Adverse events and inefficacy of PCSK9 Inhibition with evolocumab or alirocumab in hypercholesTeraemic pAtients. (AKITA)

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Study Planned

Administrative details

EU PAS number

EUPAS33787

Study ID

33788

DARWIN EU® study

No

Study countries

☐ Netherlands

Study description

Rationale: Patients with elevated plasma levels of Low Density Lipoprotein-cholesterol (LDLC) are at increased risk for cardiovascular disease. 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.Objective: To describe the characteristics of patients with either low PCSK9 inhibitor therapy efficacy or adverse effects, based on the interpretation of the treating physician.Study design: Multi-center case-control studyStudy population: 20 subjects in whom PCSK9 inhibitor therapy has been shown to result less than 30 percent reduction in LDL-C as assessed by the referring physician, and 20 subjects in whom PCSK9 inhibitor therapy was discontinued due to adverse effects will be compared with 40 controls in whom PCSK9 inhibitor therapy is considered to be successful.Main study parameters/endpoints: This is a descriptive study in which we will assess differences in clinical parameters (e.g., patient anthropometrics between patients and controls, and identify possible (novel) mutations in the PCSK9 gene possibly interfering with PCSK9 inhibitor therapy, variants in other lipid metabolism or PCSK9 related genes, assess gene expression, (semi)quantification of proteins (PCSK9 protein, other proteins involved in lipid metabolism, proteomics), PCSK9 antibody concentrations, antidrug antibodies, and (semi-) quantification of metabolites (e.g. lipids/fatty acids).

Study status

Planned

Research institutions and networks

Institutions

Amsterdam UMC

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Institution | Educational Institution | Hospital/Clinic/Other health care facility

Erasmus Medical Centre Rotterdam

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Institution

Rotterdam Erasmus UMC

Contact details

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Primary lead investigator

G Kees Hovingh

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 15/10/2018

Study start date
Planned: 15/10/2018

Date of final study report
Planned: 31/12/2020

Sources of funding

- Other

More details on funding

NWO

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Effectiveness study (incl. comparative)

Main study objective:

- To describe the patients who fail to achieve adequate LDL-C lowering on PCSK9inhibitor therapy compared to controls, due to the fact that they a) do not respond to the therapy (Group A), or b) experience adverse events. (Group B)- To unravel the cause of adverse effects and inefficacy of PCSK9-inhibition.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C10AX) Other lipid modifying agents

Other lipid modifying agents

(C10AX13) evolocumab

evolocumab

(C10AX14) alirocumab

alirocumab

Population studied

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

80

Study design details

Outcomes

Identification of genetic variants in genes possibly leading to reducedefficacy of PCSK9 inhibitors (e.g. those involved in lipid metabolism), Identification of differences in DNA expression in patients not responding totherapy compared to controls.(Semi-)quantification of proteins (e.g. anti-drug antibodies, PCSK9 protein levels, other proteins involved in lipid metabolism) in patients not responding to therapy compared to controls.· (Semi-)quantification of metabolites (e.g. lipid composition)

Data analysis plan

Data will be obtained on the patient's medical history, family history, as well as routine laboratory results. Descriptional statistics will be used to describe the current cohort. We will perform targeted sequencing of the PCSK9 gene and other genes known to be involved in lipid-metabolism, as well as proteome and metabolome analysis by ELISA and/or protein mass spectrometry. We will store samples in a biobank for further research.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No