An extended Access Program to Assess Long-Term Safety of Bardoxolone Methyl in Patients with Pulmonary Hypertension

Published: 21-03-2017
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To provide continuing open-label treatment with bardoxolone methyl as part of this extended access program while collecting ongoing safety and tolerability data of bardoxolone methyl.

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

Summary

ID

NL-OMON49960

Source
ToetsingOnline

Brief title
RANGER

Condition

- Vascular hypertensive disorders

Synonym
Pulmonary Arterial Hypertension; increased blood pressure in arteries in the lungs

Research involving
Human

Sponsors and support

Primary sponsor: Reata Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Reata Pharmaceuticals

Intervention

Keyword: Bardoxolone Methyl, Extended Access Program, Pulmonary Hypertension

Outcome measures

Primary outcome

Primary safety endpoint:

Frequency, intensity, and relationship to study drug of adverse events (AEs)

and serious adverseevents (SAEs), and change from baseline in the following

assessments: physical examinations, vital sign measurements, BNP, N-terminal

pro-brain natriuretic peptide (NT-proBNP), and

weight.

Secondary outcome

not applicable

Study description

Background summary

The established pharmacologic effects of bardoxolone methyl, including the suppression of pathologic NF-*B signaling and inflammation and mitochondrial dysfunction, are directly applicable to the treatment of PH. Despite available therapies, the prognosis for PH remains poor, especially for patients with CTD and ILD. Given the severity of the underlying disease, this study seeks to offer patients who previously participated in clinical studies extended access to bardoxolone methyl until it is available through commercial channels (including reimbursement).

Study objective

To provide continuing open-label treatment with bardoxolone methyl as part of this extended access
program while collecting ongoing safety and tolerability data of bardoxolone methyl.

Study design

extended access program - open label study

Intervention

Patients will start dosing at 10 mg of bardoxolone methyl every other day, then begin once dailydosing at Week 4. Dose de-escalation (down to 5 mg) is permitted during the study, if indicated clinically.

Study burden and risks

The most common adverse events of bardoxolone methyl are:
* Muscle spasm
* Hypomagnesemia (low level of magnesium in the blood), which primarily occurred in diabetic chronic kidney disease patients and was not associated with loss of magnesium into the urine or loss of magnesium inside cells
* Nausea
* Decreased appetite
* Weight decreased associated with a reduction in waist circumference, which primarily occurred in obese patients
* Fatigue

Less common adverse events of bardoxolone methyl are:
* Cough
* Dysgeusia (persistent metaalic taste in the mouth)
* Transient increased levels of liver enzymes, which have not been associated with liver injury in any patients
* Headache

Some participants with Stage 4 chronic kidney disease and a medical history of heart failure in previous studies experienced fluid overload. The current trial will employ risk mitigation procedures to reduce the potential for bardoxolone methyl induces fluid overload.
Th prognosis for patients with PAH is poor. The treatments that are available at the moment, do mostly not lead to functional improvements. Previous studies suggest that treatment with bardoxolone methyl may be beneficial to patients in combination with the optimal treatment with vasodilators. Patients participating in the study will be closely monitored en will continue to receive their standard of care treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Treatment-compliant patients who are participating in qualifying ongoing studies and have completed required End-of-Treatment and/or Follow-up visits in a prior clinical study with bardoxolone methyl

Exclusion criteria

1. Participation in other investigational clinical studies involving interventional products being tested or used in a way different from the approved form or when used for an unapproved indication, 2. Patients who have an ongoing SAE from a clinical study that is assessed by the investigator as related to bardoxolone methyl, 3. Unwilling to practice acceptable methods of

birth control (both males who have partners of childbearing potential and females of childbearing potential) while taking study drug, 4. Women who are pregnant or breastfeeding, 5. Patient is, in the opinion of the investigator, unable to comply with the requirements of the study protocol or is unsuitable for the study for any reason, 6. Known hypersensitivity to any component of the study drug

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):	30-08-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bardoxolone Methyl
Generic name:	Bardoxolone Methyl

Ethics review

Approved WMO

Date:	21-03-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	19-06-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2016-004365-16-NL
CCMO	NL60468.056.17