

ASCO 2015: Mismatch Repair Deficiency Predicts Response to Pembrolizumab Among Patients With Colorectal and Other Cancers



By The ASCO Post

Posted: 5/29/2015 4:32:10 PM

Last Updated: 5/29/2015 4:32:10 PM

Key Points

- Mismatch repair deficiency predicted response to the anti-PD-1 antibody pembrolizumab among patients with advanced colorectal, endometrial, and several types of gastrointestinal cancers.
- Responses occurred in 62% of patients with mismatch repair-deficient colorectal cancers but none of the patients with mismatch repair-proficient tumors.
- Disease control rates were 92% among patients with mismatch repair-deficient colorectal cancers and 16% in the mismatch repair-proficient group.
- An overall response rate of 60% was observed in patients with other mismatch repair-deficient cancers.

A phase II study identified the first genomic marker—mismatch repair deficiency—to predict clinical benefit of immune checkpoint blockade with the anti-PD-1 antibody pembrolizumab (Keytruda). Among 50 patients with colorectal cancer, 62% of the 25 patients with mismatch repair-deficient tumors responded to pembrolizumab, but no responses were seen among the 25 mismatch repair-proficient patients. The difference in disease control rates (responses plus stable disease) was even greater: 92% in the mismatch repair-deficient group and only 16% in the mismatch repair-proficient group.

An overall response rate of 60% was observed in patients with mismatch repair-deficient advanced endometrial cancer and several types of advanced gastrointestinal cancers including ampullary, duodenal, cholangiocarcinoma, and gastric cancers. “The responses were durable in a treatment-refractory patient population, and many of these responses are ongoing for over a year,” the study’s lead author, **Dung T. Le, MD**,

Assistant Professor of Oncology at Johns Hopkins Kimmel Cancer Center in Baltimore, stated at a press conference at the 2015 ASCO Annual Meeting in Chicago. The full study will be presented at the clinical science symposium on immunotherapy on Saturday, May 30 (Abstract LBA100).

All patients had previously treated progressive metastatic disease. Pembrolizumab was administered at 10 mg/kg intravenously every 14 days. Blood marker changes such as CEA levels indicating response were seen within the first few weeks of starting treatment, and patients tended to feel better almost immediately.

‘Bridging Immunotherapy and Genomics’

Mismatch repair deficiency is found in 15% to 20% of sporadic (noninherited) colorectal cancers and in nearly all colorectal cancers associated with Lynch syndrome, which constitute up to 5% of all colorectal cancers. Mismatch repair deficiency is also found in other tumor types including stomach, small bowel, endometrial, prostate, and ovarian cancer. Testing for mismatch repair deficiency is widely available and could enable identification of a larger population of patients who might benefit from pembrolizumab and other PD-1 drugs.

“This study is really about bridging immunotherapy and genomics for the benefit of patients, and it has implications for a broad range of cancers,” Dr. Le said. “Opening the door to this effective new therapy would be a breakthrough for this subset of patients with metastatic colon cancer and other hard-to-treat cancers.”

Feedback

Pembrolizumab is currently only approved by the U.S. Food and Drug Administration to treat patients with advanced melanoma that has not responded to other standard therapies. Another PD-1 therapy, nivolumab (Opdivo), is approved for the same indication, as well as in advanced squamous non-small cell lung cancer.

Thousands of Mutations

Mismatch repair deficiency leads to an accumulation of genetic mutations in a tumor. “When you have a tumor that has thousands of mutations, this increases the probability that the immune system can recognize and destroy the tumor. So, we suspected that immune checkpoint inhibitors such as pembrolizumab would work particularly well against mismatch repair-deficient tumors,” Dr. Le explained.

