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Personalized Melanoma Vaccine Cuts Relapse Risk at 5 Years

Adding a customized mRNA vaccine to checkpoint immunotherapy was associated with a 49% lower risk of melanoma recurrence or death.

June 11, 2026 By Liz Highleyman

People with advanced melanoma who received Moderna's customized messenger RNA (mRNA) vaccine and Merck's immune checkpoint inhibitor Keytruda (pembrolizumab) after surgery continue to show a sustained improvement in survival without recurrence in a mid-stage trial, according to study results presented at the American Society of Clinical Oncology Annual Meeting (ASCO 2026) and published in the Journal of Clinical Oncology.

The vaccine, intismeran autogene (also known as mRNA-4157 or V940), plus Keytruda was associated with a 49% reduction in the risk of disease recurrence or death compared with the checkpoint inhibitor alone at five years, matching previously reported three-year results.

"With each year of continued follow-up of our Phase IIb study, we gain a more complete picture of the durability of intismeran autogene in combination with Keytruda," Moderna chief development officer David Berman, MD, PhD, said in a news release. "These findings add to our confidence in the potentially transformative impact of this novel, personalized approach to cancer care made possible by mRNA technology."

Another major advance vs cancer! @ASCO #ASCO26

Personalized neoantigen mRNA vaccine 5 year follow-up vs metastatic melanoma reduced recurrence and death by 49% (on top of Keytruda)https://t.co/R5P97061FC

pic.twitter.com/1zXrSwSAzO

— Eric Topol (@EricTopol) June 1, 2026

Cancer vaccines are designed to train the immune system to recognize and attack malignant cells. They appear to be particularly good at keeping residual cancer under control and preventing recurrence after surgery to remove tumors.

Intismeran autogene, based on the same mRNA technology as Moderna's COVID-19 vaccine, contains blueprints for up to 34 neoantigens—mutated proteins expressed on cancer cells—selected by sequencing an individual patient's tumor. PD-1 checkpoint inhibitors like Keytruda restore T-cell activity against cancer. Combining a vaccine with a checkpoint inhibitor therefore effectively releases the immune system's brakes and steps on the accelerator at the same time.

The KEYNOTE-942/mRNA-4157-P201 trial (NCT03897881) is evaluating intismeran autogene for people with Stage III or IV cutaneous melanoma. The study enrolled 157 patients in the United States and Australia who had their tumors completely removed, but their cancer had spread to a lymph node, and they were considered at high risk for recurrence. More than 60% were men, the average age was approximately 60 years, about 60% had PD-L1-positive tumors (a biomarker the predicts response to PD-1 checkpoint inhibitors) and about 40% had tumors with BRAF mutations.

The participants were randomly assigned to receive intismeran autogene plus Keytruda or Keytruda alone. Those in the first group received a custom-made vaccine based on the neoantigens selected from a biopsy of their tumor. They received vaccine injections every three weeks for up to nine doses. Patients in both groups received Keytruda by IV infusion every three weeks for about one year.

Findings from the primary analysis, presented at the 2023 American Association for Cancer Research annual meeting and published in The Lancet, showed that people who received the vaccine had longer recurrence-free survival. After 18 months of follow-up, 79% of patients in the vaccine plus Keytruda group and 62% in the Keytruda monotherapy group were still alive without relapse—a 44% reduction in the risk of recurrence or death.

With an additional year follow-up, there were few new relapses, investigators reported at the 2024 ASCO annual meeting. Recurrence-free survival rates at approximately three years were 75% in the vaccine plus Keytruda group versus 56% in the Keytruda monotherapy group, a 49% risk reduction. What's more, the risk of distant metastasis or death was 62% lower in the vaccine group.

In January, Moderna and Merck announced that these results held at five years of follow-up. Matteo Carlino, MD, PhD, of the University of Sydney, presented detailed findings at ASCO 2026.

After a median 60.3 months of follow-up, people randomized to receive intismeran autogene plus Keytruda still had a 49% lower risk of melanoma recurrence or death compared with those assigned to Keytruda alone. At that time point, 69% of patients who received the combination and 49% of those on Keytruda alone were still alive and cancer-free. The risk of distant metastasis or

death was reduced by 59% in the vaccine group. Overall survival data are not yet mature, but an early exploratory analysis appears to favor vaccine recipients (92% versus 71% at five years).

Benefits were seen across subpopulations compared according to age, sex, disease stage, PD-L1 and BRAF status, tumor mutation burden and circulating tumor DNA. What's more, patients who received the vaccine showed an increase in the number and type of cancer-fighting T cells compared with those on Keytruda alone. People who remained recurrence-free had about twice the number of novel expanded T-cell clones at the long-term follow-up analysis.

Treatment was generally safe and well tolerated. Side effects were consistent with those previously seen with Keytruda alone, and there were no severe adverse events attributed to the vaccine. Immune-related adverse events occurred in 45% of people receiving the combination and 44% of those receiving Keytruda alone, showing that the vaccine does not raise the risk for these side effects.

Larger Phase III trials of intismeran autogene plus Keytruda are now ongoing for patients with high-risk advanced melanoma (INTerpath-001) and non-small-cell lung cancer (INTerpath-002, INTerpath-009 and INTerpath-014). In addition, Phase II studies are underway for other malignancies, including kidney cancer (INTerpath-004) and bladder cancer (INTerpath-005 and INTerpath-011), as well as for first-line treatment of metastatic melanoma (INTerpath-012) and lung cancer (INTerpath-013).

"Our study offers strong evidence to melanoma patients that intismeran vaccine therapy, when used in combination with immunotherapy, can demonstrably reduce their risk of having their cancer return and improve clinical outcomes," senior study author Janice Mehnert, MD, of NYU Grossman School of Medicine and Perlmutter Cancer Center, said in a news release. "Our findings also serve as encouragement to cancer researchers globally that mRNA vaccines like intismeran could work well in combination with immunotherapy for other cancers whose high rates of mutations have proven difficult to target."

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