Using pre-surgical anti-PD 1 therapy in melanoma patients can identify those most likely to benefit

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Checkpoint inhibitors that block the protein PD-1 are used in melanoma patients after they've had surgery to remove their cancer, but not all patients benefit from the immunotherapy. Now a new study from the Abramson Cancer Center of the University of Pennsylvania found that shifting use of anti-PD-1 drugs to before surgery may provide clues about which patients will benefit and which may be at increased risk for recurrence. Researchers will present their data in a symposium at the American Association for Cancer Research Annual Meeting in Chicago on Tuesday (Presentation #CT181).

"Building on our previous research that shows the effect of anti-PD-1 therapy can be seen in patients' blood as early as three weeks after treatment, we gave patients a single dose before surgery, and then looked for anti-tumor activity in the resected tumor three weeks later," said the study's lead author Alexander C. Huang, MD, an instructor of Hematology-Oncology in Penn's Perelman School of Medicine. Tara C. Mitchell, MD, an assistant professor of Hematology-Oncology at Penn, is the study's senior author.

Melanoma is a rare form of skin cancer, but it accounts for a large number of skin cancer deaths. The American Cancer Society estimates more than 91,000 new melanomas will be diagnosed in the United States in 2018, while about 9,300 people are expected to die from the disease this year. Currently, the standard of care in resectable melanoma includes surgery followed by a year of drug treatment in select high risk patients, which can include immunotherapy like anti-PD-1 drugs.

In Penn's trial, doctors gave 27 patients with stage 3 or 4 resectable melanoma a dose of anti-PD-1 therapy before surgery. Eight of the 27 (30 percent) patients had a complete or near-complete response after the single dose that was detected at the time of surgery; all of these patients with an early response remain cancer free. For patients who did not achieve that response, more than 50 percent who were evaluated at one year had recurrence of their disease. In addition, the study also revealed a high degree of tumor infiltrating lymphocytes among patients with longer recurrence-free survival.

When researchers analyzed tumor tissue from pre-treatment biopsies and compared it to tissue removed during surgery three weeks later, they found an increase in CD8 T cells and PD-L1 expression – meaning the immune system had already become active against the cancer.

"Our data suggest that giving patients this therapy before surgery may give us a sense of whether or not the therapy will be effective after surgery," Huang said.

Huang says more analysis of this trial may lead to clues that can take the concept a step further, from identifying patients at risk of recurrence, to understanding the mechanisms of the cancer's resistance.

Provided by Perelman School of Medicine at the University of Pennsylvania