A 12-Week, International, Multicenter, Double-Blind, Randomized, Placebo-Controlled Comparison of the Efficacy and Safety of Oral UT-15C Sustained Release Tablets in Subjects with Pulmonary Arterial Hypertension

Published: 01-12-2006
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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 12) in subjects with PAH who are not currently receiving ERA, PDE-5…

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

Summary

ID

NL-OMON35333

Source
ToetsingOnline

Brief title
FREEDOM-M

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

Intervention

Keyword: Double Blind, International, Pulmonary Arterial Hypertension, UT-15C

Outcome measures

Primary outcome

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

Six-Minute Walk Test at Week 12 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

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 and at the moment only a few oral medicines are on the market for this disease.

The primary hypothesis is that UT-15C SR will increase the distance traversed

in the Six-Minute Walk Test at Week 12 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 12) in subjects with PAH who are not currently receiving ERA, PDE-5 inhibitor, prostacyclin therapy, or any combination. The change in 6-Minute Walk distance will be evaluated primarily for subjects with access to 0.25 mg tablets at the time of randomization, and secondarily for the overall population.

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, 12-week study in subjects with PAH not currently receiving therapy (ERA, PDE-5 inhibitor, or prostacyclin) for the treatment of PAH.

Intervention

Each patient starts with one tablet studymedication or placebo twice daily of 0,25 mg.
This dose may be increased every three days with an additional 0,25 - 0,50 mg twice daily. Subjects unable to tolerate the 0.25 mg dose or subjects requiring

an intermediate dose may utilize the 0.125 mg tablet.

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, 11 weeks, and 12 weeks after randomization.

The treatment will start with a 0,25 mg tablet twice daily (every 12 hours +/- 1 hour) with a possible dose increase every 3 days of an additional 0,25-0,50 mg twice daily. Subjects unable to tolerate the 0.25 mg dose or subjects requiring an intermediate dose may utilize the 0.125 mg tablet.

The most common reported adverse events of UT-15C SR during previous studies include headache, flushes, dizziness and nausea. Other adverse events that might occur with UT-15C SR dosing are vomitting, low blood pressure and jaw pain.

The riscs of the 6 minute walk test may lead to fatigue, fainting, anthralgia, De risico*s verbonden aan de 6 minuten wandeltest kunnen mogelijk leiden tot vermoeidheid, flauwvallen, muscle soreness, strain or injury.

Contacts

Public
United Therapeutics Corporation

55 T.W. Alexander Drive, PO Box 14186
Research Triangle Park, NC 27709
US
Scientific
United Therapeutics Corporation

55 T.W. Alexander Drive, PO Box 14186
Research Triangle Park, NC 27709
US

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 the ages of 12 and 75 years of age at Screening.
2. The subject weighs a minimum of 40 kilograms with a Body Mass Index (BMI) less than 40kg/m2 at Screening.
3. The subject, if female, is physiologically incapable of childbearing or practicing an acceptable method of birth control. For women of childbearing potential, a negative serum 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 care anti-retroviral or other effective medication for treatment of HIV.
6. The subject must have a Baseline 6-Minute Walk distance of between 200 and 400 meters, inclusive.
7. The subject may benefit from the introduction of therapy (e.g. a prostacyclin) as determined by their medical provider.
8. The subject must be optimally treated with conventional pulmonary hypertension therapy.
9. The subject will voluntarily give informed consent to participate in the study.

Exclusion criteria

1. The subject is pregnant or lactating.
2. The subject has previously received a prostacyclin, endothelin receptor antagonist, or phosphodiesterase-5 inhibitor within 30 days of Baseline.
3. The subject has had a new type of chronic therapy for pulmonary hypertension added within 14 days of Baseline.
4. The subject has had any PAH medication except for anticoagulants discontinued within 14 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 diseasea.
11. The subject has uncontrolled systemic hypertension.
12. The subject has any disease that is likely to limit ambulation.
13. The subject is participating, or has participated in another investigational drug or device 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:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	6
Type:	Anticipated

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:	03-07-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-02-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-05-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2010

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	EUCTR2006-000801-50-NL
ClinicalTrials.gov	NCT00325403
CCMO	NL15469.029.06