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Immunotherapy drug benefits patients with high-risk local melanomas

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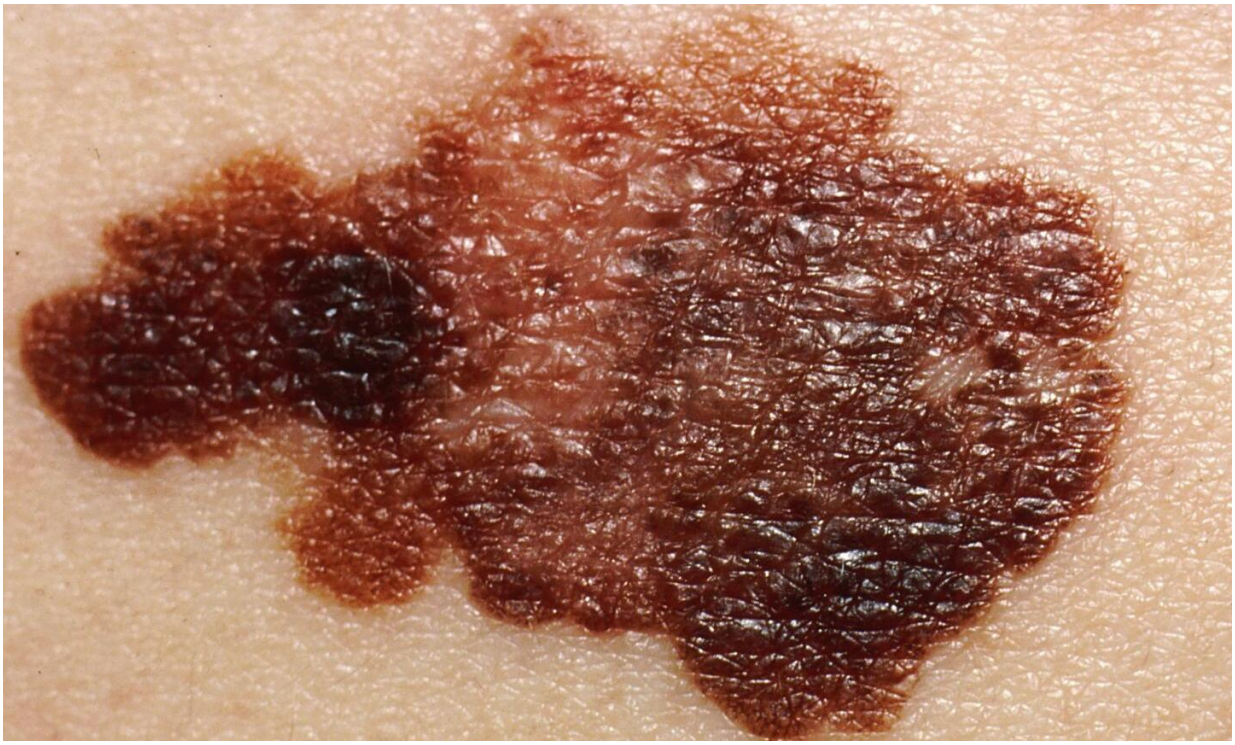

Melanoma. Credit: Wikimedia Commons/National Cancer Institute

An immunotherapy called pembrolizumab reduced cancer recurrence after surgery in patients with stage IIb and IIc melanoma, according to the results of an international, randomized phase III clinical trial led by UPMC Hillman Cancer Center. These results indicate that this immunotherapy treatment—which currently is approved only for stage

III and IV melanomas—may be appropriate for patients with earlier stages of melanoma.

The study was led by Jason Luke, M.D., director of the Cancer Immunotherapeutics Center at UPMC Hillman and associate professor of medicine at the University of Pittsburgh School of Medicine. He delivered the results on behalf of a leading international group of melanoma oncologists, including John Kirkwood, M.D., also of UPMC Hillman, as well as the study sponsor Merck, during a presentation today at ESMO Congress 2021.

"Patients with stage IIb and IIc melanomas have a high level of risk for the disease coming back after surgery," said Luke. "This is a very important clinical trial as it shows that pembrolizumab reduces that risk. Based on these results, I believe that we should be offering patients in this situation the opportunity to get this treatment after surgery."

Pembrolizumab often is used as adjuvant immunotherapy following surgical removal of stage III melanomas, in which the cancer has spread to lymph nodes, and for treatment of metastatic stage IV melanomas. But the U.S. Food and Drug Administration (FDA) has not yet approved the drug for patients with earlier stages, such as IIb and IIc melanomas—invasive tumors that extend deep into the skin or have broken the overlying skin, which is known as ulceration.

"In most cancers, it's automatically worse if the cancer moves beyond the primary location to the lymph nodes. But melanoma is idiosyncratic in that the risk of long-term relapse and death is similar among patients with stage IIIa and IIIb melanoma, with lymph node involvement, compared with stage IIb and IIc, which lack lymph node involvement," said Luke. "So in a sense, it has been unfair that these patients couldn't get pembrolizumab because they were excluded from initial trials. With this trial, we hoped to right that wrong."

The multi-country KEYNOTE-716 trial enrolled 976 patients with stage IIb or IIc melanomas. After surgery, 487 patients received intravenous pembrolizumab and 489 received a placebo every three weeks for one year. Patients were monitored for cancer recurrence via computed tomography scans and magnetic resonance imaging.

The researchers found that patients who received the drug had a 35% lower risk of death or melanoma relapse compared to those who got the placebo.

On the basis of these findings, Merck has submitted an application to the FDA for treatment of stage IIb and IIc melanoma with pembrolizumab, which is undergoing priority review.

At a median follow-up time of 14.4 months, 136 patients had disease recurrence or died: 54 in the pembrolizumab group and 82 in the placebo group.

"The fact that patients in this trial had very rapid recurrences in distant organs—which is metastatic cancer—drives home the point that stage IIb and IIc melanomas are high risk," said Luke. "There has been the idea that because these cancers don't involve the lymph nodes, they're not such a big deal. But that's clearly wrong."

The KEYNOTE-716 trial is ongoing, and the researchers will continue to monitor participants for cancer recurrence or death.

"The trial is still very early, and we expect to see the benefit of pembrolizumab increase above 35% over time," said Luke.

In part two of the trial, patients in the placebo group who had their cancer return will be offered pembrolizumab. This will help clinicians figure out whether it is better to give the treatment right after melanoma

surgery or wait until the cancer returns.

About 18% of participants receiving pembrolizumab experienced significant adverse effects that required long-term hormone replacement. According to Luke, this level of drug safety was expected based on previous trials, and they did not observe new or unexpected side effects.

Provided by University of Pittsburgh