Studie naar het effect van ursodeoxycholzuur (ursochol) en ezetimibe op de uitscheiding van vetten in de ontlasting en op de concentratie van vetten in het bloed

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON19907

Source
NTR

Brief title
EXCRETE

Health condition

Hypercholesterolemia, fecal cholesterol excretion, ABCG5/8, NPC1L1, trans-intestinal cholesterol excretion

Sponsors and support

Primary sponsor: Academisch Medisch Centrum (AMC), Amsterdam
Source(s) of monetary or material Support: Sponsor (AMC)

Intervention

Outcome measures

Primary outcome

Total faecal sterol concentration (faecal total neutral sterol concentration (FNS) + faecal bile acid concentration)

Secondary outcome

Lipid profile/composition: LDL-c, HDL-c, TG, apoB, apoA1.

Study description

Background summary

Intestinal cholesterol secretion is mediated via the ATP binding cassette (ABC) half transporters G5 and G8 (ABCG5/G8) while cholesterol absorption is mediated by the Niemann-Pick C1 Like (NPC1L1) protein, which is inhibited by ezetimibe. There is growing evidence that hydrophilic bile acids like ursochol (ursodeoxycholic acid, UDCA) promote ABCG5/G8 activity in mice.

The primary objective is to evaluate the effect of UDCA and ezetimibe on cholesterol elimination assessed as total faecal sterol concentration. Secondary objective is to assess the effect of UDCA and ezetimibe on plasma lipid profile/composition.

The current study is an investigator initiated, single-centre, randomized, double blind, placebo-controlled , cross-over, proof of concept study, to explore the translational relevance of UDCA on top of ezetimibe on cholesterol elimination.

Study objective

We hypothesize that UDCA on top of ezetimibe leads to an increased cholesterol excretion via the feces by stimulating ABCG5/8 and preventing absorption of cholesterol due to blocking NPC1L1 and therefore promoting elimination of cholesterol from the body.

Study design

Visit 1 (Day 0): Screening

Visit 2 (Day 21): Randomization

Visit 3 (Day 35): end of treatment period 1 + start washout period

Visit 4 (Day 56): start treatment period 2

Visit 5 (Day 70): end of treatment period 2 + end of study

Intervention

Ursodeoxycholicacid (UDCA) 600mg once daily or placebo

Background therapy: ezetimibe 10mg once daily

Contacts

Public
Amsterdam UMC
Rens Reeskamp
Amsterdam
The Netherlands
0031205666023
Scientific
Amsterdam UMC
Rens Reeskamp
Amsterdam
The Netherlands
0031205666023

Eligibility criteria

Inclusion criteria

- Hypercholesterolemia, with LDL plasma levels >2.6 mmol/L

- Body mass index (BMI) ¡Ý19 ¡Ü30 kg/m2

- Use of statin therapy (stable dose for 3 months) or no statin therapy at all

Exclusion criteria

- Medical, surgical, laboratory or other conditions, which in the judgment of the Physician Investigator would make the subject unsuitable for enrollment, or potentially interfere with

subject participation or completion of the study

- Suffering from an inflammatory bowel disease, e.g. Crohn¡¯s disease or ulcerative colitis.

- Suffering from gall stones or another biliary disease.

- Suffering diabetes mellitus (type I or II).

- Recent history of, or current drug or alcohol abuse

- AST or ALT levels > 2 x ULN

- Unable or unwilling to comply with the protocol requirements or deemed by the investigator to be unfit for the study.

- Presence of contra indications for the use of UDCA and ezetimibe (see SPC)

- Use of lipid lowering drugs such as the following:

o Statins and fibrates unless on a stable dose for at least 3 months prior to screening

o Use of nicotinic acid or derivates of nicotinic acid within 4 weeks prior to screening

o Use of cholestyramine or colestipol

- Use of other drugs such as the following:

o Ciclosporine

o Antacids containing aluminium hydroxide or aluminium oxide

- Likely to leave the study before its completion

- Participation in other intervention studies

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2018
Enrollment:	20
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	05-04-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 47926
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6932
NTR-old	NTR7128
CCMO	NL56321.018.16

Register	ID
OMON	NL-OMON47926

Study results