An international, multicenter, randomized, double-blind, placebocontrolled phase 3 trial investigating the efficacy and safety of rivaroxaban to reduce the risk of major thrombotic vascular events in patients with symptomatic peripheral artery disease undergoing lower extremity revascularization procedures

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

Summary

ID

NL-OMON42582

Source
ToetsingOnline

Brief title
Voyager PAD

Condition

- Platelet disorders
- Vascular therapeutic procedures
- Embolism and thrombosis

Synonym
peripheral vascular disease; reduced blood flow due to narrowed arteries

Research involving
Human

Sponsors and support

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

Intervention

Keyword: outcomes, PAD, rivaroxaban, surgical limb revascularization

Outcome measures

Primary outcome

The primary efficacy outcome variable will be a composite endpoint

consisting of the time from randomization to the first occurrence of any of the

following major thrombotic vascular events: MI, ischemic stroke, CV death,

ALI, and major amputation due to a vascular etiology.

The primary safety outcome will be major bleeding events according to the

Thrombolysis in Myocardial Infarction (TIMI) classification.

Secondary outcome

The secondary efficacy variables of the study will be:

* time from randomization to the first occurrence of an index limb

revascularization;

* time from randomization to the first occurrence of MI, ischemic stroke,

coronary heart disease mortality, ALI, and major amputation of a

vascular etiology;

* time from randomization to the first occurrence of MI, ischemic stroke,

all-cause mortality, ALI, and major amputation of a vascular etiology;

* time from randomization to the first occurrence of hospitalization for a

coronary or peripheral cause (either lower limb) of a thrombotic nature;

* time from randomization to the first occurrence of MI, all-cause stroke,

CV death, ALI, and major amputation of a vascular etiology;

* time from randomization to the first occurrence of venous

thromboembolic (VTE) events;

* time from randomization to the first occurrence of all-cause mortality

Study description

Background summary

PAD refers to the atherosclerotic obstruction of the major arteries supplying the lower
extremities, sometimes also referred to as lower extremity artery disease. Atherosclerosis of
the peripheral circulation, with underlying atheroma and chronic inflammation, leads to
progressive occlusion of medium and large arteries, with additional risks of embolism or
thrombus formation. Abrupt occlusions and plaque rupture may lead to acute complications
such as acute limb ischemia (ALI), similar to an acute coronary syndrome in the coronary
circulation.
It is now well established that symptoms, severity, and acuteness of PAD are major
determinants of subsequent risk of cardiovascular (CV) events and mortality.

Independent of
symptoms, patients diagnosed with PAD are at an increased risk of subsequent myocardial
infarction (MI) and stroke, and are 6 times more likely to die within 10 years than those
without PAD.
The most common initial symptom from underlying progressive atherosclerotic occlusion of
the peripheral vasculature is leg pain on exertion or intermittent claudication.
Overall, the currently available treatment options for PAD and evidence-based knowledge on
certain patient subsets are suboptimal. Given that the prevalence of conventional
cardiovascular risk factors for PAD is increasing, it is likely that the incidence of PAD would
grow even more dramatically overtime. The loss of mobility, functional decline, and
cardiovascular events, represents a major public health challenge. New and effective
treatments are urgently needed to reverse these trends

Study objective

The primary efficacy objective of the study is:
* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of major thrombotic vascular events (defined as MI, ischemic stroke, CV death, ALI, and major amputation of a vascular etiology) in symptomatic PAD patients with a recent lower extremity revascularization procedure.
The primary safety objective of the study is:
* to evaluate the overall safety and tolerability of rivaroxaban added to ASA compared
to ASA alone.
The secondary efficacy objectives of the study are:
* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of index limb revascularization;
* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of MI, ischemic stroke, coronary heart disease mortality, ALI, and major
amputation of a vascular etiology;
* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of MI, ischemic stroke, all-cause mortality, ALI, and major amputation of a
vascular etiology;

* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of vascular hospitalizations for a coronary or peripheral event (either limb) of
a thrombotic nature;
* to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing
the risk of MI, all-cause stroke, CV death, ALI, and major amputation of a vascular
etiology;
* to evaluate the efficacy of rivaroxaban in reducing the risk of venous thromboembolic
(VTE) events;
* to evaluate the efficacy of rivaroxaban in reducing the risk of all-cause mortality.

Study design

This study is an international multicenter, randomized, placebo-controlled, double-blind,
event-driven phase 3 study.

Intervention

Study treatment assignment will be double-blind. Study treatment consists of study
medication (rivaroxaban or matching placebo) in addition to study ASA, which is also
dispensed by the study.

Study burden and risks

Due to the event-driven study design, no firm treatment duration can be stipulated for an individual patient. However, the mean treatment duration is estimated to be approximately 30 months and the maximum treatment period for an individual patient to be approximately 42 months.

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

age *50,
* documented moderate to severe symptomatic lower extremity peripheral artery occlusive disease as evidenced by ALL of the following:
a. clinically, by functional limitations in walking activity, ischemic rest pain or ischemic ulceration,
b. anatomically, by imaging evidence of arterial occlusive disease below the inguinal ligament within 6 months prior to or at the time of the qualifying revascularization,
AND
c. hemodynamically (within 6 months prior to, or at the time of, the qualifying revascularization) by:
* an ABI * 0.80 or TBI * 0.60 of the index leg (in the event of non-compressible ankle arteries) for patients without a prior history of limb revascularization on the index leg,
OR
* an ABI * 0.85 or TBI * 0.65 of the index leg (in the event of non-compressible ankle arteries) for patients with a prior history of limb revascularization on the index leg.

Exclusion criteria

- patients undergoing revascularization for asymptomatic PAD, mild claudication without functional limitation or major tissue loss (including severe ischemic ulcers or gangrene) of the index leg,
- patients undergoing revascularization of the index leg to treat an asymptomatic or minimally symptomatic restenosis of a bypass graft or target lesion restenosis,
- prior revascularization on the index leg within 8 weeks of the qualifying revascularization,
- Planned dual antiplatelet therapy (DAPT) use for the qualifying revascularization procedure of clopidogrel in addition to ASA for >30 days after the qualifying revascularization procedure
- Planned DAPT use for any other indication(s) with any P2Y12 antagonists in addition to ASA after the qualifying revascularization procedure

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-04-2016
Enrollment:	96
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ASA
Generic name:	ASA
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:	28-09-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-12-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	04-05-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-06-2019
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	EUCTR2014-005569-58-NL

Register	ID
CCMO	NL54528.101.15