Keytruda May Benefit Patients with a Rare Type of Skin Cancer

Desmoplastic melanoma, characterized by a high tumor mutation burden, may be uniquely sensitive to immune checkpoint inhibitors.

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Single-agent Pembrolizumab May Benefit Patients with Rare Type of Skin Cancer

Monotherapy with pembrolizumab (Keytruda) led to clinical responses in 89% of patients with unresectable metastatic desmoplastic melanoma, according to results from a Phase II clinical trial presented at the AACR Annual Meeting 2023, held April 14-19.

Desmoplastic melanoma is a rare subtype of melanoma, accounting for approximately 4% of melanoma cases in the United States.

“Recent advances have led to a variety of treatment options for patients with melanoma, whether it be single drug therapy or combination therapies,” said Kari Kendra, MD, PhD, a professor of medicine and the director of cutaneous oncology at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

“The question clinicians are now posed with is how we decide the best approach for any given patient, which requires an understanding of which patient populations and/or tumor types respond to different treatments,” she said.

Previous studies have shown that desmoplastic melanoma is characterized by high levels of tumor mutational burden, a characteristic that led Kendra and colleagues to hypothesize that this subtype may be uniquely sensitive to immune checkpoint inhibition. A prior retrospective analysis found high response rates among 60 patients with desmoplastic melanoma who had been treated with an immune checkpoint inhibitor.

Based on these findings, Kendra and colleagues conducted the prospective phase II S1512 clinical trial to evaluate the efficacy of pembrolizumab, an inhibitor of the PD-1/PD-L1 immune checkpoint, in patients with desmoplastic melanoma. While pembrolizumab is approved for the first-line

treatment of patients with unresectable metastatic melanoma, Kendra noted that this is the first prospective trial testing the immune checkpoint inhibitor in patients with the desmoplastic melanoma subtype.

The trial enrolled patients with histologically and genetically confirmed desmoplastic melanoma who had not received prior systemic therapy. Patients were assigned to one of two cohorts: Cohort A of the trial evaluated neoadjuvant pembrolizumab in patients with resectable disease, while Cohort B evaluated pembrolizumab in patients with unresectable metastatic disease. Previously reported results of neoadjuvant treatment showed a 59% pathologic complete response rate among patients in Cohort A. Here, the researchers reported findings from Cohort B.

Twenty-seven patients with unresectable metastatic desmoplastic melanoma were enrolled in Cohort B and received pembrolizumab monotherapy every three weeks for two years or until disease progression or unacceptable toxicity. The primary endpoint, reported here, was complete response rate. Secondary endpoints included progression-free survival, overall survival, and safety.

Twenty-four patients had a clinical response to pembrolizumab, for an objective response rate of 89% (nine complete responses and 15 partial responses). The study met its primary endpoint with a complete response rate of 33%, exceeding the prespecified threshold of 20%. Six patients experienced grade 3 or higher adverse events.

“This study identified a subgroup of melanoma patients, those with desmoplastic melanoma, who had an exceptionally high response rate to pembrolizumab monotherapy,” concluded Kendra, adding that the response rates to pembrolizumab observed in this study exceeded those of historical data from patients with other melanoma subtypes.

Kendra suggested that the diagnosis of desmoplastic melanoma could be used as a predictive biomarker to identify patients with melanoma likely to respond to pembrolizumab. In addition, the results suggest that patients may be able to undergo monotherapy with pembrolizumab instead of combination therapies, which are commonly employed as first-line treatment for desmoplastic melanoma, according to Kendra.

“The high responses to pembrolizumab monotherapy indicate that first-line combination therapy may not be necessary for patients with desmoplastic melanoma, which could help patients avoid unnecessary toxicities,” she said.

“It is important to keep studying rare diseases and rare subsets of more common diseases so that we can better tailor therapy to each individual,” Kendra noted.

Kendra and colleagues continue to evaluate the long-term efficacy of pembrolizumab in this trial, specifically its impact on progression-free survival and overall survival. Additional ongoing studies are examining molecular features of the tumors that progressed following pembrolizumab treatment to identify biomarkers of treatment resistance.

A limitation of the study was its small sample size.

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