viruses as well as cancers. To spare normal cells, this system uses "checkpoint" molecules on T cell surfaces to "turn off" their attack against viruses when they clear the infection. The body may recognize tumors as abnormal, but cancer cells hijack checkpoints to turn off, evade and avoid immune responses. Immunotherapies like pembrolizumab seek to block checkpoints, making cancer cells more "visible" and vulnerable again to immune cells.

Immunotherapies have become the mainstay for treating melanoma, although they do not work for all patients because melanoma cells, known for their ability to evade the immune system, can become resistant to immunotherapy. For this reason, researchers have looked at adding vaccines. While most vaccines used today are designed to prevent infections, they can also be tailored to target proteins involved in cancer.

Like the COVID-19 vaccine, mRNA-4157/V940 is based on messenger RNA, a chemical cousin of DNA that provides instructions to cells for making proteins. mRNA cancer vaccines are designed to teach the body's immune system to recognize cancer cells as different from normal cells. In designing a vaccine against melanoma, researchers attempted to trigger an immune response to specific abnormal proteins, called "neoantigens," made by cancer cells.

Because the study volunteers all had their tumors removed, researchers were able to analyze their cells for neoantigens that were specific to each melanoma and create a "personalized" vaccine for each patient. As a result, T cells were produced specific to the neoantigen proteins encoded

by the mRNA. Those T cells could then attack any melanoma cells trying to grow or spread.

Scientists involved in the study say that the personalized mRNA-4157/V940 vaccine took about six to eight weeks to develop for each patient and could recognize as many as 34 neoantigens. Severe side effects were similar between the two arms of the study, they said, with fatigue being the most common side effect specific to the vaccine reported by patients.

More information: The study was funded by Moderna Inc. of Cambridge, Mass., and Merck of Rahway, NJ. mRNA-4157/V940 is being jointly developed and commercialized by Moderna and Merck. Merck is the manufacturer of pembrolizumab. About 1.3 million Americans are currently diagnosed with some form of melanoma.

Provided by NYU Langone Health

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