Reversal of oral anticoagulants rivaroxaban and apixaban, by two different dosages of prothrombin complex concentrate (Cofact®).

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21617

Source
Nationaal Trial Register

Brief title
COFACTII

Health condition

Healthy male subjects between 18 and 50 year who have no medical history of thrombotic disease or bleeding disorders will be included in the study. They must have a normal physical examination and laboratory screen tests. They will not use any medication at least 14 days before the study days.

Sponsors and support

Primary sponsor: S. Middeldorp
Academic Medical Center
Meibergdreef 9
Amsterdam
s.middeldorp@amc.uva.nl
Source(s) of monetary or material Support: Sanquin

Intervention

Outcome measures

Primary outcome

The primary outcome is the reversal (normalisation) of coagulation assays, at the end of oral f-Xa inhibitor administration and after the infusion of PCC or placebo.

Secondary outcome

N/A

Study description

Background summary

Rivaroxaban and apixaban lack a specific reversal agent. Fifty units/kg of 4-factor prothrombin complex concentrate (PCC, Cofact®) completely reversed the anticoagulant effect of rivaroxaban in healthy subjects. We hypothesized that infusion with doses of 37.5 or 25 units/kg of PCC would be able to reverse the anticoagulant effect of rivaroxaban and apixaban, both factor Xa inhibitors. In a randomized, double blind, placebo-controlled study, 12 healthy volunteers taking rivaroxaban 15 mg or apixaban 10 mg twice daily, received either a single bolus of PCC 37.5 units/kg, PCC 25 units/kg or placebo, with a wash-out period of 18 days in between infusions. The primary outcome was the effect of PCC on measures of thrombin generation, e.g. endogenous thrombin potential (ETP), after PCC or placebo infusion.

Study objective

Reversibility of oral direct factor Xa inhibitors rivaroxaban and apixaban will be the same when a lower dosage of prothrombin complex concentrate (Cofact®) is used. Infusion with doses of 37.5 or 25 units/kg of PCC would be able to reverse the anticoagulant effect of rivaroxaban and apixaban.

Study design

Day -7: Randomization for PCC or saline,
baseline coagulation tests;

Days -7 to 0:

1. Group 1: Apixaban orally, 10 mg twice daily, for 7 and a half days (15 doses);

2. Group 2: Rivaroxaban orally, 15 mg twice daily, for 7 and a half days (15 doses).

Day 0: PCC/saline administration, scheduled coagulation tests;

Day 1: Scheduled coagulation tests.

Intervention

Intravenous administration of PCC (Cofact) 25 IU/kg or PCC (Cofact) 37.5 IU/kg or placebo (saline).

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy male subjects as documented by laboratory screen tests (including HIV/HBV/HCV screening), personal medical history and normal physical examination;

2. Age ≥18 years, < 50 years;

3. No personal history of thrombotic disease/bleeding disorders;

4. No significant family history of thrombotic disease/bleeding disorders, such as recurrent thrombotic/bleeding events or thrombotic/bleeding events in the absence of any risk factors;

5. Able to provide written informed consent.

Exclusion criteria

1. History of allergic reaction to blood products;

2. Current participation in any other investigational drug study or within the past 30 days;

3. Presence of any condition that, as judged by the investigator, would place the subject at increased risk of harm if he participated in the study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-10-2012
Enrollment:	12
Type:	Actual

Ethics review

Positive opinion

Date:	02-08-2012
Application type:	First submission

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
NTR-new	NL3388
NTR-old	NTR3559
Other	:
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects.
Elise S. Eerenberg, MD; Pieter W. Kamphuisen, MD; Meertien K. Sijpkens, BSc; Joost C. Meijers, PhD; Harry R. Buller, MD; Marcel Levi, MD