Underlying Autoimmune Disease Is Not a Contraindication to the Use of Ipilimumab

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The use of immune checkpoint inhibitors, a new class of anticancer agents with a mechanism of action based on augmenting existing tumor-specific immunity, is often restricted or avoided in patients with autoimmune disease. The rationale for this restriction is that the autoimmune toxic effects observed with the use of these agents could be amplified in patients with rheumatic diseases. Moreover, patients would have an exacerbation of their underlying inflammatory condition. This restriction makes sense; however, the number of patients who would not be eligible to receive immune checkpoint inhibitor agents would be substantial. The lifetime risk of developing an inflammatory autoimmune rheumatic disease is estimated to be 1 in 12 for women and 1 in 20 for men.1 Data on the outcomes of patients with autoimmune disease who have received immune checkpoint inhibitor therapy are needed.

In this issue of *JAMA Oncology*, Johnson et al2 report, to our knowledge, the largest series of patients with melanoma with preexisting autoimmune disease who have been treated with ipilimumab to date. These patients had a diversity of autoimmune disease ranging from rheumatoid arthritis and psoriasis to more serious conditions such as ulcerative colitis and multiple sclerosis. Only a minority of patients (8 [27%]) had an exacerbation of their disease with ipilimumab therapy. All flares could be medically treated and usually were observed within 3 to 6 weeks of initiating therapy. Typical immune-related adverse events (irAEs) (grade 3-5) occurred in 10 (33%) of the patients. A recent meta-analysis of ipilimumab-mediated irAEs in 1265 patients from 22 clinical trials reported an incidence of 25% of higher-grade irAEs with treatment. At 33%, these types of adverse events may be more common in patients with underlying autoimmune disease.3 Fifteen patients (50%) with autoimmune disease experienced neither a flare of their underlying condition nor an irAE. The clinical response rate in this cohort was 20%, typical for ipilimumab, with 5 partial and 1 complete response.

These data underscore the safety of administering ipilimumab in patients with autoimmune disease. The immune checkpoint inhibitor agents are associated with unique immune-related toxic effects that often make practicing oncologists hesitant to use the drugs. Repeated studies have shown that irAEs can be medically treated and serious toxicities prevented with vigilance to identify symptoms at an early stage in evolution. The same approach would be used with patients having concurrent autoimmune disease, as has been demonstrated by Johnson et al,2 to ensure patient safety.

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