DUAL Pathway Inhibition to Improve Endothelial Function in Peripheral Artery Disease

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28220

Source
Nationaal Trial Register

Brief title
DUAL-PAD

Health condition

Peripheral arterial disease

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

The primary outcome measure is the CAR after 3 months combination treatment. The change in proportion of patients with CAR-constriction from baseline (Aspirin alone) to 3 months after adding low dose rivaroxaban will be compared for both study groups (A and B).

Secondary outcome

Serum endothelin-1 levels will be quantified as a marker for cardiovascular disease at baseline and 3 months after adding low dose rivaroxaban.

Study description

Background summary

Peripheral artery disease (PAD) is a manifestation of systemic atherosclerosis, causing patients to be at high risk of major adverse cardiovascular and limb events. Therefore, single antiplatelet therapy is recommended when patients are symptomatic or have undergone revascularization. Rivaroxaban (2.5 mg twice a day) in addition to Acetylsalicylic acid (ASA) (100 mg once a day) has shown to be effective in reducing morbidity and mortality from major cardiovascular and limb events in patients with stable peripheral or carotid artery disease compared to Aspirin alone. Although a higher rate of major bleeding was detected, the incidence of fatal or critical organ bleedings was not increased.

Endothelial dysfunction is one of the first signs of atherosclerosis and is related to major cardiovascular events. The level of vascular endothelial dysfunction can be measured using the carotid artery reactivity (CAR) test. The investigators hypothesized that a combination of low-dose rivaroxaban and antiplatelet therapy would improve endothelial function in PAD patients. The aim is to study the effectiveness of this combination therapy in improving vascular endothelial function in patients with stable or symptomatic PAD.

Therefore the investigators will study two clinical cohorts of lower extremity PAD patients (n=159) with intermittent claudication (group A: Rutherford stages 1-3) or critical limb ischemia with pain at rest and/or foot ulcers (group B: Rutherford stages 4-6) who have an indication for single antiplatelet therapy.

ASA100mg once a day + 2.5 mg rivaroxaban twice a day will be given during 3 months, preceded by a run-in period of ASA alone as reference.

The change in proportion of patients with CAR-constriction from baseline (ASA alone) to 3 months after combination treatment with low dose rivaroxaban and ASA (100mg once a day) will be compared for both study groups (A and B).

Study objective

The investigators hypothesized that a combination of low-dose rivaroxaban and antiplatelet therapy would improve endothelial function in PAD patients.

Study design

3 months

Intervention

Aspirin 100mg once a day + 2.5 mg rivaroxaban twice a day (combination therapy). The use of Aspirin alone (100 mg once a day) during the run-in period is used as reference.

Contacts

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Eligibility criteria

Inclusion criteria

• Symptomatic or stable lower extremity PAD patients (Rutherford stages 1-6) with an indication for single antiplatelet therapy according to international (ESC) guidelines
• >16 years old

Exclusion criteria

• Patients having or at risk of major bleeding:
◦ Gastrointestinal ulceration
◦ Current malignant neoplasms
◦ Brain or spinal injury
◦ Brain, spinal or ophthalmic surgery
◦ Intracranial hemorrhage
◦ Known or suspected esophageal varices
◦ Arteriovenous malformations
◦ Major intraspinal or intracerebral vascular abnormalities
◦ Hepatic disease associated with coagulopathy and clinically relevant bleeding risk,

including cirrhotic patients with Child Pugh B and C
◦ Use of selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors
• Patients with prosthetic valves
• Patients with a history of asthma attacks caused by salicylates
• Severe renal impairment (creatinine clearance <30 ml/min)
• Systemic treatment with strong CYP3A4 and/or P-glycoprotein inhibitors (i.e. azole-antimyotics, HIV protease inhibitors)
• Concomitant treatment with other anticoagulants
• Concomitant treatment with methotrexate at a weekly dosage of >15 mg
• Pregnant or lactating
• Known hypersensitivity to Aspirin or rivaroxaban

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-06-2020
Enrollment:	159
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	22-09-2020

Application type: First submission

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
NTR-new	NL8908
CCMO	NL2019-6036

Study results