A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Compare the Efficacy and Safety of Sotatercept Versus Placebo When Added to Background Pulmonary Arterial Hypertension (PAH) Therapy for the Treatment of PAH

Status: Recruiting

Eligibility Criteria

Sex: All
Age: 18 Years and over
This study is NOT accepting healthy volunteers
Key

Inclusion Criteria:

1. Age â‰¥ 18 years 2. Documented diagnostic right heart catheterization (RHC) at any time prior to screening confirming the diagnosis of WHO pulmonary arterial hypertension (PAH) Group 1 in any of the following subtypes:

• Idiopathic PAH

• Heritable PAH

• Drug/toxin-induced PAH

• PAH associated with connective tissue disease

• PAH associated with simple, congenital systemic to pulmonary shunts at least 1 year following repair 3. Symptomatic PAH classified as WHO Functional Class II or III 4. Baseline RHC performed during the Screening Period documenting a minimum pulmonary vascular resistance (PVR) of â‰¥ 5 Wood units (WU) and a pulmonary capillary wedge pressure (PCWP) or left ventricular end-diastolic pressure of â‰¤ 15 mmHg. 5. On stable doses of background PAH therapy and diuretics (i.e., patient-specific dose goal for each therapy already achieved) for at least 90 days prior to screening; for infusion prostacyclins, dose adjustment within 10% of optimal dose is allowed per medical practice. 6. 6MWD â‰¥ 150 and â‰¤ 500 m repeated twice at screening (measured at least 4 hours apart, but no longer than 1 week), and both values are within 15% of each other (calculated from the highest value) 7. Females of childbearing potential must:

• Have 2 negative urine or serum pregnancy tests as verified by the investigator prior to starting study therapy; she must agree to ongoing urine or serum pregnancy testing during the study and until 8 weeks after the last dose of the study drug

• If sexually active, have used, and agree to use, highly effective contraception without interruption, for at least 28 days prior to starting the investigational product, during the study (including dose interruptions), and for 16 weeks (112 days) after discontinuation of study treatment

• Refrain from breastfeeding a child or donating blood, eggs, or ovum for the duration of the study and for at least 16 weeks (112 days) after the last dose of study treatment 8. Male participants must:

• Agree to use a condom, defined as a male latex condom or nonlatex condom NOT made out of natural (animal) membrane (e.g., polyurethane), during sexual contact with a pregnant female or a female of childbearing potential while participating in the study, during dose interruptions and for at least 16 weeks (112 days) following investigational product discontinuation, even if he has undergone a successful vasectomy

• Refrain from donating blood or sperm for the duration of the study and for 16 weeks (112 days) after the last dose of study treatment 9. Ability to adhere to study visit schedule and understand and comply with all protocol requirements 10. Ability to understand and provide written informed consent Key

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Exclusion Criteria:

1. Diagnosis of pulmonary hypertension WHO Groups 2, 3, 4, or 5 2. Diagnosis of the following PAH Group 1 subtypes: human immunodeficiency virus (HIV)-associated PAH and PAH associated with portal hypertension. Exclusions in PAH Group I should also include schistosomiasis APAH and pulmonary veno occlusive disease 3. Hemoglobin (Hgb) at screening above gender-specific upper limit of normal (ULN), per local laboratory test 4. Baseline platelet count < 50,000/mm3 (< 50.0 x 109/L) at screening 5. Uncontrolled systemic hypertension as evidenced by sitting systolic blood pressure > 160 mmHg or sitting diastolic blood pressure > 100 mmHg during screening visit after a period of rest 6. Baseline systolic BP < 90 mmHg at screening 7. Pregnant or breastfeeding women 8. Any of the following clinical laboratory values at the screening visit:

• Estimated glomerular filtration rate (eGFR) < 30 mL/min/m2 (as defined by MDRD equation)

• Serum alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels > 3 Ã— ULN (bilirubin criterion waived if there is a documented history of Gilbert's syndrome) 9. Currently enrolled in or have completed any other investigational product study within 30 days for small molecule drugs or within 5 half-lives for biologics prior to the date of signed informed consent 10. Prior exposure to sotatercept (ACE-011) or luspatercept (ACE 536) and/or excipients or known allergic reaction to either one 11. Have full or partial pneumonectomy 12. Pulmonary function test (PFT) values of forced vital capacity (FVC) < 60% predicted at the screening visit or within 6 months prior to the screening visit. If PFT is not available, a chest CT scan showing more than mild interstitial lung disease (ILD) performed at the screening visit or 1 year prior to it. 13. Initiation of an exercise program for cardiopulmonary rehabilitation within 90 days prior to the screening visit or planned initiation during the study (participants who are stable in the maintenance phase of a program and who will continue for the duration of the study are eligible). 14. History of more than mild obstructive sleep apnea that is untreated 15. Known history of portal hypertension or chronic liver disease, including hepatitis B and/or hepatitis C (with evidence of recent infection and/or active virus replication), defined as mild to severe hepatic impairment (Child-Pugh Class A-C) 16. History of restrictive, constrictive or congestive cardiomyopathy 17. History of atrial septostomy within 180 days prior to the screening visit 18. Electrocardiogram (ECG) with Fridericia's corrected QT interval (QTcF) > 500 ms during the screening period 19. Personal or family history of long QT syndrome (LQTS) or sudden cardiac death 20. Left ventricular ejection fraction < 45% on historical echocardiogram within 6 months prior to the screening visit 21. Any symptomatic coronary disease events within 6 months (prior myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, or cardiac anginal chest pain) within 6 months of the screening visit. Note: Anginal pain can be ignored as an exclusion criterion if coronary angiography shows no obstructions. 22. Cerebrovascular accident within 3 months prior to the screening visit 23. Acutely decompensated heart failure within 30 days prior to the screening visit, as per investigator assessment 24. Significant (â‰¥ 2+ regurgitation) mitral regurgitation or aortic regurgitation valvular disease 25. Received intravenous inotropes (e.g., dobutamine, dopamine, norepinephrine, vasopressin) within 30 days prior to the screening visit

Conditions & Interventions

Interventions:
Drug: Sotatercept, Drug: Placebo
Conditions:
Pulmonary Arterial Hypertension
Keywords:
Pulmonary, Hypertension, sotatercept, Clinics and Surgery Center (CSC)

More Information

Description: The objective of this study is to evaluate the efficacy and safety of sotatercept treatment (plus background P AH therapy) versus placebo (plus background PAH therapy) at 24 weeks in adults with PAH.
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Phase: Phase 3
IRB Number: STUDY00012824
System ID: NCT04576988

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