Prospective, multi-center, randomized, heparin-controlled dose-finding trial to evaluate the efficacy and safety of rivaroxaban, a direct factor Xa inhibitor, on the background of standard dual antiplatelet therapy to support elective percutaneous coronary intervention (X-Plorer).

Published: 27-05-2011
Last updated: 29-04-2024

The aim of this study is to assess whether rivaroxaban, as compared to UFH, on the background of standard dual antiplatelet therapy (DAPT), can effectively suppress thrombosis, and related adverse ischemic events, upon balloon inflation and stent...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON35762

Source
ToetsingOnline

Brief title
X-plorer

Condition

- Coronary artery disorders

Synonym
chest pain, narrowing of the coronary artery

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: antiplatelet therapy, direct factor Xa inhibitor, percutaneous coronary intervention

Outcome measures

Primary outcome

The anticoagulant effect will be determined during the index PCI procedure

based on the number of subjects who:

-Require bail-out anticoagulant therapy in the context of an ischemic coronary

event, and/or

-Experience an angiographic flow limiting thrombotic event (i.e. abrupt vessel

closure, visible thrombus, no-reflow) and/or

-Experience thrombus formation on the PCI equipment (i.e. guiding catheter and

guidewire thrombus) and/or

-Experience an MI due to the PCI procedure (i.e. procedural MI).

Note: The PCI procedure starts when the target lesion is crossed with the

guidewire and ends when the guiding catheter is removed and the subject has

left the catheterization laboratory.

Secondary outcome

Efficacy variables

- Separate components of the primary endpoint

- Clinical ischemic events up to 30 days after index PCI assessed by the composite endpoint of:

- All death

- Non-fatal myocardial infarction (excluding those events due to the procedure alone and reported as primary endpoint)

- Stroke

- Clinically indicated target lesion revascularization (TLR)

- The incidence of clinically indicated TLR up to 30 days after index PCI

- Definite and probable stent thrombosis up to 30 days after index PCI according to the Academic Research Consortium (ARC) definition11

Safety variables

- Bleeding events up to 30 days after index PCI:

- Incidence of clinically significant bleeding according to:

- TIMI major

- TIMI minor

- Requiring medical attention

- Incidence of bleeding according to BARC type 2, 3 and 5

- Any other SAEs up to 30 days after index PCI

Study description

Background summary

During the percutaneous angioplasty procedure, the blood vessel wall can be damaged. This damage can lead to an increase formation of a blood plug or clot. A blood plug or clot is caused by blood components such as thrombin and blood platelets. This blood clot can disrupt the flow of blood in the coronary artery and can even rise the risk to block the blood vessel completely, which could result in a heart attack. In order to prevent this it is generally recommended to be on oral treatment with so called antiplatelet inhibitors as aspirin and clopidogrel which decrease the effect of thrombin and blood platelets. In addition to this an anticoagulant such as heparin will be given intravenously during the procedure.

For more than 50 years heparin has been the most important drug for indirectly inhibiting thrombin and therefore preventing clot formation. Despite its unmistakable advantages, this drug also has some disadvantages such as:
- finding the correct individual dose (which is often difficult),
- risk of antibody production and
- route of administration as heparin needs to be administered via a vein (intravenously).
Other new drugs with a similar effect as heparin are now being developed. The study drug, Rivaroxaban (Xarelto®), which in contrast to heparin is a tablet and will be taken orally, is a new anticoagulant that is being developed by Bayer HealthCare AG in Germany.
Rivaroxaban is an oral active direct factor Xa inhibitor approved in September 2008 by the European Commission for the prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. Rivaroxaban (Xarelto®) inhibits factor Xa which plays a central role in the formation of a clot. Inhibiting factor Xa ensures that the effect of thrombin is inhibited and thus prevents from clot formation.

Study objective

The aim of this study is to assess whether rivaroxaban, as compared to UFH, on the background of standard dual antiplatelet therapy (DAPT), can effectively suppress thrombosis, and related adverse ischemic events, upon balloon inflation and stent expansion, during elective PCI, without increasing bleeding.

The secondary objective is to investigate the safety of rivaroxaban plus DAPT in the setting of elective PCI. Secondary objectives are safety criteria with respect to bleeding Safety criteria with respect to bleeding (TIMI major, TIMI minor and BARC type 2, 3 and 5) and the composite of clinical ischemic events (all death, non-fatal MI, non-fatal stroke and target Lesion Revascularization)

be determined up to 30 days.
The coagulation profile and the plasma concentration of rivaroxaban will be captured at various time points.

Study design

This is a prospective, randomized, heparin-controlled, multi-dose, semi-blind study, conducted in Europe (Netherlands and Belgium). Prior to the elective PCI a screening visit will be performed. The duration of the study will be 30 ± 7 days and ends with a follow-up telephone call at that time point.

Intervention

Study-specific intervention/therapy (e.g. apart from standardly performed PCI):

Patients participating in the study will receive 1 of the 2 doses rivaroxaban (10 or 20 mg), or 10 mg rivaroxaban followed by 50 IU/kg unfractionated heparin pre procedure (NB: the fourth group of patients will receive standard therapy with heparin).

Study burden and risks

- Physical examination is done once
- Blood will be drawn 6-9 times (max 40 ml each time), depending on the duration of the PCI. Every half hour a sample will be taken.
- 4 ECGs will be recorded
- A pregnancy test will be done for women.

.

Contacts

Public
Bayer

Kaiser-Wilhelm-Allee
51368 Leverkusen
DE
Scientific
Bayer

Kaiser-Wilhelm-Allee
51368 Leverkusen
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Male or female subject aged 18 years or more with no upper age limit and willing to comply with the protocol.;2) Symptomatic coronary artery disease due to undergo an elective (non- emergent) PCI on one or two lesions in the native coronary vessel(s). Cardiac standard troponin at baseline is within the normal limits.;3) Subject is able to read and give written informed consent and has signed an informed consent form approved by the Investigator's IRB/IEC after receiving detailed written and oral information prior to any study specific procedures.;4) Ability to understand and follow study-related instructions.

Exclusion criteria

1) Conditions that may increase the risk of the PCI procedure
• Lesion-specific conditions
• Clinical condition at screening visit:
2) Conditions that may increase the risk of bleeding (e.g. a clinically significant gastrointestinal bleeding within 12 months before randomization; history of hemorrhagic stroke; active internal bleeding etc.)
3) Concomitant conditions or diseases (e.g. known HIV infection at time of screening; significant valvular heart disease etc.)
40 Concomitant medication (e.g. current use of anticoagulant drugs; Chronic treatment with non-steroidal anti-inflammatory drugs, NSAIDs)
The complete list can be found in the protocol chapter 5.1.2 on page 33 till 35.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-10-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	27-05-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	12-07-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-11-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2011-001094-58-NL
CCMO	NL36665.060.11