An Open-Label Extension Study of UT-15C in Subjects with Pulmonary Arterial Hypertension - A Long-Term Follow-Up to Protocol TDE-PH-310

Published: 10-08-2012
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To provide UT-15C for eligible subjects who participated in study protocol TDE-PH-310

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vascular hypertensive disorders
Study type	Interventional

Summary

ID

NL-OMON50371

Source
ToetsingOnline

Brief title
Open-label study of UT-15C in PAH patients

Condition

- Vascular hypertensive disorders

Synonym
increased pressure in pulmonary arteries, PAH

Research involving
Human

Sponsors and support

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

Intervention

Keyword: open-label, Pulmonary hypertension, UT-15C

Outcome measures

Primary outcome

The primary objective of this study is to provide UT-15C sustained release tablets for eligible subjects who participated in TDE-PH-310.

Secondary outcome

- To assess the long-term safety of oral UT-15C

- To assess the effect of continued long-term therapy with UT-15C on exercise capacity (six minute walk distance [6MWD] Borg dyspnea score), World Health Organization (WHO) Functional Class, and N- terminal pro-brain natriuretic peptide (NT proBNP) (at Week 48 only)

Exploratory Objective: Optional evaluation of pharmacogenomics

Study description

Background summary

Pulmonary arterial hypertension (PAH), defined as an elevation in pulmonary arterial pressure and pulmonary vascular resistance, is a severe hemodynamic abnormality common to a variety of diseases and syndromes. Elevation in pulmonary arterial pressure causes an increase in right ventricular afterload, impairing right ventricular function and ultimately leading to heart failure and death.
The typical etiologies of PAH include idiopathic, heritable or associated with collagen vascular/connective tissue disease, portal hypertension, infection with the human immunodeficiency virus (HIV), a history of cocaine inhalation, or exposure to appetite suppressant drugs. An estimated annual incidence of approximately 2 cases per million has been reported for idiopathic PAH. [Rich, 1987; Rubin 1997]

There are three major factors thought to contribute to the increased pulmonary vascular resistance seen in this disease: vasoconstriction, remodeling of the vessel wall, and thrombosis. There are a number of metabolic pathways which contribute to these changes that involve vasoactive mediators such as the vasodilators nitric oxide and prostacyclin, and the vasoconstrictor endothelin-1. These substances affect both vascular tone and remodeling leading to their use as pharmacologic targets. [Farber, 2004]
Approved pharmacotherapies for PAH include: (1) intravenous prostacyclin (epoprostenol sodium or Flolan®); (2) the prostacyclin analogues, subcutaneous (SC), intravenous (IV), and inhaled treprostinil sodium (Remodulin®; Tyvaso®) and inhaled iloprost (Ventavis®); (3) the oral phosphodiesterase-5 inhibitors (PDE5-I), tadalafil (Adcirca®) and sildenafil (Revatio®); and (4) the oral endothelin receptor antagonists, bosentan (Tracleer®) and ambrisentan (Letairis®, Volibris®) [Barst, 2009].

Study objective

To provide UT-15C for eligible subjects who participated in study protocol TDE-PH-310

Study design

Multi-center, open-label study for eligible patients who participated in TDE-PH-310.

Intervention

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Study burden and risks

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Contacts

Public
United Therapeutics Corp

T.W. Alexander Drive 55
Research Triangle Park, NC 27709
US
Scientific
United Therapeutics Corp

T.W. Alexander Drive 55
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 voluntarily provides informed consent to participate in the study.
2. The subject participated in study TDE-PH-310 and met the definition of clinical worsening (as specified in Protocol TDE PH 310), remained on study drug, was compliant with study procedures and assessments during the TDE-PH-310 Study or was currently enrolled in that study at the time the study was discontinued by the sponsor.
3. All WOCBP must practice true abstinence from intercourse when it is in line with their preferred and usual lifestyle, or use 2 different forms of highly effective contraception for the duration of the study, and for at least 30 days after discontinuing study medication. Medically acceptable forms of effective contraception include: (1) approved hormonal contraceptives (such as birth control pills), (2) barrier methods (such as a condom or diaphragm) used with a spermicide, (3) an intrauterine device or (4) partner vasectomy. For women of childbearing potential, a negative urine pregnancy test is required at Baseline (study entry) prior to initiating study medication. WOCBP includes any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or is not postmenopausal [defined as amenorrhea for at least 12 consecutive months].
4. Males participating in the study must use a condom during the length of the study, and for at least 48 hours after their last dose of study medication.

Exclusion criteria

1. The subject is pregnant or lactating.
2. The subject has received infused or inhaled prostacyclin therapy for 29 days or more.
3. The subject was prematurely discontinued from study TDE-PH-310 for reasons other than a clinical worsening event.
4. The subject developed a concurrent illness or condition during the conduct of TDE PH 310 which, in the opinion of the Investigator, would represent a risk to overall health if they enrolled in this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-07-2014
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	/
Generic name:	oral treprostinil diethanolamine

Ethics review

Approved WMO Date:	10-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	15-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	27-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2020
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	EUCTR2012□000098□21-NL
ClinicalTrials.gov	NCT01560637
CCMO	NL41022.029.12