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(866) 423-7849

Emerging PH Therapeutics: Vardenafil

Announcer:
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Dr. Preston:
Hello, I'm Dr. Ioana Preston. I'm Director of the Pulmonary Hypertension Center at Tufts Medical Center in Boston. Thank you for joining me today to talk about emerging therapeutics in PAH, vardenafil.

We know that there are no treatments for PAH to acutely improve exercise capacity and symptoms on an as-needed basis in patients with pulmonary arterial hypertension, much as like patients with asthma who can use their inhaled therapies on a PRN basis. We also know that oral PDE5 inhibitors are effective and approved for the treatment of PAH. Oral vardenafil is a PDE5 inhibitor that is approved for the treatment of erectile dysfunction, and its safety profile is well established. However, it has not been formally properly tested in PAH.

A phase 2A RT234 dose escalating study used vardenafil in an inhaled formulation, not an oral, which was very novel, and demonstrated a dose-dependent reduction in pulmonary vascular resistance, and was safe and well tolerated in patients with PAH. Therefore, a phase 2B study has been developed to evaluate the efficacy and safety of inhaled vardenafil RT234 in a DPI device on exercise capacity and symptoms assessed by cardiopulmonary exercise test, or CPET, and 6-minute walk test in PAH participants who are on stable background therapy.

The study is called VIPAH PRN, and is a prospective, multicenter, open-label, dose escalation phase 2B study. And the objective is to evaluate the efficacy and safety of RT234 on exercise capacity and symptoms. The study design is depicted here. Patients with PAH and functional class II, II, or IV on stable PAH background therapy are enrolled in this open-label study. The first cohort will receive 0.5 mg of vardenafil inhaled, the second will receive 1 mg of inhaled vardenafil. After a baseline screening visit, where a 6-minute walk test and CPET will be performed, the following visit will include a CPET 30 minutes after dose inhalation, and visit 4 will include a 6-minute walk test 30 minutes after post dose inhalation. The pharmacokinetics will also be obtained after each of the two doses.

So the key endpoints of the trial will include the change from baseline in peak VO2, 6-minute walk distance, ventilatory inefficiency slope as measured by VE/VCO2 slope, and duration of exercise from baseline to compared to the inhaled treatment. There will be several safety components who will be measured, such as incidence and severity of adverse events, and changes from baseline in vital signs, physical examination, and EKG.

The key eligibility criteria include adult patients with Group 1 PAH who are up to three PAH-specific background therapies that include oral or inhaled. But patients are excluded if they are on parenteral medications or on riociguat. The right heart catheterization criteria are listed here, and the VE/VCO2 slope has to be at least a 36. And this will ensure that patients are symptomatic with exercise.

So the preliminary characteristics of the first 9 patients are listed here, where patients have Group 1 PAH, and they are on a combination or therapy with PDE5 inhibitors and endothelin receptor antagonists or prostacyclin, or their analogs.

These are the preliminary results of the patients so far included in the trial. And it shows the change in 6-minute walk distance between baseline and after the low-dose vardenafil 0.5 mg. And also on the right-hand side, the 6-minute walk distance change from baseline to after dosing in patients who, at baseline, walked less than 500 meters.

This is an example of a patient enrolled in the VIPAH study, a 35-year-old female with idiopathic PAH, who showed improvement in several parameters measured after inhalational treatment. And these included peak VO2, VE/VCO2 slope, peak blood pressure with peak exercise, to exercise time, and peak dyspnea.

In summary, PAH patients remain symptomatic even on background therapies, especially in their everyday activities. PDE5 inhibitors are known effective treatments for PAH. VIPAH PRN is the first study investigating RT234, vardenafil inhalation powder for an as-needed treatment for PAH in addition to stable disease-specific background therapy to acutely improve exercise and/or quality of life. Preliminary results suggest that inhaled RT234 may offer a clinical benefit with minimal side effects for patients with PAH. This proof-of-concept study is actively enrolling in the U.S., and will inform the design of the global RT234 phase 3 clinical program.

Thank you for joining me today.

Announcer:
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