Comparing daytime plasma levels of rivaroxaban with a morning versus evening dose

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To determine and compare plasma levels of rivaroxaban during daytime with a morning and evening intake in patients treated for venous thromboembolism

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON47973

Source
ToetsingOnline

Brief title
TIME-X study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Bayer,derde geldstroom

Intervention

Keyword: bleeding risk, DOAC, rivaroxaban, thrombosis

Outcome measures

Primary outcome

Plasma-levels of rivaroxaban during daytime, i.e. 14.00 p.m.,determined with

liquid chromatography-mass spectrometry (LC-MS)

Secondary outcome

Trough plasma level of rivaroxaban (Cmin), peak plasma level of rivaroxaban

(Cmax), T1/2 and area under the concentration curve (AUC), accuracy of plasma

level detection of anti-Xa level assay compared to LC-MS

Study description

Background summary

Currently, no specific recommendations are made for the timing of intake of rivaroxaban in patients treated for venous thrombo-embolism. In clinical practice this means that patients are advised to take rivaroaxaban with either breakfast or supper. As rivaroxaban is accompanied by a bleeding risk, specifically in the case of trauma and emergency invasive procedures, the lowest plasma-levels should preferably occur during daytime. This could be achieved by an evening dose rather than an morning dose. However, it remains unclear whether plasma levels of an evening dose are relevantly more lower than from a morning dose and whether the achieved plasma levels are adequately low enough to perform invasive procedures safely.

Study objective

To determine and compare plasma levels of rivaroxaban during daytime with a morning and evening intake in patients treated for venous thromboembolism

Study design

Crossover study

Study burden and risks

We will ask eligible subjects informed consent for participation in this study. Subjects will not benefit from participation to this study. However, the burden and risk of this study are considered limited. First, subjects wil be asked to keep a diary of dietary pattern and timing of rivaroxaban intake. This diary is not detailed and is mostly focused on ticking boxes. Secondly, we will change dose-timing by prolonging or shortening the dosing interval with 6 hours in two steps. We do not expect complications from this temporary change in dosing interval, as this is method is used in clinical practice to adjust dose-timing for clinical or patient's personal reasons. Lastly, we will sample 6x7 mL blood by a venous puncture. Besides discomfort from the puncture, we are not aware of any risks or harms of this blood sampling. The results of this study may contribute to improving the safety of anticoagulation therapy.

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

- Adults (>18 years)
- Treated for venous thrombo-embolism with rivaroxaban 20 mg once daily for at least three months
- Ingestion of rivaroxaban either in the morning with breakfast or in the evening with supper
- Both breakfast and supper incorporated in daily dietary pattern

Exclusion criteria

- Impaired renal function, i.e. estimated glomerular filtration rate <50 ml/min/1.73 m2
- BIM of >40 kg/m2 or weight of >120 kg
- Liver cirrhosis
- History of gastric- or bowelresection
- Concomitant use of medication interacting with rivaroxaban (CYP3A4 inhibitors and P-glycoprotein inhibitors)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-12-2020
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	14-01-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL70187.042.19