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

Published: 16-10-2012
Last updated: 26-04-2024

-Assess the incidence of major bleeding and clinically relevant non-major bleeding -Assess the incidence of recurrent venous thromboembolism -Characterize the pharmacokinetic/ pharmacodynamic profile of a 30-day treatment with oral rivaroxaban

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

Summary

ID

NL-OMON43577

Source
ToetsingOnline

Brief title
EINSTEIN Junior

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
venous 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

Composite of major and clinically relevant non-major bleeding

Secondary outcome

Composite of all recurrent venous thromboembolism; results of pharmacokinetics

(PK) / pharmacodynamics (PD).

Study description

Background summary

Rivaroxaban is registered in The Netherlands for the treatment of DVT and the prevention of recurrent DVT and pulmonary embolism (PE) after an acute DVT in adults. In this study, rivaroxaban will be evaluated in children with venous thrombosis, in order to be able to make a choice in the future for children between the (new) anticoagulantia.

See also protocol pages 15-19.

Study objective

-Assess the incidence of major bleeding and clinically relevant non-major bleeding
-Assess the incidence of recurrent venous thromboembolism
-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 between 6 and < 18 years with various manifestations of symptomatic and asymptomatic venous thrombosis.

Intervention

Randomization into 1 group:
1.rivaroxaban (tablets [once daily] or suspension [twice daily]), for 30 days

Study burden and risks

For this study, the patient will visit the hospital 5x, which is for some patients more often than normal (depending on the standard treatment which differs slightly per site). A total of 4 PK/PD blood samples will be taken during visit 3 and 4, which will normally not be taken. This is the minimum amount of blood needed for adequate analysis. However, these patients will require no INR-monitoring or daily heparin injections. A "taste and texture" questionnaire (for children below 12 years of oral rivaroxaban suspension) and a simple study booklet need to be completed. There is a chance for (unknown) side effects, as is documented in the SmPC of rivaroxaban.

In this study, rivaroxaban will be administered after at least 2 months of treatment with standard of care anticoagulant, when the risk of recurrence of thrombotic complications and bleeding is expected to diminish compared to the first months of anticoagulant treatment. In adults, rivaroxaban is administered orally and is characterized by stable and predictable pharmacokinetics and, therefore, does not require laboratory monitoring with subsequent dose adjustments. Furthermore, selected rivaroxaban dose regimen was extensively tested in large phase III studies in adults in which it had a similar efficacy and safety profile as standard of care anticoagulant.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Children aged 6 years to < 18 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 and alanine aminotransferase (ALT) evaluated within 10 days prior to visit 2;3. Informed consent provided and, if applicable, child assent 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 coagulopathy leading to a clinically relevant bleeding risk;6. Platelet count < 50 x 10^9/L;7. Hypertension defined as > 95th age percentile ;8. Concomitant use of strong inhibitors of both CYP3A4 and P-gp, i.e. all human immunodeficiency virus protease inhibitors and the following azole-antimycotics agents: ketoconazole, itraconazole, voriconazole, posaconazole, if used systemically (fluconazole is allowed);9. Concomitant use of strong inducers of CYP3A4, i.e. rifampicin, rifabutin, phenobarbital, phenytoin and carbamazepine

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):	16-09-2013
Enrollment:	12
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:	16-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-04-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2015
Application type:	Amendment
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	EUCTR2011-004539-30-NL
ClinicalTrials.gov	NCT01684423
CCMO	NL41912.018.12