An open-label, long term extension study for treatment of pulmonary arterial hypertension in paediatric patients aged 8 years up to 18 years who have participated in AMB112529 and in whom continued treatment with ambrisentan is desired (AMB114588)

Published: 25-11-2010
Last updated: 03-05-2024

Primary: Longterm safety and tolerability of 2 dosages of ambrisentan. Secundary: Supportive efficacy data.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Pulmonary vascular disorders
Study type	Interventional

Summary

ID

NL-OMON34600

Source
ToetsingOnline

Brief title
AMB114588

Condition

- Pulmonary vascular disorders

Synonym
Pulmonary Arterial Hypertension, Pulmonary Hypertension

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: ambrisentan, paediatric patients, pulmonary arterial hypertension

Outcome measures

Primary outcome

Adverse events.

Secondary outcome

E.g. all cause mortality, exercise tolerance, time to clinical worsening, NT

proBNP, NYHA class, SF-10 questionnaire.

Study description

Background summary

Pulmonary arterial hypertension (PAH) is a life threatening disease, characterized by a serious persistent increase of PA pressure. This results in right ventricular failure and death.
There are various treatment options, but no single drug is effective for all patients. Morbidity and mortality is high among patients with PAH, who remain symptomatic despite treatment.
Ambrisentan is a endothelin receptor antagonist (ERA). It targets the ETA receptor and blocks the undesired effects if the vasoconstrictive endothelin-1. The drug has been regsitered under the name Volibris for the treatment of adults with PAH.
Except bosentan no drugs have been regstred for the treatment of adolescents or children, but they are frequently used off-label. In line with the current opinion, the sponsor would like to collect structured data on the effects of ambrisentan in youngsters.
This is an extension study of the study AMB112529, that has been designed to collect data on efficacy, safety and PK of 2 dosages of ambrisentan in minors

as of the age of 8 with PAH. The purpose of this extension study is to collect longterm safety and tolerability data and, on the other hand, to enable participants to continue with ambrisentan until the drug has been registered for the treatment of people under 18 years of age.

Study objective

Primary: Longterm safety and tolerability of 2 dosages of ambrisentan.
Secundary: Supportive efficacy data.

Study design

Multicenter open label non-comparative phase III study.
Treatment with ambrisentan in a dose to be determined by the investigator.
Minimal duration 6 months. Thereafter continuation is possible until
* The subject turns 18 years of age (when the subject can receive marketed product);
* The product is approved and available for use in the subject*s age group;
* Development for use in the pediatric population is discontinued;
* The subject decides he/she no longer wants to participate in the study;
* The investigator considers it is in the best interest of the subject to discontinue ambrisentan (e.g. for safety reasons).
Max. 66 patients.

Intervention

Treatment with ambrisentan.

Study burden and risks

Risk: Adverse events of study medication.
Burden: Monthly blood tests (2.5-3.5 ml/visit) and pregnancy test (if relevant). Visit to investigator every 3 months. Duration 1-3 h.
Every 3 months: SF-10 questionnaire.
Every 6 months: physical examination, ECG, echocardiogram, 6 min. walk test.
Extra in comparison to regular care: longer (1-2 h) hospital visits, possibly somewhat more frequent blood tests. 6 min. walk test, pregnancy test and questionnaire: in most cases only because of study participation.

Contacts

Public
GlaxoSmithKline

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

* Participation in and complied, to the best of their ability, with the protocol for AMB112529 and have met one of the following:
a. Completed the Week 24 visit in AMB112529;
b. Required additional targeted treatment for PAH due to inadequate response to the current treatment or worsening of their clinical condition prior to week 24 in AMB112529;
c. Required reduction in dose of baseline targeted treatment for PAH after ambrisentan was added to the treatment regimen;
d. In the opinion of the investigator, continued treatment with ambrisentan is warranted.
* Females of childbearing potential: reliable method of contraception.

Exclusion criteria

* Withdrawn from ambrisentan and/or non-compliance in study AMB112529
* Estimated creatinine clearance <30 mL/min.
* Clinically significant fluid retention.
* Clinically significant anaemia.

* Pregnancy or breastfeeding.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Volibris
Generic name:	ambrisentan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-11-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	19-07-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-11-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	13-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
Other	clinicaltrials.gov, registratienummer n.n.b.
EudraCT	EUCTR2010-021572-29-NL
CCMO	NL34702.042.10