Pembrolizumab Yields Lasting Merkel Cell Carcinoma Responses

In a phase II single-arm study, the PD-1 checkpoint inhibitor pembrolizumab (Keytruda; Merck) produced durable responses in 56% of patients with advanced Merkel cell carcinoma (MCC), a disease for which there are no FDA-approved treatments. Although that response rate is on par with the response rate to standard treatment with platinum chemotherapy and etoposide, the study showed that pembrolizumab proved significantly superior in controlling the disease.

The findings, which were simultaneously published in The New England Journal of Medicine, were presented by Paul Nghiem, MD, PhD, head of dermatology at the University of Washington in Seattle, on April 19 at the American Association for Cancer Research Annual Meeting 2016 in New Orleans, LA.

MCC affects 2,000 people in the United States each year, often appearing as fast-growing skin lumps. Exposure to ultraviolet light is a risk factor, and the disease strikes more often in people over age 50 and individuals with a compromised immune system.

Merkel cell polyomavirus drives about 80% of cases. Discovered in 2008, this virus infects most people during childhood, but typically causes no problems. However, the unlikely acquisition of multiple genetic mutations enables the virus to evade immune system surveillance and trigger MCC. More than 40% of patients develop advanced MCC, and among those, roughly 60% die in less than a year.

Benefits of treatment with standard chemotherapy are short-lived, as about half of patients experience progressive disease within 3 months. Because previous research found that patients with MCC whose tumors showed evidence of a killer T-cell response fared better, researchers thought that pembrolizumab, which ramps up the immune system's response and has already been approved for the treatment of certain melanomas and lung cancers, might be worth a try.

Nghiem and colleagues enrolled 26 patients with advanced MCC who had not received prior systemic therapy; 17 had virus-positive disease. All received pembrolizumab every 3 weeks for up to 2 years, with tumor evaluations every 9 to 12 weeks.

Overall, among the 25 patients who had at least one radiologic assessment, 56% responded to the drug. That rate is nearly twice the response rate seen in melanoma, the first cancer for which this immunotherapy drug was approved, Nghiem said.

The response rate was higher in patients with virus-positive than virus-negative disease (63% versus 44%), although this difference was not statistically significant. Baseline tumor expression of PD-L1, the ligand of PD-1, did not predict response to pembrolizumab, Nghiem added.

Most notable, Nghiem said, was that 88% of the responders continued to respond to treatment after 6 months, on average, significantly longer than with chemotherapy. In addition, the initial 3-month evaluation seemed to indicate a patient's trajectory for the rest of the study, with benefits persisting for responders, and nonresponders continuing to worsen.

Aiming to confirm these results, Nghiem said his team will expand the trial to include 24 more patients. —Esther Landhuis

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