

Some Patients May Experience Durable Disease Control Even After Discontinuing Immunotherapy

Some lung cancer patients who stop immune checkpoint inhibitors due to side effects continue to see benefits.

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A subset of patients with non-small cell [lung cancer](#) (NSCLC) who discontinued immune checkpoint inhibitor (ICI) therapy due to immune-related adverse events (irAEs) continued to experience long-term disease control, [according to findings](#) published in [Clinical Cancer Research](#), a journal of the American Association for Cancer Research (AACR).

Immune checkpoint inhibitors have revolutionized the treatment landscape for NSCLC, offering significant survival benefits in both early-stage and advanced disease. However, by stimulating the immune system, ICIs can cause irAEs, such as pneumonitis, colitis, and hepatitis, which can also lead to permanent treatment discontinuation.

“When immunotherapy activates the immune system, the goal is to selectively target cancer cells. But this activation can also cause inflammation in other organs,” said senior author [Mark Awad, MD, PhD](#), chief of the Thoracic Oncology Service at Memorial Sloan Kettering Cancer Center. “Whenever we see these side effects, we question whether we should keep giving immunotherapy or if we need to stop treatment temporarily or permanently.”

Between 3% and 12% of patients treated with a single ICI and up to 25% of patients treated with dual ICI combination therapy may need to discontinue treatment due to irAEs, Awad explained. Many of these patients face concerns about whether their cancer will progress or recur if they stop treatment.

Awad and colleagues sought to characterize the outcomes of patients with NSCLC who discontinued ICIs. In a multi-institutional cohort of 2,794 patients who were treated with ICIs alone or in combination with other therapies, approximately 10% discontinued treatment due to irAEs; among these patients, the median post-discontinuation progression-free survival (PFS) was 12.7 months, and the median post-discontinuation overall survival (OS) was 43.7 months.

“These outcomes suggest that patients can experience prolonged disease control and survival

after stopping treatment due to toxicity or if side effects are impacting their quality of life,” said Federica Pecci, MD, a research fellow at Dana-Farber Cancer Center and first author of the study.

Next, the researchers evaluated clinical and pathological characteristics that were associated with longer PFS and OS after discontinuation.

Among patients who received treatment before discontinuing for less than three months, between three and six months, and more than six months, the median PFS after discontinuation was 6.2 months, 13.9 months, and 25.8 months, respectively; the median OS after discontinuation was 21.7 months, 42.7 months, and 86.9 months, respectively.

In a multivariable analysis, predictors of longer post-discontinuation PFS included high PD-L1 expression, a complete or partial response (CR/PR) to treatment, and a treatment duration of either three to six months or more than six months before discontinuation. Furthermore, factors associated with prolonged post-discontinuation OS were nonsquamous histology, CR/PR to treatment, and a treatment duration exceeding six months.

The use of steroids or other immunosuppressants to treat irAEs was not associated with a difference in PFS or OS after discontinuation in the study, suggesting that such treatments may not jeopardize the anticancer response.

“We identified clinical and pathological features that can help physicians to better understand which patients can benefit longer without any additional treatment after discontinuing for toxicity,” Pecci said. “Our study can serve as a valuable resource to support clinicians in the complex considerations of treatment discontinuation for irAEs.”

While discontinuation is clearly warranted in cases of severe irAEs, the management of grade 2 irAEs often presents a more nuanced challenge for clinicians. These findings may help physicians provide patients with a clearer, more individualized assessment of their risk of disease progression, Pecci said, taking into account factors such as treatment duration before discontinuation, response to therapy, and other clinicopathologic characteristics.

Limitations of this study include its retrospective design, which could be hindered by missing or inaccurate data annotations. Additionally, comparisons based on treatment duration before discontinuation may be confounded by an overrepresentation of long-term responders in the longer-duration groups. To mitigate this, landmark analyses and multivariable Cox regression models were used to help reduce potential biases and enhance the reliability of the findings.

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