Arterial wall inflammation measured with 18F-FDG PET/CT in patients with statin intolerance before and after treatment with a PCSK-9 inhibitor

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON45376

Source
ToetsingOnline

Brief title
VISTA

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arterial wall thickening, Atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vasculaire geneeskunde, Academisch Medisch Centrum

Source(s) of monetary or material Support: EU,Sanofi-aventis

Intervention

Keyword: Arterial wall inflammation, Artherosclerosis, PCSK9 inhibition, Statin intolerance

Outcome measures

Primary outcome

The primary endpoint is the change in 18F-FDG target-to-background ratio (TBR)

following 12 weeks of PCSK-9 inhibition

Secondary outcome

- The secondary endpoints are the difference in hematopoietic 18F-FDG activity

in bone marrow before and after PCSK-9 inhibition and to evaluate whether there

is a correlation between 18F-FDG PET activity in arterial wall and

hematopoietic organs (i.e. bone marrow)

- circulating immune cell phenotype including but not limited to monocytes.

- epigenetic changes before and after treatment

Study description

Background summary

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are relatively novel therapeutic agents to treat dyslipidaemia. It prevents degradation of low-density lipoprotein cholesterol (LDL-C) receptors in the liver, thereby promoting uptake of LDL-C from the circulation into the liver, resulting in lower plasma LDL-C levels. Phase II/III studies showed strong LDL-C lowering after PCSK-9 inhibition (i.e. 50-75%) without clinically relevant adverse events. Therefore, PCSK-9 inhibitors are promising agents for use in patients with elevated LDL-C levels and increased cardiovascular (CV) risk.
Besides LDL-C, inflammation is a critical pathway contributing to destabilisation of atherosclerotic lesions. Consequently, inhibiting inflammatory activity has emerged as potential therapeutic target in patients at increased cardiovascular risk. In contrast to statins which decrease both

LDL-c as well as the acute phase reactant C-reactive protein (CRP), PCSK-9 inhibition does not lower CRP levels. The latter has fueled the question whether PCSK9-inhibition may lack the ability to lower inflammatory activity, which may theoretically limit the clinical efficacy of PCSK-9 inhibition in high-risk CV patients.

Study objective

In the present study, we set out to evaluate arterial wall inflammation in patients at increased CV-risk with statin-associated muscle symptoms (SAMS), precluding effective statin therapy. Following twelve weeks of treatment with PCSK9-Ab, the change in both lipid levels as well as arterial wall inflammation is assessed. The results of this study will help unravel whether PCSK9-Ab induced LDL-c lowering reduces inflammatory activity in patients with SAMS, in absence of significant changes in CRP.

Study design

This is a multi-center, double-blind, placebo-controlled, intervention study using PCSK9 inhibition (alirocumab).

Intervention

Treatment with Alirocumab (or placebo) for 3 months.

Study burden and risks

Awaiting the outcome studies for PCSK9-Ab, individual patients will not gain direct *health* benefit from this study. The results are expected to provide insight into the relation between LDL-C changes and inflammatory activity in atherosclerotic arteries. The burden and risk of participating in this study are estimated to be intermediate. The study requires a maximum of 4 study visits and 1 phone consultation. The exposure to radiation related to 18F-FDG PET/CT is 8.2 mSv for 2 consecutive PET/CT scans in this study. Maximal blood withdrawal including clinical laboratory assessment will be 144 ml.

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

Patients aged 50 years or older. With Statin-associated Muscle symptoms (SAMS) and Increased cardiovascular risk with high LDL-cholesterol.

Exclusion criteria

- Malignant diseases or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator.
- Chronic or recent (<1 month) infections and/ or clinical signs of acute infection and/or CRP >10
- Auto-immune diseases
- Recent or chronic immunosuppresant / antibiotic usage
- Diabetes (type 1/ type 2)
- Standard contra-indications to 18F-FDG PET/CT based on psysicians experience and current practice.

Study design

Design

Study phase:	2
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):	20-04-2017
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alirocumab
Generic name:	Praluent
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-02-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-03-2017
Application type:	First submission
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	EUCTR2016-004794-41-NL
CCMO	NL60006.018.16

Study results

Date completed:	29-06-2018
Actual enrolment:	53