MODULATION OF POSTPRANDIAL LIPEMIA, INFLAMMATION, AND VASCULAR FUNCTION BY PCSK9 INHIBITION IN DIABETES.

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To explore the inflammatory changes of a PCSK-9 inhibitor compared with placebo on postprandial lipemia and postprandial leukocyte activation, oxidative stress and endothelial function in men with type 2 diabetes mellitus.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON43374

Source
ToetsingOnline

Brief title
PLEIADES-pcsk9

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Lipid metabolism disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
fat loading, Postprandial lipemia

Research involving
Human

Sponsors and support

Primary sponsor: Sint Franciscus Gasthuis
Source(s) of monetary or material Support: Stichting Onderzoek Interne specialisme Franciscus Gasthuis

Intervention

Keyword: Atherosclerosis, Leukocyte activation, PCSK9-inhibition, Postprandial lipemia

Outcome measures

Primary outcome

Postprandial leukocyte inflammation markers

Secondary outcome

Postprandial lipemia, oxidative stress parameters and vascular function.

Study description

Background summary

Diabetes mellitus type 2 (T2DM) is characterized by a 2-fold increased risk in cardiovascular mortality. Several risk factors are involved. The presence of small dense LDL, low HDL-C but also postprandial hyperlipidemia with increased concentrations of chylomicron and VLDL remnants leading tot postprandial inflammation and impaired vascular function, have been implicated. Current therapies like statins and fibrates have only minor effects on these risk factors. Since remnant particles are also cleared by the LDL-R, upregulation of this system may lead to improved postprandial lipemia and inflammation and consequently to decreased cardiovascular risk.

Study objective

To explore the inflammatory changes of a PCSK-9 inhibitor compared with placebo on postprandial lipemia and postprandial leukocyte activation, oxidative stress and endothelial function in men with type 2 diabetes mellitus.

Study design

Randomized, double blind pilot study.

Study burden and risks

The use of a pcsk9 inhibitor every two weeks (Q2W) has been established to be a safe and effective treatment for hypercholesterolemia. Volunteers will be hospitalized on 2 different days (day 1, day 43) for approximately nine hours each day and receive an oral fat load. The volunteers* general practitioner will be informed on their participation. A total of 222ml (111ml for each postprandial test) of blood will be drawn. Volunteers will be allowed to drink only water during the tests. Volunteers receive 250 euros for full participation. Furthermore, volunteers will be informed and given advice if there are additional cardiovascular risk factors or any other conditions

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

- Age of 18 years or older
- Male
- Fasting triglycerides levels between 1.8 mmol/L and 7.0 mmol/L
- Diabetes mellitus type 2 on intensive insulin treatment (three times short acting and one daily long acting) (unchanges for >10 weeks prior to consent)
- Stable glucose regulation last 6 months (HbA1c >6.5% - < <9.0%)
- Stable lipid lowering therapy last 2 months (no changes in regiments or dose)

Exclusion criteria

- Current smoking
- Impaired renalfunction (MDRD <60 ml/min/1.73 m2)
- Recent cardiovascular event (<6 months) (myocardial infarction, coronary artery bypass grafting, stroke)
- Severe hyperglycemic events in the past 6 months (hyperglycemia >20 mmol/L requiring hospital admittance)
- Recent or current use of pcsk9 antibodies
- HIV-infection
- Uncontrolled hypothyroidism

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	27-11-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	30-12-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-01-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2018
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

ID: 22535
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2016-003253-15-NL
CCMO	NL58836.101.16
OMON	NL-OMON22535

Study results

Date completed:	07-11-2018
Actual enrolment:	12