Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/seralutinib-for-treatment-of-group-1-pah/15741/

Time needed to complete: 1h 23m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Seralutinib for Treatment of Group 1 PAH

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Shlobin:
Hi my name is Oksana Shlobin, and I'm a Medical Director for Pulmonary Hypertension Program at Inova Fairfax Hospital. Today I'm going to talk about seralutinib for treatment of Group 1 pulmonary arterial hypertension.

This slide shows mechanism of action of seralutinib. And let me walk you through it. CSF1R positive macrophages secrete PDGF and contribute to both inflammation and vascular remodeling. C-KIT positive cells are thus increased, and they further drive both the inflammatory and proliferative process. Aberrant PDGFR signaling drives overgrowth of vascular smooth muscle cells, thus leading to medial hypertrophy, neointimal lesion formation, and fibrosis. Furthermore, PDGF activation decreases BMPR2, and that causes pulmonary arteries small muscle cell proliferation. Seralutinib, a tyrosine kinase inhibitor, targets all of these receptors and cytokines and it modulates expression of BMPR2.

This slide shows the TORREY phase 2 trial design. It's a 24-week, double-blind, placebo-controlled study of 1:1 randomization with a total of 86 patients. The inclusion criteria were functional class II to III, including patients on triple therapy. And just about 50% of patients were on triple therapy with a PVR of equal or more than 5, and there was a dose titration from 45 to 90 mg twice a day. The primary endpoint was pulmonary vascular resistance change from baseline, and a secondary endpoint was 6-minute walk test change from baseline. Most patients completed the study with only about 16% of patients who discontinued treatment, and 13% of patients who withdrew from the study, mostly due to side effects.

This slide shows some demographic data, and I'd like to draw your attention to functional class distribution. As you can see, patients enrolled in a seralutinib were more likely to be in functional class II, so they were a bit less sick. It is a prevalent population with almost 9 years from a diagnosis of pulmonary hypertension to enrollment of the study. The 6-minute walk test distance at baseline is a little bit higher than we normally see in PAH trials. And NT-proBNP is a little bit lower overall. If you break the population into functional class II and functional class III, the demographic data is what we would normally expect for the respective classes. The other parameter that was used in baseline demographics was REVEAL 2.0 risk score. And in functional class II patients, about 30% of the patients had a score more than 6. And in the functional class III cohort, 60% of patients had a REVEAL 2.0 Lite score more than 6.

So the topline results from the study that were announced by the company show that the drug met primary endpoint of statistically significant PVR reduction of 14%. And it did appear that the patients with more severe disease had a larger effect. So you can see patients who had functional class III symptoms at baseline had a PVR reduction of 21%, and patients who had REVEAL 2.0 score of 6 or above at baseline kind of decrease in PVR of 23%. The 6-minute walk test analysis also showed that as an entire treated group, there was a favor towards seralutinib treatment group, again with enhanced effect in patients with more severe disease. So, for the entire group, there was a 6.5-meter improvement. But if you look at the patients in functional class III group, there was an improvement of 37.3 meters. Similarly, for patients who had a REVEAL 2.0 score of 6 or more at baseline, there was an improvement of almost 22 meters. In

addition, patients who were received seralutinib had significantly significant reduction in NT-proBNP, and also significant reduction in echo-assessed RV parameters, and specifically the parameters that were looked at right atrial area, RV free wall strain, and pulmonary artery compliance.

So in the summary, seralutinib resulted in statistically significant PVR reduction, 6-minute walk test distance favorite seralutinib treated group, with enhanced effect in patients with more severe disease. And the results of the study are also supported by NT-proBNP and echo RV parameters data.

Thank you very much.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.