30-day, single-arm study of the safety, efficacy and the pharmacokinetic and pharmacodynamic properties of oral rivaroxaban in young children with various manifestations of venous thrombosis

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- Assess the incidence of major bleeding and clinically relevant non-major bleeding- Assess the incidence of recurrent venous thromboembolism- Assess the asymptomatic deterioration in the thrombotic burden on repeat imaging- Characterize the...

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

Summary

ID

NL-OMON41837

Source
ToetsingOnline

Brief title
EINSTEIN Junior Phase IIb

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
blood clot, thrombosis

Research involving

Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer B.V.

Intervention

Keyword: efficacy and safety, pediatric study, rivaroxaban, venous thrombosis

Outcome measures

Primary outcome

Assess the incidence of major bleeding and clinically relevant non-major

bleeding

Secondary outcome

- Assess the incidence of recurrent venous thromboembolism

- Assess the asymptomatic deterioration in the thrombotic burden on repeat

imaging

- Characterize the pharmacokinetic/harmacodynapic profily of a 30-day treatment

with oral rivaroxaban

Study description

Background summary

Treatment with heparins and VKA (vitamin K antagonist) has several unsatisfying aspects. For heparins, this includes the requirement for intravenous or subcutaneous injection and monitoring of the activated partial thromboplastin time (aPTT) and assessment of anti Xa. For VKA, this includes frequent INR (international normalized ratio) monitoring. An oral anticoagulant drug that requires no monitoring of its effect, with a rapid onset of action and a high benefit-risk ratio is of considerable interest for the pediatric population.

Study objective

- Assess the incidence of major bleeding and clinically relevant non-major bleeding
- Assess the incidence of recurrent venous thromboembolism
- Assess the asymptomatic deterioration in the thrombotic burden on repeat imaging
- Characterize the pharmacokinetic/pharmacodynamic profile of a 30-day treatment with oral rivaroxaban

Study design

This is a single arm study evaluating the safety, efficacy and PK/PD profile of a 30 day treatment with age- and body weight-adjusted oral rivaroxaban in children aged 6 months < 6 years with various manifestations of symptomatic or asymptomatic venous thrombosis.

Intervention

1. rivaroxaban (suspension), twice daily for 30 days

Study burden and risks

The study includes 5 planned visits. 4 blood samples will be taken and the total blood volume taken will be 12 ml. The child will receive a diary to collect information regarding drug intake at the day before each visit and at visit. Children older than 4 years
will complete a Taste and Texture questionnaire about oral suspension during one of the visits.General physical exam will be performed during each visit. There is a chance for (unknown) side effect, as is documented ion the SmPC of rivaroxaban.

Contacts

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Bayer

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Scientific
Bayer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Children aged between 6 months to < 6 years who have been treated for at least 2 months or, in case of catheter related thrombosis, for at least 6 weeks with LMWH, fondaparinux and/or VKA for documented symptomatic or asymptomatic venous thrombosis ;2. Hemoglobin, platelets, creatinine, alanine aminotransferase (ALT) and bilirubin evaluated within 10 days prior to randomization;3. Informed consent provided

Exclusion criteria

1. Active bleeding or high risk for bleeding contraindicating anticoagulant therapy;2. Symptomatic progression of venous thrombosis during preceding anticoagulant treatment;3. Planned invasive procedures, including lumbar puncture and removal of non-peripherally placed central lines during study treatment;4. An estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m2;5. Hepatic disease which is associated with either: coagulopathy leading to a clinically relevant bleeding risk, or ALT > 5x upper level of normal (ULN) or total bilirubin > 2x ULN with direct bilirubin > 20% of the total;6. Platelet count < 50 x 109/L;7. Hypertension defined as > 95th age percentile ;8. Life expectancy < 3 months;9. Concomitant use of strong inhibitors of both cytochrome P450 isoenzyme 3A4 (CYP3A4) and P-glycoprotein (P-gp), i.e. all human immunodeficiency virus protease inhibitors and the following azole-antimycotics agents: ketoconazole, itraconazole, voriconazole, posaconazole, if used systemically;10. Concomitant use of strong inducers of CYP3A4, i.e. rifampicin, rifabutin, phenobarbital, phenytoin and carbamazepine;11. Hypersensitivity or any other contraindication listed in the local labeling for the comparator treatment or experimental treatment;12. Inability to cooperate with the study procedures;13. Previous randomization to this study;14. Participation in a study with an investigational drug or medical device within 30 days prior to randomization.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-02-2016
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xarelto
Generic name:	rivaroxaban
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	02-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	15-09-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-11-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-09-2015
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2014-000566-22-NL
ClinicalTrials.gov	NCT02309411
CCMO	NL48610.078.14