An Open-Label Long-term Follow-up Study to Evaluate the Effects of Sotatercept When Added to Background Pulmonary Arterial Hypertension (PAH) Therapy for the Treatment of PAH

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Primary:The primary objective of this open-label, LTFU study is to evaluate the long-term safety and tolerability of sotatercept when added to background PAH therapy in adult participants with PAH.Secondary:The secondary objective is to follow...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Pulmonary vascular disorders
Study type	Interventional

Summary

ID

NL-OMON56380

Source
ToetsingOnline

Brief title
A011-12 SOTERIA

Condition

- Pulmonary vascular disorders

Synonym
Pulmonary Arterial Hypertension - lung hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Acceleron Pharma, Inc., a wholly-owned subsidiary of Merck&Co., Inc.
Source(s) of monetary or material Support: betaald door Acceleron (de verrichter)

Intervention

Keyword: ActRIIA, Pulmonary Arterial Hypertension, Sotatercept, Soteria

Outcome measures

Primary outcome

Primary (safety) endpoints.

The following endpoints will be evaluated as a measure of safety and

tolerability:

• Adverse events (AEs)

• Anti-drug antibodies (ADA)

• Clinical laboratory assessments (hematology and serum chemistry /

follicle-stimulating hormone (FSH), and urinalysis)

• Vital signs

• 12-lead electrocardiogram (ECG)

Secondary outcome

Secondary (Efficacy) endpoints

The following efficacy endpoints will be evaluated:

• 6-minute walk distance

• N-terminal pro-hormone B-type natriuretic peptide

• World Health Organization functional class

• Pulmonary vascular resistance

• Overall survival

• Simplified French Risk score

Study description

Background summary

This Phase 3 study is being conducted to assess the long-term safety, tolerability, and efficacy of sotatercept in PAH. Long-term follow-up of patients receiving sotatercept is important to understand the maintenance and durability of treatment effect (especially in the presence of background PAH therapy) and to provide greater opportunity for pharmacovigilance following sotatercept treatment in the selected patient populations.

This LTFU study is supported by data from the PULSAR study (Phase 2, NCT03496207), in which treatment with sotatercept resulted in hemodynamic and functional improvements in the study participants, including those receiving maximal PAH therapy with double/triple drug combinations and intravenous prostacyclin.

Study objective

Primary:
The primary objective of this open-label, LTFU study is to evaluate the long-term safety and tolerability of sotatercept when added to background PAH therapy in adult participants with PAH.

Secondary:
The secondary objective is to follow participants from parent sotatercept studies that were treated with sotatercept or placebo and assess continued efficacy

Study design

This open-label, LTFU study will evaluate the safety, tolerability, and efficacy of sotatercept in participants with PAH previously treated with sotatercept or placebo.

Consenting participants who meet the eligibility criteria can roll over to A011-12 study to receive/continue receiving sotatercept plus background PAH therapy. Administration of sotatercept will be via subcutaneous (SC) injection(s) every 21 days.

Participants rolling over to the A011-12 study from a blinded parent study will begin sotatercept treatment at a dose of 0.3 mg/kg (SC).

The dose for participants with stable hemoglobin (Hgb) and platelet counts should be titrated up to 0.7 mg/kg at Visit 2 (Study Day 22 ± 3 days). However, if at Visit 2 Hgb increases by more than 2.0 g/dL from baseline (Visit 1) and this value is above the gender specific- upper limit of normal (ULN) per local laboratory test, dosing should be delayed. All other study procedures, with the exception of study drug administration, should be performed. At Visit 3, if Hgb has increased by less than 2.0 g/dL from baseline (Visit 1) or Hgb value is below the gender-specific ULN per local laboratory test, dosing should be restarted at 0.3 mg/kg. At Visit 4, if Hgb has increased by less than 2.0 g/dL from baseline (Visit 1) or
Hgb value is below the gender-specific ULN per local laboratory test, the dose may be escalated to the target dose of 0.7 mg/kg.

