A randomized, double-blind, placebo-controlled, 4-period, two part cross-over study to evaluate the potential interaction effect between 4 mg/kg and 16 mg/kg sugammadex and enoxaparin or unfractionated heparin on anticoagulation activity in young healthy male volunteers

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To investigate the potential of an interaction between 4 mg/kg and 16 mg/kg sugammadex and enoxaparin or UFH on anticoagulant activity in young healthy male volunteers.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Embolism and thrombosis
Study type	Interventional

Summary

ID

NL-OMON36201

Source
ToetsingOnline

Brief title
Anticoagulant interaction study (Sugammadex)

Condition

- Embolism and thrombosis

Synonym

coagulation, thrombus

Research involving
Human

Sponsors and support

Primary sponsor: Schering-Plough
Source(s) of monetary or material Support: Pharmaceutical company - Schering-Plough

Intervention

Keyword: anticoagulation, enoxaparin, sugammadex, UFH

Outcome measures

Primary outcome

part 1 - to investigate the potential effect of 4 mg/kg and 16 mg/kg sugammadex

on the Anti-Xa anticoagulant activity of enoxaparin.

part 2 - to investigate the potential effect of 4 mg/kg and 16 mg/kg sugammadex

on the APTT anticoagulant activity of UFH.

Secondary outcome

part 1:

- To investigate the potential effect of 4 mg/kg and 16 mg/kg sugammadex on the

APTT anticoagulant activity of enoxaparin.

- To evaluate the effect of enoxaparin on the potential APTT anticoagulant

activity of 4 mg/kg sugammadex.

- To evaluate the potential anticoagulant activity of 4 mg/kg sugammadex as

compared to baseline. Anti-Xa activity and APTT will be the secondary endpoint

measures.

- To evaluate the safety and tolerability of sugammadex alone or in combination

with enoxaparin.

part 2

- To evaluate the effect of UFH on the potential APTT anticoagulant activity of

16 mg/kg sugammadex.

- To evaluate the potential anticoagulant activity of 16 mg/kg sugammadex as

compared to baseline; APTT and anti-Xa activity will be the secondary endpoint

measures.

- To evaluate the safety and tolerability of sugammadex alone or in combination

with UFH.

Study description

Background summary

Sugammadex has been designed to specifically bind rocuronium and vecuronium with very high affinity. Upon complexation with a neuromuscular blocking agent (NMBA) such as rocuronium, sugammadex reduces the amount of NMBA available to bind to nicotinic receptors in the neuromuscular junction, and hence results in the reversal of neuromuscular blockade (NMB). Sugammadex is approved for use in humans since September 2008 in the EU under the brand name Bridion®, and is currently approved in over 60 countries.
The current study will investigate the interaction between sugammadex and enoxaparin or unfractioned heparin (UFH), as enoxaparin and UFH are frequently used for the prophylaxis of deep vein thrombosis (DVT) during surgery.

Study objective

To investigate the potential of an interaction between 4 mg/kg and 16 mg/kg sugammadex and enoxaparin or UFH on anticoagulant activity in young healthy male volunteers.

Study design

Randomized, double-blind, placebo-controlled, 4 period, 2 part cross-over,

drug-drug interaction study in young healthy male volunteers

Intervention

part 1 - intereractiion sugammadex and enoxaparine: administration of sugammadex (2x 4 mg/kg, 1x 16 mg/kg, 1x placebo) and enoxaparin (3x 40 mg, 1x placebo)

part 2 - interaction sugammadex and UFH: administration of sugammadex (1x 4 mg/kg, 2x 16 mg/kg, 1x placebo) and UFH (3x 5000 units, 1x placebo)

Study burden and risks

- Relatively frequent blood collection.
- The insertion of the cannula can be painful and result in a bruise.
- The use of sugammadex could influence coagualation and may uncommonly cause a hypersensitivity reaction.
- Enoxaparin and UFH may reduce blood coagulation and therefore may cause bruises. In addition, liver function may be transiently affected or an injection side reaction may occur.

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
- 18-45 years of age
- BMI 18-32
- Subjects must be free of any clinical significant disease that would interfere with the study evaluations.
- No clinically significant abnormalities in laboratory tests (chemistry, hematology, virology, urinalysis)
- APTT and PT within normal limits and anti-Xa activity below LLOQ
- Normal physical examination (including vital sign measurements), normal ECG

Exclusion criteria

- Subject's female partner is pregnant, intends to become pregnant (within 3 months of ending the study), or is breastfeeding
- Subject who will not be able to participate optimally in the study
- Contraindications to heparin or enoxaparin or history of heparin induced thrombocytopenia
- A (suspected) history of hypersensitivity or hypersensitivity-like reaction to sugammadex, history of sensitivity/idiosyncrasy to chemically related compounds or excipients which could be employed in the study or to any other unknown drug used in the past
- Subject is not able to refrain from alcohol, grapefruit, xanthines as described in protocol
- Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism or excretion of any drug
- History of infectious disease during past month that in the opinion of the investigator, affects subject's ability to participate in the study
- History of an unexplained reaction or hypersensitivity reaction during previous surgery and/or anesthesia
- Subject who underwent surgery during past year
- History of anaphylaxis from any cause, a suspected history of hypersensitivity reactions to cyclodextrins, or multiple drug hypersensitivities
- History of allergic reactions (eg, food, drug, atopic reactions or asthmatic episodes) which, in the opinion of the investigator, interfere with their ability to participate in the study
- Positive screen for drugs or alcohol
- Drug or alcohol abuse in the past 2 years
- Smoking more than 10 cigarettes or equivalent tobacco use per day
- Clinically significant abnormalities in laboratory tests (chemistry, hematology, virology,

coagulation) or physical examination
- Subjects with hereditary vitamin K dependent clotting factor deficiencies and/or pre-existing coagulopathies
- History of gastrointestinal bleeding, easy bruising, frequent nose bleeds
- Previous exposure to sugammadex

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):	26-09-2011
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bridion
Generic name:	sugammedex
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Clexane
Generic name:	enoxaparin sodium
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Heparin LEO

Generic name:	heparin sodium
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-07-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	21-09-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-09-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2011-001969-41-NL
CCMO	NL37049.058.11