TIGIT Checkpoint Inhibitor Improves Response in People with Lung Cancer

Combination therapy that includes a novel antibody is superior to immunotherapy alone for advanced non-small-cell lung cancer.

December 23, 2022 By American Society of Clinical Oncology

A Phase II randomized clinical trial in people with Stage IV non-small-cell lung cancer (NSCLC) showed that adding a novel, engineered antibody to an immunotherapy resulted in better overall response rates (ORR) and progression-free survival (PFS) compared to treatment with the immunotherapy drug alone. The results of the study [were presented at the ASCO Plenary Series session on December 20].

The novel antibody, domvanalimab, works by binding to, and blocking, TIGIT, a checkpoint receptor expressed on immune cells. TIGIT inhibits the immune system's natural ability to detect and kill cancer cells, so blocking its activity could aid cancer treatment. Importantly, TIGIT and PD-1, a marker that is targeted by the immunotherapy used in the trial (zimberelimab), have distinct functions in controlling antitumor immune responses, hence the hope that combining the two drugs could be beneficial. Previous TIGIT-directed agents have shown mixed benefit in clinical trials, but domvanalimab, unlike other TIGIT-targeted drugs, is designed to avoid depleting peripheral immune cells as they can be key to a robust immune response.

"The current standard-of-care for many patients with Stage IV non-small cell lung cancer is a single immunotherapy drug but only a fraction of patients will truly benefit over the long term. Identifying novel combination treatments is critical to improving patient outcomes," said Melissa L. Johnson, MD, Director, Lung Cancer Research for Sarah Cannon Research Institute at Tennessee Oncology, Nashville, and the presenting author of the study. "We are particularly encouraged by the number of patients benefiting at six months as evidenced by tumors being stable or shrinking. It should be noted that this is an interim analysis and the data will continue to mature with longer follow up."

The trial, called ARC-7, enrolled people with Stage IV, non-small cell lung cancer who had high expression levels of the PD-L1 marker and had no previous treatment for their disease. There were 150 patients randomly assigned to one of three treatment regimens. Of the 150 patients enrolled, 133 patients had results that were evaluable. The trial arms were:

- Arm Z: Zimberelimab intravenously every 3 weeks. Patients with disease that progressed were allowed to cross over to arm EDZ.
- Arm DZ: Domvanalimab intravenously every 3 weeks plus zimberelimab.
- Arm EDZ: Etrumadenant, a drug that modulates immune response and has anti-cancer activity, orally once a day, in addition to the DZ regimen.

Patients were followed for a median of about one year. Both the DZ and EDZ arms demonstrated improved ORR with 27% of patients responding in arm Z compared to 41% of patients in the DZ and 40% in the EDZ arms; the combination arms included domvanalimab.

Both DZ and EDZ containing arms reduced the risk of disease progression or death (PFS) compared to Z alone: DZ vs Z was 12 months vs 5.4 months, respectively, and EZD vs Z was10.9 months vs 5.4 months, respectively. Additionally, for PFS at six months, 43% of patients showed no signs of disease progression compared to 65% of patients in arm DZ and 63% of patients in arm EDZ.

Grade three or greater treatment-related adverse events occurred in about half of all groups. Significantly, there wasn't an increase in immune-related adverse events for the DZ arm.

With proof-of-concept established by this Phase II trial, several global Phase III trials are now in progress to confirm the activity of domvanalimab combination treatments in different types of NSCLC.

"There have been mixed signals from prior studies looking at TIGIT targeting. The promising results of the combination immunotherapy treatment in this study support further investigation, and if confirmed, could lead to a new standard of care for patients with advanced lung cancer," said ASCO lung cancer expert Lauren Byers, MD.

Abstract: ARC-7: Randomized phase 2 study of domvanalimab + zimberelimab ± etrumadenant versus zimberelimab in first-line, metastatic, PD-L1-high non-small cell lung cancer (NSCLC).

This news release was published by the American Society of Clinical Oncology on December 19, 2022.
