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/emerging-ph-therapeutics-ralinepag/15736/

Time needed to complete: 1h 23m

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

Emerging PH Therapeutics: Ralinepag

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. Preston:
Hello, I'm Ioana Preston, the Director of the Pulmonary Hypertension Center at Tufts Medical Center in Boston. Welcome, and thank you for joining me to discuss today emerging therapies in PAH, ralinepag.

We know that pathological mechanisms of pulmonary arterial hypertension are related, at least in part, to a prostacyclin pathway deficiency and prostacyclin production deficiency. Ralinepag is a novel next generation highly selective IP receptor agonist that has demonstrated positive findings in a phase 2 clinical study of pulmonary arterial hypertension. In addition, preclinical findings on pharmacology, pharmacokinetics, and efficacy with ralinepag have been reported before. The table on the slide shows the distribution and the importance of various prostacyclin and prostaglandin receptors in our body and the affinity of ralinepag to each receptor.

Let's talk about the phase 2 trial with ralinepag. This was a randomized, parallel group, placebo-controlled trial. The primary efficacy endpoint was absolute change in pulmonary vascular resistance from baseline to week 22. Several secondary endpoints were included such as changes in 6-minute walk distance, hemodynamics, percent change in pulmonary vascular resistance, as well as safety and tolerability. Exploratory endpoints included changes in BNP and NT-proBNP from baseline to week 22.

This is the phase 2 ralinepag trial study design, where PAH patients were randomized in a 2:1 fashion to either ralinepag or placebo. The first part of the study included a up-titration to maximum tolerated dose. And the second part of the study, patients were maintained on their maximum tolerated dose up to week 22.

If we look at the demographics and baseline characteristics of the 61 PAH patients enrolled, we see that patients had Group 1 PAH, and they have been mostly on combination therapy with an ERA and PDE5, or an ERA and soluble guanylate cyclase stimulators.

Ralinepag significantly reduced pulmonary vascular resistance when compared to placebo. On the left-hand side, it's the result of the primary endpoint with absolute reduction in pulmonary vascular resistance in the ralinepag arm versus no change in the placebo. And on the right-hand side, there is the percent change in pulmonary vascular resistance in ralinepag and the placebo arms.

Regarding the secondary hemodynamic parameters and their change from baseline to week 22, we note a decrease in mean PA pressure in the ralinepag arm, but as well as a decrease in main PA pressure and systemic vascular resistance, suggesting some systemic effects of ralinepag. Importantly, ralinepag also reduced NT-proBNP compared to placebo, as shown in this graph. Six-minute walk distance increased from baseline by over 36 meters with ralinepag, but it also increased almost 30 meters with placebo. Serious adverse events occurred in 10% of ralinepag patients, and 29% of placebo patients, and study discontinuations occurred in 13% of ralinepag, and 10% of placebo patients.

Going back to the improvement in 6-minute walk distance in placebo arm, I think this effect occurred because patients in this particular study were enrolled very soon after the diagnosis of PAH.

The frequency of patient-reported adverse events are depicted here, where prostacyclin-type adverse events have been recorded, such as headache, nausea, and diarrhea. And of note, with more frequency during the up-titration period of the phase 2 trial compared to the maintenance phase.

In conclusions, phase 2 study of ralinepag was designed to assess the efficacy, safety, and tolerability of twice-daily ralinepag administered orally in a cohort of adult patients with PAH. Ralinepag caused a statistically significant absolute change in PVR, meeting the primary efficacy endpoint. When expressed as percentage change relative to placebo, an almost 30% difference was observed, including a 20.1% decrease from baseline for the ralinepag treated group. Additional signs of efficacy were also observed in other hemodynamic parameters. Of note ralinepag produced greater mean reductions in both systolic and mean PA pressures compared with placebo. Twenty-two weeks of treatment with ralinepag was well tolerated by most patients in this study, and the treatment-related adverse events generally consistent with known safety profile of prostacyclin receptor agonist. Ralinepag, next generation orally available non-prostanoid, selective prostacyclin receptor agonist, significantly reduced pulmonary vascular resistance compared with placebo in patients with symptomatic PAH. This effect was observed in subjects who were taking either monotherapy or combination therapy at the time of enrollment.

As a consequence, the phase 3 clinical trial program with ralinepag advanced outcomes is currently recruiting. The study is designed to assess the efficacy and safety of ralinepag when added to background therapy in patients with Group 1 PAH.

Primary endpoint is the time and days from randomization to the first adjudicated protocol-defined clinical worsening event. Worsening event includes death, nonelective hospital admission for worsening PAH, initiation of parenteral or inhaled prostacyclin agent for treatment of worsening PAH, disease progression, which is also a clearly defined point, or unsatisfactory long-term clinical response, a very important aspect of PAH treatment.

Several secondary endpoints include change in the REVEAL risk score, a 6-minute walk distance, NT-proBNP, and functional class. The formulation in this trial is a new once a day extended-release tablet, and the trial is planning to enroll 1,000 patients.

With that, I thank you for your participation.

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.