Background

- Pulmonary arterial hypertension (PAH) is characterized by abnormally high mean pulmonary arterial pressures and remodeling of the pulmonary vasculature culminating in progressive right ventricular dysfunction.
- Current disease-specific treatments for PAH include endothelin-receptor antagonists (ERAs), phosphodiesterase (PDEs) inhibitors, and prostanoids and are used with general supportive care agents (e.g., anticoagulants, diuretics, digoxin).
- Therapies that attenuate the development and progression of PAH are needed.
- Mutations in bone morphogenetic protein receptor 2 (BMPR2) underlie many heritable cases of PAH; however, the relevance of the BMPR2 pathway extends far beyond familial PAH.
- Disruptions in transforming-growth-factor (TGF)-β and BMP signaling are associated with the development of PAH.

Study Design

**STUDY POPULATION**

- One hundred participants with WHO Group 1 PAH (Functional Class II–III) at clinical sites in 9 countries

**TREATMENT PERIOD**

- This ongoing, Phase 2, randomized, double-blind, placebo-controlled, parallel-group study is comprised of 3 periods (Fig. 2):
  - Screening period (up to 28 days)
  - Treatment period
  - Post-treatment follow-up period (8 weeks)

**EXTENSION PERIOD**

- Participants who have not discontinued early from the Placebo-controlled Treatment Period can directly rollover into the 18-month Extension Period and be treated as follows (Fig. 2):
  - Participants initially randomized to placebo will be re-randomized to receive sotatercept (0.3 mg/kg or 0.7 mg/kg) SC every 21 days plus SOC
  - Participants initially randomized to sotatercept will continue on their current dose level, administered SC every 21 days, plus SOC

**OBJECTIVE**

- To determine the efficacy and safety of sotatercept (ACE-011) plus standard care of SOC* versus placebo plus SOC in adults with PAH (World Health Organization [WHO] Group 1).

**STUDY ENDPOINTS**

- **Efficacy endpoints**
  - Change from baseline in 6MWD
  - Change from baseline in quality of life
  - Change from baseline in pulmonary vascular resistance (PVR)
  - Change from baseline in echocardiographic parameters

- **Safety endpoints**
  - Change from baseline in NT-proBNP (Figure 1)
  - Change in safety and endpoints

**REFERENCES**


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