Protocol CV185074: evaluation of multiple dose pharmacokinetics and pharmacodynamics of apixaban and rivaroxaban in healthy subjects

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Primary:- to assess the multiple-dose pharmacokinetics of apixaban and rivaroxaban - to compare plasma concentration peak to trough ratio (Cmax/Cmin) of rivaroxaban to apixaban Secondary:- to assess the multiple dose pharmacodynamics (anti-Factor Xa...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON34739

Source
ToetsingOnline

Brief title
Apixaban/Rivaroxaban multiple dose PK/PD study

Condition

- Other condition
- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Venous varices

Synonym
Trombose

Health condition

Veneuze trombose

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Anticoagulant, Apixaban, Rivaroxaban, Venous thromboembolism (VTE)

Outcome measures

Primary outcome

Pharmacodynamics.

Pharmacokinetics.

Safety.

Secondary outcome

n.a.

Study description

Background summary

The drug to be given, apixaban, is a so-called Factor Xa inhibitor. Factor Xa is one of the coagulation factors that play a key role in blood clotting after an injury or surgery. Apixaban is a new, investigational compound that may eventually be used for the treatment and prevention of venous thromboembolism (VTE) which may occur after knee or hip replacement surgery. Venous thromboembolism (VTE) is the formation of a blood clot in one of the deep veins within the body, such as in the leg or pelvis. This kind of thrombosis can occur after surgery and may cause redness, pain and swelling as well as pulmonary embolism and stroke. Apixaban is an antithrombotic drug which reduces thrombus or blood clot formation by limiting the ability of the platelets to clot.

Study objective

Primary:
- to assess the multiple-dose pharmacokinetics of apixaban and rivaroxaban
- to compare plasma concentration peak to trough ratio (Cmax/Cmin) of rivaroxaban to apixaban

Secondary:
- to assess the multiple dose pharmacodynamics (anti-Factor Xa activity) of apixaban and rivaroxaban
- to assess the safety and tolerability of apixaban

Exploratory:
- to explore the metabolites of rivaroxaban in plasma in healthy subjects

Study design

Design:
An open-label, randomized, crossover study.

Procedures and assessments
Screening and follow-up:
Clinical laboratory, pregnancy test (females only), vital signs (including body temperature, respiratory rate) full physical examination, weight, 12-lead ECG.

Observation period:
16 continues days, divided in two periods.

Blood sampling:
- for pharmacokinetics and pharmacodynamics of Rivaroxaban: up to Day 4
- for pharmacokinetics and pharmacodynamics of Apixaban: up to Day 4
- for biotransformation sample: 4 and 24 h post-dose on Day 4 during Treatment A

Urine sampling:
N.A.

Faeces sampling:
N.A.

Safety assessments:
Adverse events: throughout the study; physical examination: on Day 8 (Day -1, Period 2) clinical laboratory: once on Day 8 (Day -1, Period 2) and once on Day 8 (Day -1, Period 2); vital signs (including oral temperature): pre-dose and once on Day 8 (Day -1, Period 2) and once on Day 8 (Day -1, Period 2); 12-lead ECG: pre-dose and once on Day 1 (Part 1) and pre-dose (Day -1, Period 2); pregnancy test (females only) on Day 8 (Day -1 Period 2).

Bioanalysis:
- analysis of plasma rivaroxaban and apixaban samples using a validated method

at PRA
- analyse of FxA activity using a validated method by PRA

Intervention

Study Medication
Active substance:
Rivaroxaban and Apixaban.

Study burden and risks

Procedure:
Pain, light bleeding, heamatoma, possibly an infection.

Contacts

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Scientific
Bristol-Myers Squibb

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United States of America

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- healthy male/female
- age between 18 and 45 years old
- BMI between 18 and 30 kg/m2
- non-smoker
- at screening state of health must satisfy the entry requirements

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 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 (for men) / more than 1.0 liters of blood (for women) in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2010
Enrollment:	14
Type:	Actual

Ethics review

Approved WMO

Date:	18-01-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-01-2010
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	EUCTR2009-017278-19-NL
CCMO	NL30983.056.10