An adaptive Phase I/II study to assess safety, efficacy, pharmacokinetics and pharmacodynamics of RO7112689 in healthy volunteers and patients with paroxysmal nocturnal hemoglobinuria (PNH)

Published: 05-09-2016
Last updated: 14-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Red blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON43007

Source
ToetsingOnline

Brief title
RO7112689 phase I/II study (Part 1a conducted in NL)

Condition

- Red blood cell disorders

Synonym
PNH

Research involving

Human

Sponsors and support

Primary sponsor: F. Hoffmann-La Roche Ltd
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: PNH, RO7112689

Outcome measures

Primary outcome

- Evaluate the safety and tolerability of single doses of RO7112689 in HVs.

Secondary outcome

- Characterize the pharmacodynamic (PD) effects of a single-dose of RO7112689

on complement activity and other related biomarkers.

- Describe the single-dose pharmacokinetic (PK) profile of RO7112689.

- Explore the PK/PD relationship of single-ascending doses of RO7112689 on

complement activity and other related biomarkers.

- Evaluate the immunogenicity of RO7112689 in healthy volunteers.

- Assess the bioavailability of SC administration of RO7112689.

- Assess ethnic sensitivities across Japanese and non-Japanese healthy

volunteers.

Study description

Background summary

RO7112689 is a new investigational compound that may eventually be used for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). PNH is a rare, acquired, chronic disease of the blood characterized by destruction of red

blood cells by the complement system, a part of the body's immune system. RO7112689 is a monoclonal antibody, a type of protein that is normally made by the immune system to help defend the body from infection and cancer. RO7112689 binds to the complement protein C5 and is expected to stop complement mediated destruction of red blood cells in the blood vessels of patients with PNH.

RO7112689 is not registered as a drug and has not been given to humans before.

Study objective

The purpose of Part 1A is to investigate how safe RO7112689 is and how well RO7112689 is tolerated. Part 1A will also investigate how quickly and to what extent RO7112689 is absorbed into, distributed in, and eliminated from the body (this is called pharmacokinetics). In addition, the effect of RO7112689 on certain blood markers will be investigated (this is called pharmacodynamics).

Study design

The actual study will consist of 1 period during which the volunteer will stay in the clinical research center for a minimum of 8 days (7 nights): from the afternoon of Day -1 (1 day before administration of the study compound) to the morning of Day 7. Depending on the results for safety and blood markers the volunteer may be asked to stay longer than the planned 8 days. The in-clinic stay will be followed by 7 days (Days 14, 21, 28, 35, 42, 56 and 84) during which the volunteer will visit the clinical research center for a short visit during which blood will be collected; the volunteer will be informed at what time he is expected at the clinical research center for these short visits.

Intervention

The volunteer will receive a single dose of RO7112689 or placebo as an intravenous (iv) infusion of 1 hour or as a subcutaneous injection on Day 1. The placebo dose is an iv infusion or a subcutaneous injection without the active ingredient RO7112689.

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. As RO7112689 will be administered to man for the first time in this study, adverse effects of RO7112689 in man have not been reported to date.

In patients who were treated with eculizumab, a registered drug with the same mechanism of action as RO7112689, serious to fatal cases of meningitis were seen. These were, however, patients who were treated with this compound for a long time. Also, infections with other bacteria were reported. Because RO7112689 (and also eculizumab) are biologicals, there is a chance that your

body will develop antibodies against RO7112689, especially with prolonged use. In animal studies there were sporadic cases in which immune complexes of these antibodies with RO7112689 were formed. These immune complexes caused an inflammation process in the vessels of arteries, which however did not lead to permanent damage.

Procedures: pain, minor bleeding, bruising, possible infection

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 volunteers
21-55 yrs, inclusive
BMI: 18-30 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-09-2016
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bexsero
Product type:	Medicine
Brand name:	Nimenrix

Ethics review

Approved WMO

Date:	05-09-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-03-2017
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	EUCTR2016-002128-10-NL
CCMO	NL59050.056.16