Immune checkpoint inhibitors (ICIs) are becoming first-line therapeutic options in oncology for more and more malignancies, including metastatic melanoma, non–small cell lung cancer, and kidney cancer, as well as adjuvant therapy for certain forms of melanoma. However, because of immune-related adverse events (irAEs), patients with preexisting autoimmune diseases (PADs) have been excluded from clinical trials of ICIs, even though many clinicians suspect these patients might benefit from these drugs. The main concern is that unleashing severe inflammatory and autoimmune toxicity might exacerbate a patient’s PAD or compromise their ability to tolerate ICI therapy.

A new study conducted in France investigated whether patients with cancer and an array of PADs could benefit from ICIs (Arthritis Rheumatol. Published online August 5, 2019. doi:10.1002/art.41068). “How to manage these patients is a real question in clinical practice,” says study author Divi Cornec, MD, PhD, professor of rheumatology at Brest University Hospital in Brest, France. “More than safety, our study assesses the efficacy of ICI, especially when an immunosuppressive treatment (IS) is used at ICI initiation.”

Dr. Cornec notes that the new study adds to information from recent reports that explored cancer immunotherapy in patients with PADs. “However, our much larger population allowed us to compare different subgroups of patients and to draw firmer conclusions,” he says.

Study Details
This multicenter, retrospective cohort study included 112 patients who were identified by surveys of experts participating in 3 French national networks: the Groupe Français de Pneumo-Cancérologie (French Lung Cancer Group), Groupe de Cancérologie Cutanée (Cutaneous Cancer Group), and Club Rhumatismes et Inflammations (Rheumatism and Inflammation Club). All patients were identified as having PADs and as having a cancer that was treated with ICIs between January 2017 and January 2018. Researchers collected data from questionnaires and medical records regarding the type of ICI, the occurrence of PAD flare and/or other irAEs, and tumor response. They assigned grades to the AEs (grades 1-2 for mild events and grades 3-4 for severe events) and noted the use of glucocorticoids or other IS therapy.

The cohort included patients with psoriasis or psoriatic arthritis (31 patients), rheumatoid arthritis (20 patients), polymyalgia rheumatic and/or giant cell arteritis (7 patients), systemic lupus (4 patients), skin-limited lupus (3 patients), or inflammatory bowel disease (14 patients).

Immune-Related Adverse Events
Among these 112 patients, 79 (71%) experienced an immune toxicity, with 53 patients (47%) experiencing a PAD flare, 47 (42%) experiencing an irAE that was not related to the treatment.
PAD, and 20 (18%) experiencing both. One death was reported due to an immune toxicity, and 24 patients (21%) permanently discontinued their ICI because of immune toxicity.

Nearly one-half of PAD flares were treated with glucocorticoids (24 patients); 6 patients received a conventional synthetic disease-modifying antirheumatic drug and 3 patients were treated with a biological disease-modifying antirheumatic drug. A total of 24 patients with non-PAD de novo irAEs were treated with glucocorticoids and 7 also received an additional IS agent (methotrexate, a tumor necrosis factor inhibitor, or intravenous immunoglobulin).

According to Dr. Cornec, overall the researchers found the use of ICIs in patients with PAD to be rather safe. “[Patients] are exposed to immune-related adverse events that might be severe, but for most are mild and manageable with steroids,” he says. “A close monitoring is mandatory, along with collaboration between the oncologist and the specialist of the PAD.”

**Oncologic Outcomes**

The authors did find that IS treatment at the time of ICI initiation appeared to have a negative impact on cancer outcomes, Dr. Cornec says, and for patients with a stable PAD, minimal IS therapy should be used. In contrast to prior reports, Dr. Cornec and his colleagues found that the occurrence of irAEs was associated with worse cancer outcomes. “This discrepancy can be explained by the different statistical method used,” he says. Patients with a more favorable prognosis and better responses to ICIs would have enough time to experience an irAE, in contrast to those patients with a much shorter survival. This phenomenon could lead some researchers to conclude that patients with an irAE have better survival. To avoid this bias, “we considered irAE occurrence as a time-dependent covariate,” Dr. Cornec says.

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“I think this study does a good job of highlighting that the risk of potentially reactivating the underlying disorder is high, but it’s not 100%,” says April Salama, MD, an associate professor of medicine at Duke University School of Medicine and a member of the Duke Cancer Institute in Durham, North Carolina. “So, categorically, clinicians should not rule out immunotherapy in a cancer patient who could potentially benefit because of an underlying rheumatologic disorder. That’s an important piece of information that clinicians can discuss with their patients, in terms of whether or not they would consider moving forward with some of these types of therapies.”

Dr. Cornec says that for patients with a stable PAD, minimal IS treatment should be advised at the initiation of ICIs so as not to reduce the response of the cancer to treatment. “This is already applicable in clinical practice in the general population, since several studies highlighted a negative impact of [cortico]steroids of more than 10 mg/day at ICI initiation after adjustments on bad prognostic factors in patients treated with steroids for palliative indications such as dyspnea, fatigue, or brain metastases,” he says. “But there is clearly a need for prospective studies in larger populations to confirm these findings.”

“There is also a need in basic research to identify predictive factors for immune toxicity and for cancer response,” he says.

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