Local delivery of CER-001 in advanced plaques
Proof-of-concept for apoA-1 as initiator of reverse cholesterol transport

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON22856

Source
NTR

Brief title
LOCATION

Health condition

Atherosclerosis, cardiovascular disease

Sponsors and support

Primary sponsor: Academic Medical Center Amsterdam
Source(s) of monetary or material Support: Investigator initiated

Intervention

Outcome measures

Primary outcome

The CER-001 uptake in the plaque over time by means of PET imaging of the aorta and

carotid arteries, reported as Standardized Uptake Value (SUV) of the plaque

Secondary outcome

Further quantification of CER-001 uptake at the plaque

- 89Zr-CER-001 uptake in the plaque over time assessed as the Target to Background Ratio (TBR), via PET imaging

- Difference between SUV and TBR at the level of the plaque and SUV and TBR of non-diseased arterial wall on PET

Relation between CER-001 uptake and plaque characteristics

- Relation between SUV and TBR of the plaque on PET and structural plaque dimensions on MRI i.e. normalized wall index, vessel wall area. - Relation between SUV and TBR of the plaque and plaque permeability on DCE-MRI, i.e. Ktrans

Relationship between the CER-001 uptake in the plaque by means of PET imaging reported as SUV of the plaque and the cholesterol efflux capacity.

Study description

Background summary

Atherosclerosis is considered a chronic inflammatory disease in which macrophages play a major role by taking up (oxidized) low-density lipoprotein (LDL). The lipid-laden macrophages accumulate and undergo apoptosis leading to the formation of a necrotic core and eventually the vulnerable plaque. Cholesterol efflux from lipid-laden macrophages is a key atheroprotective mechanism, a process referred to as reverse cholesterol transport (RCT) in which apolipoprotein (apo)A-1 and HDL particles remove cholesterol from peripheral cells. In view of the abundant evidence for apoA-1 on stimulating efflux from macrophages in vitro, it is reasonable to assume that apoA-1 will also stimulate efflux from vessel wall macrophages in vivo if apoA-1 succeeds in getting into the proximity of plaque macrophages. The radio-isotope Zirconium-89 (89Zr) has emerged as a ‘gold-standard’ in the field of antibody-based PET imaging. The experience in oncology and the fact that 89Zr-labeling is a GMP-approved method makes this a suitable candidate for proving target delivery of apoA-1/HDL into advanced atherosclerotic plaques in humans using non-invasive imaging techniques. With this project we aim to show that exogenously infused apoA-1 (CER-001®) penetrates into advanced plaques in patients, making it ‘highly likely’ that efflux of cholesterol from macrophages to the apoA-1/HDL complex will occur.

Study objective

To demonstrate that 89Zr-CER-001 penetrates into atherosclerotic plaques in patients by means of PET imaging.

Study design

PET/CT scans will be performed at timepoints 10 minutes, 24 hours and 72 hours after 89Zr-CER-001 infusion.

Intervention

Infusion with (89Zr-)CER-001 and PET-CT imaging

Contacts

Public
Department of Vascular Medicine - Academic Medical Center

K.H. Zheng
Meibergdreef 9

Amsterdam 1105 AZ
The Netherlands
+31 20 5667516
Scientific
Department of Vascular Medicine - Academic Medical Center

K.H. Zheng
Meibergdreef 9

Amsterdam 1105 AZ
The Netherlands
+31 20 5667516

Eligibility criteria

Inclusion criteria

Patients must meet the following criteria for study entry:

- Adult patients (either gender) ≥ 50 years

- Documented atherosclerotic vascular disease; defined as either peripheral arterial disease or documented aortic or carotid atherosclerosis on clinical vascular MRI or ultrasound

- Clinically stable for at least 3 months prior to inclusion

- Very high CV-risk (based on Framingham risk engine)

Exclusion criteria

Patients are not eligible if they meet one of the criteria listed below:

- Creatinine clearance < 50 ml/min (MDRD) 6 months prior to inclusion

- Auto-immune disease/vasculitis, other active inflammatory diseases, proven or suspected bacterial infections. Recent (<1 month prior to inclusion) or ongoing serious infection requiring IV antibiotic therapy that could interfere with the conduct of the study in the opinion of the investigator

- Known systemic disorders such as hepatic, renal, hematologic, and malignant diseases or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator

- Standard contra-indications to MRI, PET, and CT

- Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2014
Enrollment:	8
Type:	Actual

Ethics review

Positive opinion

Date:	06-05-2015
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40758
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5040
NTR-old	NTR5178
CCMO	NL49081.018.14
OMON	NL-OMON40758

Study results