Keytruda Reduces Recurrence of High-Risk Melanoma

Immunotherapy lowered the likelihood of relapse after surgery.

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People with Stage III melanoma who used Keytruda (pembrolizumab) after surgical removal of the cancer had improved recurrence-free survival, meaning they were still alive without relapse, according to research presented at the American Association for Cancer Research annual meeting and published in the New England Journal of Medicine.

Alexander M.M. Eggermont, MD, PhD, of Gustave Roussy Cancer Campus Grand Paris in Villejuif, France, conducted the Phase 3 KEYNOTE-054 study to evaluate Keytruda versus a placebo as adjuvant therapy for people with resected, or surgically removed, high-risk Stage III melanoma. Adjuvant therapy is administered after a primary treatment (usually surgery) to prevent cancer relapse.

Melanoma typically starts as a skin cancer, but it can spread to other parts of the body, a process known as metastasis. If it is not caught early, it often invades the lungs, liver, bones and brain. People with Stage III melanoma have evidence of cancer in one or more regional lymph nodes, but it has not yet spread to other parts of the body, according to Eggermont. These patients are considered to be at high risk of post-surgery recurrence.

Keytruda is a monoclonal antibody that blocks PD-1, a receptor on T cells that plays a role in regulating immune function. Some tumors can use PD-1 to turn off immune responses against them; drugs that block PD-1—or its binding partner PD-L1—can restore T-cell activity. Keytruda is currently approved for the treatment of unresectable or metastatic melanoma. Another PD-1 inhibitor, Opdivo (nivolumab), and the CTLA-4 checkpoint inhibitor Yervoy (ipilimumab) are already approved as adjuvant therapy for high-risk melanoma after surgery.

The KEYNOTE-054 trial enrolled 1,019 adults with surgically removed skin melanomas that had spread to lymph nodes. About 60 percent were men, and the median age was 54. Forty-four percent had one affected lymph node, 34 percent had two or three affected nodes and 21 percent had cancer in four or more nodes. About 83 percent were PD-L1 positive, meaning PD-L1 was present on more than 1 percent of tumor cells or immune cells within tumors.

Study participants were randomly assigned to receive 200 milligrams of Keytruda or a placebo

every three weeks for a total of 18 doses (about a year) or until disease recurrence or development of unacceptable side effects. Those who experienced recurrence but did not have metastasis to the brain could cross over from placebo to Keytruda, or they could start Keytruda again if they relapsed more than six months after the first treatment.

After a median 1.25 years of follow-up, people who took Keytruda had 135 recurrence events compared with 216 events in the placebo group. This was a statistically significant difference, meaning it was probably not attributable to chance. The Keytruda group overall had a significantly higher one-year recurrence-free survival rate compared with the placebo group: 75.4 percent versus 61.0 percent, respectively, or a 43 percent risk reduction. Both PD-L1 positive and PD-L1 negative patients saw improvements in recurrence-free survival.

Treatment was generally safe and well tolerated. About 15 percent of people taking Keytruda and 3 percent of placebo recipients experienced serious or life-threatening adverse events. By unleashing T cells, checkpoint inhibitors can cause an overactive immune response that harms healthy organs and tissues. The most common immune-mediate adverse event seen among Keytruda recipients in this study was endocrine gland disorders (23 percent), mostly mild or moderate. Lung, liver and intestinal inflammation were rare (2 percent or less). There was one Keytruda-related death due to myositis (muscle inflammation).

“We were pleased to see that adjuvant pembrolizumab, given as a flat dose of 200 milligrams every three weeks after surgery for up to a year, which is 18 doses, significantly reduced the risk of recurrence for patients with high-risk Stage III melanoma that has been completely resected,” Eggermont said in an AACR press release. “We hope that these data will lead to regulators in the United States and Europe approving pembrolizumab as a new treatment option for these patients.”

Eggermont noted that more follow-up time is needed to see whether recurrence-free survival translates into overall survival, the ultimate goal of cancer treatment.

Click here to read an AACR press release about the study.

Click here to read the AACR study abstract.

Click here to read the full report in the New England Journal of Medicine.

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