

# 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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<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Platelet disorders
<b>Study type</b>	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:** pharmaceutische 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, ALL, 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**

### **Public**

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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  $\geq 50$ ,

\* 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  $\geq 0.80$  or TBI  $\geq 0.60$  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  $\geq 0.85$  or TBI  $\geq 0.65$  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**

CCMO

**ID**

NL54528.101.15