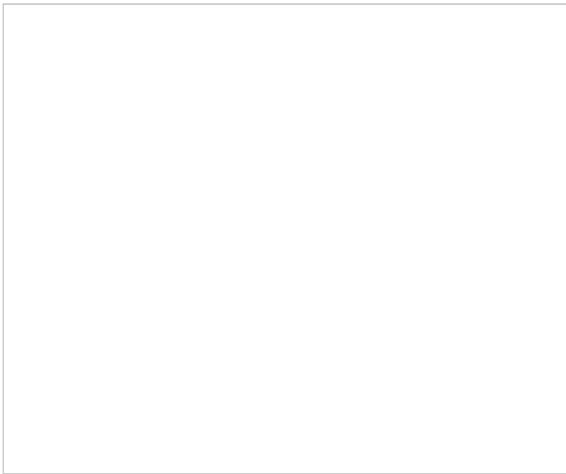
In this study, mismatch repair-deficient tumors had an average of 1,782 mutations, compared to 73 mutations in mismatch repair-proficient tumors. Higher numbers of mutations were linked to better response to pembrolizumab. Commenting on the more than 1,700 mutations, press conference moderator **Lynn Schuchter, MD, FASCO**, said: “It’s like you put a red flag on the cancer cell and say to the immune system, ‘Here I am!’” Dr. Schuchter is the University of Pennsylvania’s C. Willard Robinson Professor of Hematology/Oncology, Chief of the Hematology/Oncology Division, and Program Leader of the Abramson Cancer Center’s Melanoma Research Program.

Dr. Le indicated that the next step is to reproduce the findings of this prospective study in a larger group of patients to solidify the observation that mismatch repair deficiency is a predictor of response to therapies targeting PD-1. She noted that the durability of response with little toxicity could eventually lead to testing this approach as initial treatment for these patients.

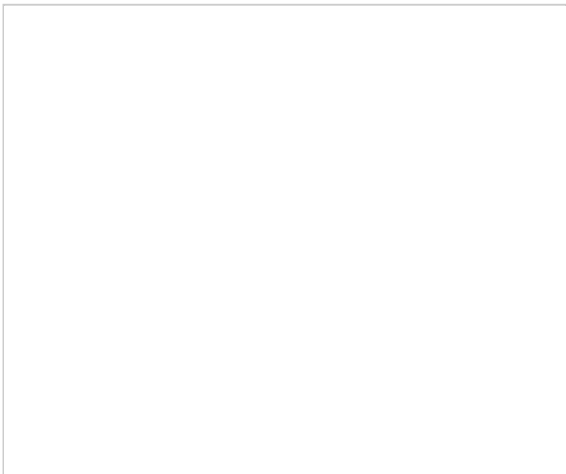
This study received funding from Swim Across America, The Commonwealth Fund, The Ludwig Center at Johns Hopkins, and the National Institutes of Health.

The content in this post has not been reviewed by the American Society of Clinical Oncology, Inc. (ASCO®) and does not necessarily reflect the ideas and opinions of ASCO®.

ADVERTISEMENT



ADVERTISEMENT



Feedback

SEP 20 TODAY IN ONCOLOGY

Long-Term Outcomes With Adjuvant Trastuzumab for 9 Weeks or 1 Year in HER2-Positive Breast Cancer:
Analysis From SOLD Trial

Phase III CABINET Trial Cabozantinib in Advanced Neuroendocrine Tumors

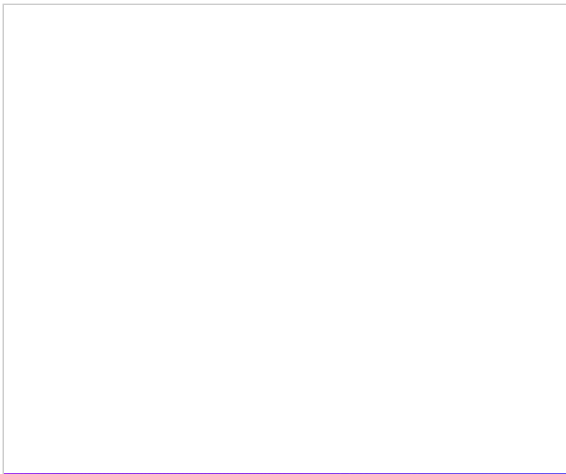
Immunotherapy Combination May Improve Long Term Survival in Patients With Metastatic Melanoma

Tarlatamab in Previously Treated Small Cell Lung Cancer

Atezolizumab, Venetoclax, and Obinutuzumab in Richter Transformation Diffuse Large B-Cell Lymphoma

[VIEW MORE ▶](#)

ADVERTISEMENT



Feedback

© 2024 HSP News Service, L.L.C.



[Editorial Board](#) [Advertising](#) [Disclosures](#) [Contact](#) [Privacy Policy](#) [Disclaimer](#) [ASCO.org](#)