Beginning to unravel the cause of familial hypercholesterolemia of unknown origin (FH4)

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To unravel the cause(s) of the FH phenotype in patients with no mutations in well-established lipid genes (LDLR, APOB, PCSK9).

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

Summary

ID

NL-OMON44591

Source
ToetsingOnline

Brief title
BEAVER

Condition

- Lipid metabolism disorders

Synonym
Familial hypercholesterolemia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Vidi grant [016.156.445] from the Netherlands Organisation for Scientific Research (NWO)

Intervention

Keyword: Cholesterol, Familial hypercholesterolemia, Genetics, LDL

Outcome measures

Primary outcome

The main study parameters are novel mutations/SNP*s associated with hypercholesterolemia, methylation of target genes, DNA expression, (semi-)quantification of proteins (proteomics), (semi-)quantification of metabolites (e.g. lipids/fatty acids) in FH4 patients compared with matched controls

Secondary outcome

nvt

Study description

Background summary

Familial hypercholesterolemia (FH) is characterized by increased low density lipoprotein (LDL) cholesterol and increased cardiovascular risk. There are 3 known genes (LDLR, ApoB, PCSK9) in which mutations can lead to the FH phenotype (FH1 to 3 respectively). However, in approximately 5-10% of patients such a mutation cannot be found, despite family-based linkage studies (the so called FH4 group). Therefore, a more elaborate approach is deemed necessary, where data derived from the genome, epigenome, transcriptome, proteome, and metabolome are combined to find novel genes and metabolic pathways in lipid metabolism.

Study objective

To unravel the cause(s) of the FH phenotype in patients with no mutations in well-established lipid genes (LDLR, APOB, PCSK9).

Study design

Matched case-control study.

Study burden and risks

Patients will be subjected to venous blood sampling (60 ml total). A subgroup of FH4 cases, those on lipid lowering therapy for primary prevention, might be asked to participate again after a washout period of 4 weeks of those medication. This will result in temporarily higher LDL-C levels, mildly increasing the risk for CVD. However, we think that this additional risk is minimal in the light of a life time exposure to high LDL-C levels in FH4 patients.

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

- Diagnosis of familial hypercholesterolemia based on Dutch Lipid Clinic Network criteria (Nordestgaard et al. 2013) in combination with a negative DNA-testing (mutations in LDLR, ApoB, PCSK9).
- Untreated LDL-cholesterol levels of > 95th percentile for age and gender, or between 20-60th percentile for family controls
- >18 years of age

Exclusion criteria

- Heavy alcohol use
- Dysthyroidism
- Renal insufficiency (creatinine >150 µmol/L)
- Diabetes mellitus

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-01-2018
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	05-10-2017
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2021
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

ID: 27045
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL62407.018.17
OMON	NL-OMON27045