Many Immunotherapy Recipients Experience Persistent Adverse Events

However, a majority of these chronic immune-related side effects were mild.

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Lasting immune-related side effects of PD-1 checkpoint inhibitor immunotherapy for people with advanced melanoma are quite common, according to study results published in JAMA Oncology. While most of these adverse events were on the mild end of the spectrum, few resolved by the end of the follow-up period.

“Chronic and long-lasting side effects were more common than we expected and involved a variety of often overlooked organs, like the thyroid, salivary glands and joints,” Douglas Johnson, MD, of the Vanderbilt University Medical Center in Nashville, said in a press release. “While these side effects are important to monitor and treat, anti–PD-1 therapies remain lifesaving for many patients with melanoma.”

PD-1, a receptor on T cells that regulates immunity, can sometimes be commandeered by a tumor to turn off immune responses. Checkpoint inhibitor drugs that block PD-1 or its binding partner, known as PD-L1, can release the brakes and restore T-cell activity. But these medications can also activate the immune system more broadly, causing it to attack healthy tissues. In the short term, such side effects can be severe and even fatal. But long-term effects have not been well studied.

Johnson and his colleagues analyzed various features of chronic immune-related adverse events following adjuvant, or post-surgery, therapy with the PD-1 inhibitors Keytruda (pembrolizumab) or Opdivo (nivolumab) for advanced melanoma. Events were considered chronic if they continued for at least 12 weeks after therapy wound up.

The team carried out a multicenter study involving 387 participants across eight centers in the United States and Australia between 2015 and 2020. Only individuals with advanced melanoma (Stages III and IV) who had received these drugs as adjuvant therapy were included. Of the 387 people, 235 (61%) were men.

Across the study population, the team identified 267 instances of acute immune-related adverse events, meaning those occurring during the course of treatment. Of these, 52 (20%) ranged between severe and fatal (Grades 3 to 5). One individual died due to myocarditis (heart inflammation) and another due to neurotoxicity.

The researchers found that 167 individuals (43%) treated with adjuvant Keytruda or Opdivo experienced a chronic immune-related adverse event, of which only 14% cleared up. Of these 167 people, 161 (96%) reported mild to moderate (Grade 1 or 2) adverse events. Most (86%) experienced such events through the final follow-up.

These persistent adverse events were more likely to affect the endocrine glands, joints, eyes, salivary glands and peripheral nerves. On the other hand, immune-related adverse events that affected organs such as the lungs, liver, kidneys and colon were less likely to become chronic.

The persistence of side effects did not depend on age, sex, the time of onset or the need for steroids to manage inflammation.

“In this multicenter cohort study, chronic immune-related adverse events associated with anti–PD-1 therapy appear to be more common than previously recognized and frequently persisted even with prolonged follow-up, although most were low grade,” wrote the researchers. “The risks of chronic immune-related adverse events should be integrated into treatment decision-making.”

Click here to read the study abstract in JAMA Oncology.

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