Phase 3 eXalt3 study shows significantly longer progression-free survival

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Patients with non-small cell lung cancer (NSCLC) carrying anaplastic lymphoma kinase (ALK) gene alterations who received ensartinib experienced substantially longer progression-free survival than a matched group of patients who received crizotinib, according to a presentation at the International Association for the Study of Lung Cancer World Conference on Lung Cancer Virtual Presidential Symposium.

The results were presented today by Leora Horn, MD, Ingram Associate Professor of Cancer Research in the Division of Hematology/Oncology and director of the Thoracic Oncology Program at Vanderbilt-Ingram Cancer Center, Nashville, Tenn.

ALK-positive lung cancer occurs in approximately 5% to 7% of patients with NSCLC, mostly in patients younger than age 55. Mutated forms of the ALK gene and proteins have also been found in other types of cancer, such as neuroblastoma, and anaplastic large cell lymphoma. These changes directly contribute to the uncontrolled growth of cancer cells.

Ensartinib (X-396) is a novel next-generation ALK tyrosine kinase inhibitor (TKI). According to Dr. Horn, in Phase 1 and 2 studies, ensartinib showed promising activity in patients with ALK+ NSCLC who were ALK TKI treatment naive or received prior crizotinib or second-generation ALK TKIs, including strong activity in patients with brain metastases.

Crizotinib is an anti-cancer drug acting as an ALK, MET, and ROS1 inhibitor, approved for treatment of some subtypes of patients with NSCLC (including ALK+) in the United States and other countries worldwide.

Dr. Horn and her colleagues at the participating cancer centers randomized 290 patients with ALK+ NSCLC to either ensartinib or crizotinib—the prespecified intent to treat (ITT) population with locally determined ALK+ NSCLC. Patients were stratified by prior chemotherapy, Eastern Cooperative Oncology Group performance status, brain metastases, and geographic region. Baseline characteristics were well balanced between the two groups: median age was 54.1; 26% of patients had prior chemotherapy, and 36% of patients had baseline brain metastases (5% had prior brain radiotherapy). The modified ITT population (the prespecified patient population that was ALK+ as confirmed by central Abbott FISH test) included 247 patients, of which 121 received ensartinib and 126 received crizotinib.

At the July 1, 2020 data cutoff, based on a pre-planned interim analysis design (at 75% of progression-free survival events) treatment was ongoing in 64 ensartinib-treated patients (45%) and 25 crizotinib-treated patients (17%). There were 139 patients who experienced disease progression (as assessed by blinded independent review committee, BIRC) or death, which represented 73% of progression events in the ITT population and 119 BIRC-events or deaths (63%) in the mITT population.

According to Dr. Horn, the trial's analysis demonstrated a statistically significant difference between patients who received ensartinib, with a median progression-free survival of 25.8 months compared with 12.7 months with crizotinib, with a median follow-up of 23.8 and 20.2 months, respectively (HR, 0.52; 95% CI, 0.36-0.75; P=.0003 by log-rank test). In the mITT population, the median progression-free survival has

not been reached yet for the ensartinib arm vs. 12.7 months for the crizotinib arm (HR, 0.48; 95% CI, 0.32-0.71; P=.0002 by log-rank test).

The overall response rate was 75% versus 67% with crizotinib; among patients with measurable brain metastases, the BIRC-assessed intracranial overall response rate was 64% with ensartinib versus 21% with crizotinib.

The time-to-treatment-failure rate in the brain in patients with no baseline brain metastases was also significantly lower with ensartinib compared to crizotinib (4% vs 24% at 12 months).

"In patients with ALK-positive NSCLC, ensartinib significantly prolonged progression-free survival over crizotinib with a favorable safety profile, representing a new option in the first-line setting," Dr. Horn concluded.

"This is a remarkable achievement that gives patients with ALK+ lung cancer and treating physicians a safe and effective new treatment choice to control the disease before any other ALK TKI has been used. The study continues to follow patients that are on treatment and will be updated at upcoming conferences," said Li Mao, M.D. and CEO of Xcovery Holdings, Inc., the sponsor of the study.

Provided by International Association for the Study of Lung Cancer

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