Long-term Metastatic Melanoma Survival Dramatically Improves on Immunotherapy

Half of patients treated with Opdivo plus Yervoy combination are still alive and cancer-free a decade later.

September 17, 2024 By Dana-Farber Cancer Institute

Long-term data from a landmark international trial show about half of patients with metastatic melanoma treated with a combination of immune checkpoint inhibitors survive cancer-free for 10 years or more, according to a new report from Dana-Farber Cancer Center and Weill Cornell Medicine investigators and their colleagues.

The 10-year follow-up study, published September 15 in the New England Journal of Medicine, will bring the Phase 3 CheckMate 067 trial to a close. The trial, which followed 945 patients treated at 137 sites in 21 countries, demonstrated that combining nivolumab [Opdivo] and ipilimumab [Yervoy], immunotherapies that inhibit two different immune checkpoint proteins, dramatically improved outcomes for a condition that had been nearly universally fatal. Subsequent analyses of patient outcomes at 3, 5, and 6.5 years after the trial launched demonstrated that the effect persisted for several years for patients who responded to the treatment.

"This trial is a key part of how we talk to patients about the lasting benefits of immune checkpoint therapy and the potential of combining multiple immune therapies to improve treatment outcomes," said Dr. F. Stephen Hodi, the director of the Melanoma Center and the Center for Immuno-Oncology at Dana-Farber and the co-senior author of the study. Dr. James Larkin of The Royal Marsden Hospital in the U.K. is the other co-senior author.

In 2011, the median survival for patients with metastatic melanoma was just six and a half months. However, the emergence of immune checkpoint inhibitors, which facilitate the ability of the immune system to attack cancer, as a treatment option gradually began to increase survival. The CheckMate 067 trial demonstrated that nivolumab alone or in combination with another checkpoint inhibitor, ipilimumab, is a more effective approach than ipilimumab alone.

"This was a practice-changing trial," said first author Dr. Jedd Wolchok, the Meyer Director of the Sandra and Edward Meyer Cancer Center and professor of medicine at Weill Cornell Medicine and an oncologist at NewYork-Presbyterian/Weill Cornell Medical Center. "The median survival for this

population is now a little over six years, and people who are free from cancer progression at three years have a high likelihood of remaining alive and disease-free at the 10-year time point."

In addition to confirming long-term survival in about half of patients treated with the combination, the 10-year analysis found no new safety signals for the treatment. Some physicians worried that treatment-related health problems might emerge later because patients must continue taking the drugs long-term. But the 10-year analysis found no concerning signals of long-term toxicity. There was also no resurgence of well-documented acute toxicities and few recurrences of melanoma.

The team analyzed melanoma-specific survival and overall survival at 10 years and found the two diverge long-term, showing that metastatic melanoma survivors become increasingly likely to die of other causes as they age, an indication of long-term treatment success, according to the investigators.

"After a decade of follow-up, we can now confidently tell our patients that there are treatments available with the potential to transform metastatic melanoma into a manageable, long-term condition, instilling confidence about the future," said Dr. Hodi.

In addition to demonstrating a reassuring long-term efficacy and safety profile for this immune checkpoint inhibitor combination, the investigators hope the data will also help improve the care protocols for metastatic melanoma survivors. The data suggest that patients who are still doing well at five or even three years are likely to continue doing well, which may allow physicians to reduce the frequency of follow-up visits or tests, they said.

These long-term data from the CheckMate 067 trial may help patients with metastatic melanoma understand their prognosis. Dr. Wolchok noted that patients are often understandably very afraid or depressed by the news that their cancer spread.

"We try to reorient them toward an attitude of hope and more optimistic expectations," he said. "We can now say half of patients treated with this combination therapy will live 10 years or longer without the concern of dying from metastatic melanoma."

This study was funded by Bristol Myers Squibb (Princeton, NJ, USA), a grant (P30CA008748) from the National Cancer Institute, part of the National Institutes of Health; and a grant from the National Institute for Health Research Royal Marsden–Institute of Cancer Research Biomedical Research Centre.

This news release was published by Dana-Farber Cancer Institute on September 15, 2024.

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