Adverse events and inefficacy of PCSK9 Inhibition with evolocumab or alirocumab in hypercholesteraemic patients

Published: 15-10-2018
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To describe the characteristics of patients with either low PCSK9 inhibitor therapy efficacy or adverse effects.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Observational invasive

Summary

ID

NL-OMON55799

Source
ToetsingOnline

Brief title
AKITA

Condition

- Lipid metabolism disorders

Synonym
hypercholesterolemia; high cholesterol

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Inkomsten uit presentaties en lezingen

Intervention

Keyword: Adverse effects, non-responders, PCSK9 inhibitor

Outcome measures

Primary outcome

The main study parameters are differences in clinical parameters (e.g., patient anthropometrics between patients and controls, mutations in the PCSK9 gene possibly interfering with PCSK9 inhibitor therapy, variants in other lipid metabolism or PCSK9 related genes, gene expression, (semi)quantification of proteins (PCSK9 protein, other proteins involved in lipid metabolism, proteomics), (semi-)quantification of metabolites (e.g. lipids/fatty acids).

Secondary outcome

nvt

Study description

Background summary

High plasma levels of Low Density Lipoprotein-cholesterol (LDL-C) result in increased cardiovascular risk. Monoclonal antibodies against proprotein convertase subtilisin/kexin type 9 (PCSK9) have been shown to result in LDL-C lowering and CVD risk reduction. This relatively new class of drugs has not been widely studied in daily clinic, and anecdotal evidence has suggested that a small proportion of patients do either not respond to this medication or suffer from side effects.

Study objective

To describe the characteristics of patients with either low PCSK9 inhibitor therapy efficacy or adverse effects.

Study design

Multi-center case-control study, in which blood samples will be collected at

two different time-points. One sample when patient is on therapy, one sample when patient is off therapy.

Study burden and risks

Blood will be collected from participants by venous blood sampling on two occasions (86 ml total). Patients in whom therapy fails will be subjected to a washout period of 6 weeks of PCSK9 inhibitor therapy before restarting PCSK9 inhibitor therapy as a re-challenge. This washout period and a re-challenge are normal clinical practice and are not part of this study. Only the collection of blood samples is part of this study. The period without PCSK9-inhibitor therapy is not deemed a clinical risk, as these patients were shown not to respond to the PCSK9 antibody therapy prior to enrolment.

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
- On therapy or discontinued therapy with alirocumab 75mg 1x/2weeks or 150mg 1x/2weeks, or with evolocumab 140mg 1x/2weeks.
- Failure of PCSK9 inhibitor therapy, due to adverse effects leading to discontinuation of the drug
OR
- Failure of PCSK9 inhibitor therapy, due to less than 30 percent reduction in LDL-C observed by the referring physician
- >18 years of age, Controls:
- On therapy with alirocumab or with evolocumab
- On therapy with alirocumab or with evolocumab
- No adverse effects leading to discontinuation of the drug
- LDL-C reduction above 30 percent., - >18 years of age.

Exclusion criteria

None

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-11-2018
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	15-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2019
Application type:	Amendment
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
CCMO	NL66234.018.18

Study results

Date completed:	26-10-2022
Actual enrolment:	71

Summary results
Trial is onging in other countries