Participants rolling over to the A011-12 study from an unblinded parent study will continue sotatercept treatment at their current dose (SC) and, if they are at dose < 0.7 mg/kg, they will have the opportunity to titrate up to a dose of 0.7 mg/kg (SC) per investigator discretion. The above guidelines for dose escalation will be followed.

Participants will complete, at minimum, the first 5 consecutive visits at the clinical site. In order to qualify for optional at home self-administration, participants must meet the following criteria for the previous 3 consecutive visits:
- Stable Hgb levels (within 2 g/dL, below the gender-specific upper ULN per local laboratory test)
- Stable platelet count levels (within the normal range by local laboratory test; if below the lower limit of normal, within 10% of the previous values)
Participants who meet these criteria qualify for optional self-administration of sotatercept at home starting at Study Day 106 (±3 days) or later. Each self--administration of sotatercept at home will be accompanied by a phone call from the clinical investigative site to confirm proper storage, dosing, and administration of sotatercept and to document concomitant medications as well as incidence of any adverse events (AEs), medication errors, accidental exposure of others, or product inquiries.
On-site visits will continue for participants who are ineligible for and opt out of optional self-administration of sotatercept at home. For participants eligible for and opting into self-administration of sotatercept at home, quarterly on-site visits will be performed approximately every 3 months according to the Schedule of Events in table 2, page 18 of the protocol.

Intervention

Sotatercept, up to the target dose of 0.7 mg/kg.

Study burden and risks

Participation in the study requires amongst other the following of the patient:
- number of visits (in 4 years about 68 visits)
- procedures can be a burden, like right heart catherisation (RHC). However, this procedure is only performed once, at the end of trial.
- during the study and till 112 days after the last dose, women are not allowed to get pregnant
- if a patient is not eligible for self administration of sotatercept, the patient has to visit the hospital every 3 weeks for an injection with sotatercept
- adverse events (see E9 and E9a)

Currently, PAH cannot be treated and treatment only aims to relieve symptoms or slow down clinical worsening. In general the disease shows progression.
In the PULSAR study Sotatercept was able to demonstrate hemodynamic and functional improvements in these participants, including those receiving maximal PAH therapy with double/triple drug combinations and intravenous prostacyclin.
Through a novel mechanism of action, sotatercept may open up a new treatment paradigm for PAH

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Eligible participants must meet the following criteria to be enrolled in the study:
1. Participants must have completed their current respective PAH sotatercept clinical study, must have completed the parent study requirements, and must not have discontinued early.
2. Participants must be willing to adhere to the study visit schedule and understand and comply with all protocol requirements.
3. Participants must have the ability to understand and provide documented consent.
4. Females of childbearing potential must:
a. Have a negative pregnancy tests as verified by the investigator prior to starting study drug administration; she must agree to ongoing pregnancy testing during the course of the study and until 8 weeks after the last dose of the study drug.
b. If sexually active, have used, and agree to continue to use highly effective contraception in combination with a barrier method 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 drug.
c. 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 drug.
5. Male participants must:
a. Agree to use a condom, defined as a male latex condom or non-latex 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
b. Refrain from donating blood or sperm for the duration of the study and for 16 weeks (112 days) after the last dose of study drug.
6. Participants must agree not to participate in any other trials of investigational drugs/devices while they are enrolled in the A011-12 study

Exclusion criteria

Participants will be excluded from the study if any of the following criteria are met:
1. Did not participate in a sotatercept PAH parent trial.
2. Missed more than the equivalent of 4 consecutive doses between the end of parent study and the start of this study.
3. Presence of an ongoing serious adverse event (SAE) that occurred during a PAH sotatercept clinical study that is assessed to be possibly or probably related to sotatercept.
4. Pregnant or breastfeeding females.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-10-2022
Enrollment:	24
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	NA
Generic name:	Sotatercept

Ethics review

Approved WMO Date:	25-11-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-02-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-10-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-11-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-02-2023
Application type:	Amendment
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Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-08-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-11-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-02-2024

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-03-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-05-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	31-05-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-005061-13-NL
ClinicalTrials.gov	NCT04796337
CCMO	NL79145.028.21