A 16-Week International, Multicenter, Double-Blind, Randomized, Placebo Controlled Comparison of the Efficacy and Safety of Oral UT-15C Sustained Release Tablets in Combination with an Endothelin Receptor Antagonist and/or a Phosphodiesterase-5 Inhibitor in Subjects with Pulmonary Arterial Hypertension

Published: 01-12-2006
Last updated: 10-05-2024

Primary: To assess the effect of UT-15C sustained release (SR) on exercise capacity compared to placebo (as measured by the change in 6-Minute Walk distance from Baseline to Week 16) in subjects with PAH.Secondary: To assess the effect of UT-15C SR...

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

Summary

ID

NL-OMON30667

Source
ToetsingOnline

Brief title
FREEDOM-C

Condition

- Pulmonary vascular disorders

Synonym
high blood pressure in the small circulation; Pulmonal Arterial Hypertension

Research involving
Human

Sponsors and support

Primary sponsor: United Therapeutics Corporation
Source(s) of monetary or material Support: bedrijf: United Therapeutics Corporation

Intervention

Keyword: Double-Blind, Endothelin Receptor Antagonist, Phosphodiesterase-5 Inhibitor, Pulmonary Arterial Hypertension

Outcome measures

Primary outcome

The primary study parameter is the change in the distance traversed in the

Six-Minute Walk Test at Week 16 over placebo in subjects with PAH.

Secondary outcome

Borg Dyspnea Score

Combined Walk and Borg Dyspnea Score

Clinical Worsening

Dyspnea-Fatigue Index

WHO Functional Class

Symptoms of PAH

Study description

Background summary

Combination treatment of PAH with therapies targeting different mechanisms of action has great promise in addressing the multiple pathophysiologic mechanisms that are implicated in PAH. These combinations may produce an additive effect or enhance and prolong the effect of other therapeutic agents.
Remodulin (treprostinil sodium) is an effective agent given by subcutaneous or intravenous delivery. UT-15C is a diethanolamine salt of treprostinil and is being investigated as a solid-dose oral compound. An oral product is easier to use.

The primary hypothesis is that UT-15C SR will increase the distance traversed in the Six-Minute Walk Test at Week 16 over placebo in subjects with PAH.

Study objective

Primary: To assess the effect of UT-15C sustained release (SR) on exercise capacity compared to placebo (as measured by the change in 6-Minute Walk distance from Baseline to Week 16) in subjects with PAH.

Secondary: To assess the effect of UT-15C SR on the following:
* Combined Walk Distance/Borg Dyspnea Score
* Clinical Worsening*
* Borg Dyspnea Score
* Dyspnea-Fatigue Index
* World Health Organization (WHO) Functional Class
* Symptoms of PAH
* Safety (adverse events, clinical laboratory parameters, electrocardiogram findings)

*Definition of clinical worsening requires one of the following:
1. Death (all causes excluding accident)
2. Transplantation or atrial septostomy
3. Clinical deterioration as defined by:
a. Hospitalization as a result of PAH, or
b. * 20% decrease in 6-Minute Walk distance from Baseline (or too ill to walk) and a decrease in WHO Functional Class And
c. Initiation of new PAH specific therapy (i.e., endothelin receptor antagonist, phosphodiesterase-5 inhibitor, prostacyclin).

Study design

Multi-center, randomized, double-blind, placebo-controlled, 16-week study in subjects with PAH currently receiving oral therapy for the treatment of PAH.

Intervention

Each patient starts with one tablet studymedication or placebo twice daily. This dose may be increased every five days with an additional 1 mg.

Study burden and risks

Subjects will be assessed during Screening and Baseline Phases to determine eligibility for the study.
Once enrolled in the study following the Baseline Visit, four Treatment Phase visits to the clinic will be required at 4 weeks, 8 weeks, 12 weeks, and 16 weeks after
randomization.
Treatment will be initiated at 1 mg twice daily (every 12 hours +/- 1 hour) with dose escalation of an additional 1 mg twice daily every 5 days.

The most commonly observed side effects of UT-15C SR during previous studies included headache, facial flushing, dizziness and nausea. Other side effects that may occur with UT-15C SR are vomiting, low blood pressure, and jaw pain.

The risks associated with the 6-Minute Walk Test may include the possibility of fatigue, fainting, muscle soreness, strain or injury.

Contacts

Public
United Therapeutics Corporation

One Park Drive, PO Box 14186
Research Triangle Park, NC 27709
USA
Scientific
United Therapeutics Corporation

One Park Drive, PO Box 14186
Research Triangle Park, NC 27709
USA

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. The subject is between 12 and 70 years of age at Screening.
2. The subject weighs a minimum of 45 kg at Screening.
3. The subject, if female, is incapable of chilbearing of practicing an acceptable method of bith-control. For women of childbearing potential, a negative blood pregnancy test will be required at Screening.
4. The subject has a diagnosis of symptomatic Idiopathic or Familial PAH (including PAH associated with appetite suppressant/toxin use), PAH associated with repaired congenital systemic-to-pulmonary shunts (repaired * 5 years), PAH associated with Collagen Vascular Disease, or PAH associated with HIV.
5. The subject, if HIV positive, has a CD4 lymphocyte count * 200 within 30 days of Baseline and is receiving current standard of casr anti-retroviral or other effective treatment for HIV.
6. The subject must have a Baseline 6-Minute Walk distance of between 150 and 450 meters inclusive.
7. The subject may benefit from the introduction of additional therapy (e.g. a prostacyclin) as determined by their medical provider.
8. The subject must have been optimally treated with approved oral therapies. Specifically, the subject:
a. Has been receiving approved PDE-5 inhibitor or approved ERA therapy alone for at least 90 days and at the current stable dose for 30 days prior to Baseline and is willing to remain on PDE-5 inhibitor or ERA alone and at the same dose for the duration of the 16-week Treatment Phase
or
b. Has been receiving the combination of approved PDE-5 inhibitor and approved ERA therapy for at least 90 days prior to Baseline with both treatments at the current stable dose at least 30 days prior to Baseline and is willing to remain on the combination of PDE-5 inhibitor and ERA at the same dose for the duration of the 16-week Treatment Phase.
9. The subject must be optimally treated with conventional pulmonary hypertension therapy
10. The subject voluntarily gives informed consent to participate in the study.

Exclusion criteria

1. The subject is pregnant or lactating.
2. The subject has received epoprostenol, treprostinil, iloprost, beraprost, or any other prostacyclin therapy within 30 days of Baseline.
3. The subject has had a new type of chronic therapy for pulmonary hypertension added

within 30 days of Baseline.
4. The subject has had any PAH medication except for anticoagulants discontinued within 30 days of Baseline.
5. The subject has any disease associated with pulmonary arterial hypertension other than mentioned in the inclusion criteria.
6. The subject has a current diagnosis of uncontrolled sleep apnea.
7. The subject has chronic renal insufficiency.
8. The subject has anemia.
9. The subject has a history or current evidence of left-sided heart disease.
10. The subject has significant parenchymal lung disease.
11. The subject has uncontrolled systemic hypertension
12. The subject has any disease that is likely to limit ambulation.
13. The subject participates is another study or has participated in a study within 30 days prior to Screening.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-08-2007
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not applicable

Generic name:	Treprostinil Diethanolamine

Ethics review

Approved WMO Date:	01-12-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-02-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2006-000800-17-NL
ClinicalTrials.gov	NCT00325442
CCMO	NL15413.029.06