Studies Show Immunotherapy Improves Long-Term Survival in Growing Number of Cancers

Researchers report good 10-year survival for people with melanoma and improvements for those with triple-negative breast cancer and bladder cancer.

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Immunotherapy, which works by enabling the body's immune system to recognize and destroy cancer cells, improves long-term overall survival in patients with advanced melanoma in results from large international studies reported at the European Society for Medical Oncology Congress (#ESMO2024).

Researchers leading the longest follow-up study to date suggest that immunotherapy offers the potential for cure in patients who respond to this treatment (1). Further clinical trials reported at ESMO 2024 show improved long-term survival with immunotherapy given before and after surgery in women with early-stage, hard-to-treat breast cancer (triple negative breast cancer) and in patients with muscle-invasive bladder cancer.

"The main message from all of these studies is that immunotherapy continues to keep its promise and hope of long-term survival for many patients with different types of cancer," said Dr. Alessandra Curioni-Fontecedro, professor of oncology at the University of Fribourg and director of oncology at the Hospital of Fribourg, Switzerland, who was not involved in the study. "At ESMO 2024 we are seeing many studies in many different cancers showing that immunotherapy can work for a long time."

Melanoma Survival

Results of a Phase III trial of immunotherapy with an anti–PD-1- based therapy showed continued long-term survival benefit in patients with advanced melanoma (1). After follow-up of at least 10 years, the median overall survival was 71.9 months (about six years) in patients randomized to combination immunotherapy with nivolumab [Opdivo] plus ipilimumab [Yervoy] in the CheckMate 067 trial. Very few of the patients showing good initial response to anti-PD-1-based immunotherapy, with no disease progression for at least three years, had died of melanoma at 10 years (10-year melanoma specific survival rate 96%). The researchers suggested that there is now a potential for cure in patients responsive to these treatments.

“The results from this trial do confirm the potential for cure with immunotherapy in patients with advanced melanoma,” agreed Dr. Marco Donia, associate professor of clinical oncology at the National Center for Cancer Immune Therapy of Denmark, Copenhagen University Hospital Herlev, Denmark, who was not a study author either. He added, “For patients who show no disease progression beyond three years, these longer-term results demonstrate that most of them never progress. The melanoma-specific survival is very high in this group of patients.”

“Importantly, the long-term survival benefit with immunotherapy is also seen in routine clinical practice, outside clinical trials,” Donia continued. “Immunotherapy has transformed advanced melanoma from something that was previously a deadly disease with a median survival of less than one year to what we see today, with half of patients surviving for many years.”

He considered this raises practical questions about how best to follow these patients up, including whether they need long-term check-ups. “It also supports their right ‘to be forgotten’ as former cancer patients after five years of being cancer-free following the end of treatment, so they don’t suffer discrimination compared to the general population when seeking financial credit.”

Breast and Bladder Cancer
Improved overall survival with immunotherapy was also reported in early-stage triple negative breast cancer (TNBC) and in muscle-invasive bladder cancer. Triple negative breast cancers are particularly difficult to treat because they do not have oestrogen or progesterone receptors or raised HER2 levels, so fail to respond to commonly used breast cancer treatments. Results showed a statically significant and clinically meaningful improvement in overall survival with immunotherapy [Keytruda, or pembrolizumab] plus chemotherapy before surgery and continued immunotherapy after surgery; the five-year overall survival rate was 86.6% in patients given immunotherapy and 81.2% in the placebo group (3).

“This study shows improvements with immunotherapy in patients with the most aggressive subtype of breast cancer, where previously we could only offer chemotherapy,” said Curioni-Fontecedro. “We had thought that breast cancer may not be sensitive to immunotherapy alone but giving it in combination with chemotherapy before surgery and then further afterwards improves overall survival in many patients. The finding suggests the possibility that the combination of treatments might lead to a sensitization of TNBC to immunotherapy.”

A similar improvement in overall survival with giving immunotherapy before surgery was seen in a study of patients with muscle-invasive bladder cancer. The Phase III NIAGARA study randomized patients to immunotherapy with durvalumab [Imfinzi] plus chemotherapy before radical cystectomy followed by continued immunotherapy or to only chemotherapy before surgery.

Patients treated with immunotherapy showed significantly longer event-free survival (hazard ratio 0.68 [95% confidence interval 0.56-0.82] $p<0.001$) and overall survival (hazard ratio 0.75 [95% CI 0.59-0.93] $p=0.0106$) compared to those receiving chemotherapy alone (4). The researchers noted that giving immunotherapy before surgery did not compromise the ability to perform radical cystectomy, which was completed in 88% of the immunotherapy group and 83% of the

comparator arm.

Looking to the future of research with immunotherapy, Curioni-Fontecedro suggested, “We still have some major questions that are unanswered. The first is understanding why cancers recur in some patients despite initial response to immunotherapy. We still don’t understand how resistance to immunotherapy can occur in some patients. We need to understand what happens in these patients, what are the mechanisms of resistance and how we can overcome them.”

She suggested that it is important that clinical researchers and pharmaceutical companies all work together to approach the issue of resistance to immunotherapy effectively. “As long as the issue of resistance is investigated in isolation, looking at individual immunotherapy agents, it will not be enough. We should all put our forces together to improve understanding and promote better treatment for the future.”

References

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