Randomized, double-blind (for clazosentan), placebo- and moxifloxacin-controlled, 3-way cross-over Phase 1 study to assess the effect of two intravenous doses of clazosentan on the QTc interval duration in healthy subjects

Published: 16-08-2018
Last updated: 11-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Aneurysms and artery dissections
Study type	Interventional

Summary

ID

NL-OMON46268

Source
ToetsingOnline

Brief title
CS0297 (ID-054-107)

Condition

- Aneurysms and artery dissections

Synonym
cerebral vasospasm (cerebral hemorrhage)

Research involving

Human

Sponsors and support

Primary sponsor: Idorsia Pharmaceuticals Ltd
Source(s) of monetary or material Support: Idorsia Pharmaceuticals Ltd.

Intervention

Keyword: Cardiodynamic ECG, Pharmacokinetic, Safety

Outcome measures

Primary outcome

Cardiodynamic variables

Secondary outcome

pharmacokinetic parameters

safety parameters

Study description

Background summary

When bleeding occurs in the brain, the brain tissue responds by contracting the blood vessels near the bleeding. This cramping of
blood vessels can result in local brain cells receiving not enough blood. The brain areas that receive too little blood may in turn die.
Clazosentan is being developed to prevent and/or reverse cramping of blood vessels after a stroke.

Study objective

This study aims at investigating potential relevant QT effects of clazosentan at supra therapeutic doses in healthy male and female subjects using a concentration/response analysis approach in compliance with the ICH E14 guidance [FDA 2017].

Primary objective:
To assess potential QT liability of clazosentan at two supra-therapeutic i.v. doses.

Secondary objectives:
To assess the safety and tolerability of clazosentan at supra-therapeutic doses.
To investigate the PK of clazosentan.
To ensure assay sensitivity using concentration/QT analysis with moxifloxacin.
To assess the effect of clazosentan on heart rate (HR), PR and QRS intervals, T-wave morphology, and U-wave presence.

Study design

This is a single-center, randomized, double-blind (for clazosentan), placebo- and moxifloxacin-controlled, 3-way cross-over, study to investigate the effect of clazosentan on the duration of the QT interval in healthy male and female subjects.

Intervention

The study will start with a screening. At the screening a physical examination will take place and a few other standard
medical assessments will be performed (ECG,vital signs). Furthermore a blood and urine sample will be taken for
laboratory tests and an alcohol breathtest and drug screen will be done.

All subjects will receive a continuous infusion of either clazosentan (Treatment A, doses of 20 and 60 mg/h, 3 h each), placebo for 6 h (Treatment B), and moxifloxacin (400 mg oral, Treatment C) immediately followed by clazosentan placebo i.v. for 6 h. Subjects will be randomly assigned to one of the 6 treatment sequences. On several time points blood will be taken, Holter ECG will be measured, and urine will be collected . The subjects will be asked for possible side effects on regular basis. Furthermore several safety assessments will be done frequently.

Finally, a end of study visit will take place and a follow-up phone call will take place .

Study burden and risks

The risk to health at the chosen dose is limited, but the volunteers may experience any of the side effects written in the ICF or
symptoms that have not reported before.

Volunteers health is closely monitored during the study to minimize these risks.

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

Healthy male and female (non-childbearing potential) between 18 and 65 years (inclusive) with a Body mass index (BMI) of 18.0 to 30.0 kg/m2 (inclusive) at Screening.;Further inclusion criteria can be found in the protocol section 3.2.2.

Exclusion criteria

1. Previous exposure to clazosentan.
2. Previous exposure to Moxifloxacin within 3 months prior to Screening.
3. Known hypersensitivity to clazosentan or Moxifloxacin or treatments of the same class, or any of their excipients.;Further exclusion criteria can be found in the protocol section 3.2.3.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-09-2018
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	16-08-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2018
Application type:	First submission
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	EUCTR2018-002118-12-NL
CCMO	NL66989.056.18