ASCO and NCCN Issue Guidelines on Managing Immunotherapy Side Effects

Taking the brakes off the immune system can lead to excessive responses that harm healthy organs and tissue.

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The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have developed new guidelines to help clinicians assess and manage side effects related to immune checkpoint inhibitors, according to a recent ASCO Post report.

Checkpoint inhibitors are among the first immune-oncology therapies that work by helping the immune system fight cancer. They have shown promise for several different cancer types, including melanoma, lymphoma and bladder, kidney, liver and lung cancers. They produce long-term remission in some people, but they do not work for everyone and it is difficult to predict who will respond well.

“With rapidly increasing use of immune checkpoint inhibitors, it is imperative that clinicians are knowledgeable about their unique toxicity profiles,” said ASCO chief executive officer Clifford A. Hudis, MD. “These new guidelines from ASCO and NCCN will help our community continue to provide the highest quality of care to all patients as they incorporate these agents into routine care.”

Most first-generation checkpoint inhibitors interfere with PD-1, an immune checkpoint on T cells that plays a role in regulating immune function. Some tumors can hijack PD-1 to turn off immune responses against them. Drugs that block the interaction between the PD-1 receptor and PD-L1, its binding partner on cancer cells or immune cells inside tumors, can release the brakes and restore T-cell activity. CTLA-4 is another immune checkpoint that turns off immune responses by suppressing T-cell multiplication.

Keytruda (pembrolizumab) and Opdivo (nivolumab) are monoclonal antibodies that block PD-1. Bavencio (avelumab), Imfinzi (durvalumab) and Tecentriq (atezolizumab) block PD-L1. Yervoy (ipilimumab) is a CTLA-4 blocker.

In some ways, immunotherapy is better tolerated than traditional chemotherapy or radiation therapy, which kill not only cancer cells but also rapidly dividing healthy cells throughout the body, causing side effects such as nausea, blood cell deficiencies and hair loss.

But immune-based therapies can cause their own side effects. Taking the brakes off the immune system can lead to overactive responses that harm healthy tissue, with symptoms ranging from fever to organ failure. These side effects can involve multiple organs including the skin, lungs, intestines, liver, thyroid, heart and central nervous system. These adverse events may occur soon after starting therapy or may be delayed and occur at any time during treatment. Although typically mild, sometimes symptoms can be severe, irreversible or even life-threatening.

Because this type of treatment has entered clinical practice fairly recently, most providers are not yet knowledgeable about or experienced in recognizing and managing the associated side effects, according to the ASCO Post article.

To develop the guidelines, ASCO and NCCN convened multidisciplinary panels that included specialists in medical oncology, dermatology, gastroenterology, endocrinology, neurology and other relevant fields. They also included nurses, emergency medicine practitioners and patient advocates. The panel members reviewed the relevant medical literature and used an informal consensus process.

The guidelines state that, in general, checkpoint inhibitors can be continued with close monitoring in people with mild side effects, with the exception of neurological and some blood-related toxicities. For moderate side effects, the drugs should be stopped temporarily until symptoms or lab values improve; corticosteroid medications may be used. Patients with severe side effects should receive high-dose corticosteroids and treatment should be resumed with extreme caution or not at all. Life-threatening toxicities require stopping checkpoint inhibitors permanently.

The latest guidelines are only for immune checkpoint inhibitors. Later this year NCCN plans to update its guidelines to include chimeric antigen receptor T-cell (CAR-T) therapies, another type of cancer immunotherapy that has led to remarkable benefits for some patients but also can cause potentially fatal side effects if not recognized and managed promptly.

“Some people will brush their symptoms aside, but any unusual symptom should be reported to the doctor,” said Julie Brahmer, MD, of Johns Hopkins, chair of the expert panel that developed the ASCO guideline. “These guidelines will help all providers who care for patients treated with immune checkpoint inhibitors—not just oncologists but also emergency room and primary care doctors—assess and manage these side effects.”

ASCO and NCCN encourage feedback on their guidelines from oncologists, other practitioners and patients.

Click here to read Management of Immune-related Adverse Events in Patients Treated with Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline, published in the Journal of Clinical Oncology.

Click here to read NCCN Guidelines for Management of Immunotherapy-Related Toxicities.

Click here for more information about immunotherapy and its side effects.

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