ABILITY OF PROTHROMBIN COMPLEX CONCENTRATE (COFACT ®) TO REVERSE THE ANTICOAGULANT EFFECT OF NOVEL ANTITHROMBOTIC AGENTS

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Study questionWhat is the effect of a single administration of prothrombin complex concentrate (CoFact) on the anticoagulant effect of a novel oral thrombin inhibitor (Dabigatran) and a novel oral factor Xa inhibitor (Rivaroxaban) in healthy human...

Ethical review	Approved WMO
Status	Pending
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON33208

Source
ToetsingOnline

Brief title
Cofact study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
anticogulant therapy, bleeding

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antidote, dabigatran, prothrombine complex concentrate, rivaroxaban

Outcome measures

Primary outcome

The primary outcome is activation and inhibition of coagulation, as reflected

by coagulation tests.

Secondary outcome

none

Study description

Background summary

In recent years a large number of new antithrombotic agents has been developed and tested in clinical trials and many of these new agents will become available for clinical practice in the very near future. However, there is no antidote available for these agents if immediate reversal of their effect is required, e.g. in case of bleeding or when emergency surgery or invasive procedures is indicated.
Based on its general pro-hemostatic potential, prothrombin complex concentrate may be effective in (completely or partially) reversing the anticoagulant effect of these new antithrombotic agents.

Study objective

Study question
What is the effect of a single administration of prothrombin complex concentrate (CoFact) on the anticoagulant effect of a novel oral thrombin inhibitor (Dabigatran) and a novel oral factor Xa inhibitor (Rivaroxaban) in healthy human subjects?

Study design

Study design

The study will be performed as a double blind cross-over study. Two groups of 6 healthy human subjects will be enrolled (group 1 and 2). Subjects in group 1 will take Dabigatran 2dd 150 mg on day -2, -1 and 0. Subjects in group 2 will take Rivaroxaban 2dd 20 mg on day -2, -1 and 0. After the fifth dose (on day 0) subjects will be randomized to receive Cofact (50 U/kg) or a similar volume of Saline as a single bolus dose i.v. over 15 minutes. After a 10 day wash-out period the procedure is repeated but the alternative treatment (Saline of Co-fact) is administered.

Intervention

Administration of Rivaroxaban or Dabigatran
Administration of Prothrombin Complex Concentrate or Placebo

Study burden and risks

Subjects will be screened and instructed. They will start their oral medication at day -2. They will be admitted to the study ward on day 0. An i.v. catheter will be placed to administer Cofact or saline and can be used to withdraw blood samples. Blood samples are collected at the following times: T= day -2 (before starting the oral anticoagulants), T= 0 (before the administration of Cofact/ Saline), and after the administration of Cofact/Saline at T= 15 min, 30 min, 60 min, 120 min, 240 min, 360 min and at 24 hrs.
Risk of rivaroxaban and dabigatran is related to the anticoagulant effect and volunteers will be instructed to avoid trauma (for example contact sports). The collection of blood will be done as much as possible from the i.v. line. Separate venipunctures may be associated with limited inconvenience.

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 males between 18-50 year will be recruited.

Exclusion criteria

Subjects will have no medical history of thrombotic disease or bleeding disorders. They must have a normal physical examination and laboratory screen. They will not use any medication at least 14 days before the study days.

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:	Pending
Start date (anticipated):	01-10-2009
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Cofact
Generic name:	prothrombin complex concentrate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Pradaxa
Generic name:	dabigatran
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xarelto
Generic name:	rivaroxaban
Registration:	Yes - NL intended use

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Amsterdam UMC

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	EUCTR2009-014667-40-NL
CCMO	NL29183.018.09