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Working with Rheumatologists to Manage irAEs

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Caring for patients experiencing toxicities from treatment with immune checkpoint inhibitors (ICIs) requires multidisciplinary input and coordination. Rheumatologists evaluate and treat patients experiencing a wide variety of immune-related adverse events (irAEs), including inflammatory arthritis, sicca syndrome, polymyalgia rheumatica, myositis, vasculitis, and scleroderma. It's important for rheumatologists to know that these irAEs can vary significantly in their time of onset, severity, and treatment. Accurately diagnosing and treating rheumatic irAEs requires that providers obtain a tailored patient history and physical examination, since there are no definitive diagnostic laboratory tests for these complications.

While myositis can occur within days to weeks of beginning treatment with ICI and can ultimately cause death, inflammatory arthritis and sicca syndrome do not cause death and can appear at almost any time during ICI treatment. Some patients may only require supportive care, as with sicca syndrome, for which artificial saliva and tears, and saliva-stimulating medications are useful. Other irAEs may require corticosteroids or additional immunosuppression, such as intravenous immunoglobulin or tumor necrosis factor (TNF) inhibitors. Because of these potential problems, oncologists should involve rheumatologists early when rheumatic irAEs are suspected.

When treating patients with irAEs, rheumatologists try to prevent morbidity, improve quality of life, and increase physical function. Qualitative research shows that, due to their under-recognition, persistence, and impact on the activities of daily life, rheumatic irAEs such as inflammatory arthritis can have more of an effect on patients compared to other irAEs. Because patients experiencing an irAE are also facing a major health crisis from their underlying cancer, it is important that rheumatologists be able to balance the need to continue cancer therapy with the need to address the symptoms brought on by irAEs. For patients who experience a mild to moderate irAE that does not require their ICI therapy to be stopped, rheumatologists may offer supportive care, direct corticosteroid therapy (e.g., an intra-articular steroid injection), or low-dose systemic corticosteroids. In the future, simultaneous treatment with ICIs and immune-modulating therapy for irAEs may become more common. For example, there have been reports of successful treatment of colitis with TNF-inhibitors while ICI therapy continues to be administered.[1]

It is important for patients and cancer team members to recognize that rheumatic irAEs may persist after ICI cessation. In one study performed by our group at Johns Hopkins, longer duration of ICI therapy, treatment with combination therapy (anti-CTLA-4 + anti-PD-1), and the presence of irAEs were all associated with a higher likelihood of having persistent inflammatory arthritis. Since patients may experience extended symptoms from irAEs, involving a rheumatologist in treatment is critical to improve quality of life and function.[2]

When referring patients to a rheumatologist, the oncology care team should provide background information about the patient's cancer and current and prior treatment(s) to help rheumatologists develop their own treatment plan. Knowing how long a patient is expected to survive can also guide therapy choice. If a patient's cancer has progressed on ICI therapy and they have few treatment options remaining, the oncologist may decide with the rheumatologist to pause or stop ICI treatment. This would enable the rheumatologist to be more liberal with prescribing high-dose immunosuppression drugs for symptomatic relief.

1. Badran YR, Cohen JV, Brastianos PK, Parikh AR, Hong TS, Dougan M. Concurrent therapy with immune checkpoint inhibitors and TNFa blockade in patients with gastrointestinal immune-related adverse events. *J Immunother Cancer*. 2019;7(1):226.

2. Braaten TJ, Brahmer JR, Forde PM, Le D, Lipson EJ, et. al. Immune checkpoint inhibitor-induced inflammatory arthritis persists after immunotherapy cessation. *Ann Rheum Dis*. 2020;79(3):332-338.

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