# Double-blinded, randomised, placebo-controlled, multicentre , Phase IIa study to investigate the effect, safety and tolerability of phosphorylcholine human monoclonal antibody (PC-mAb) 3G10 on arterial inflammation, together with safety and tolerability, in subjects with elevated lipoprotein a (Lp[a ])

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Coronary artery disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON44302

**Source**
ToetsingOnline

**Brief title**
ATH-3G10-005

### Condition

- Coronary artery disorders
- Vascular disorders NEC

**Synonym**
arterial inflammation in cardiovascular disease

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Athera Biotechnologies AB
**Source(s) of monetary or material Support:** Industry funding

## Intervention

**Keyword:** arterial inflammation, atherosclerosis, human monoclonal antibody, safety and tolerability

## Outcome measures

### Primary outcome

• Change in TEM in monocytes isolated from treated subjects from baseline to

visit 11

### Secondary outcome

• Change in tissue to background ratio (TBRmax) in common carotid arteries by

fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG

PET/CT) from baseline to Visit 11

• Change in PWV (m/sec) assessed by Sphygmocor Xcel from baseline to Visit 11

• Safety and tolerability: number of AEs/SAEs, vital signs, physical

examination, ECG and Laboratory assessments including haematology, clinical

chemistry and immunogenicity.

# Study description

### Background summary

Inflammation and dyslipidaemia are key factors for the development and progression of atherosclerosis and cardiovascular disease (CVD). Atherosclerotic lesions are characterised by the presence of activated immune cells, which produce pro-inflammatory cytokines, including interleukin-12 (IL-12), IL-18, interferon-gamma and tumour-necrosis factor (TNF) in the lesions. Low density lipoprotein (LDL) plays a major role for these inflammatory reactions in the arterial wall, accelerates the atherogenic process and is a major determinant of plaque instability and increased thrombogenicity. Another pro-inflammatory plasma lipoprotein is lipoprotein (a) (Lp[a]), composed of apolipoprotein (a) bound to apolipoprotein B-100 of LDL-like particles, where several studies show strong, independent and likely causal relationship of increased plasma levels to risk of CVD. Vascular inflammation generates a range of effects, including endothelial dysfunction and migration of white blood cells into the vessel wall, which results in increased risk of cardiovascular events. There are currently no drugs available on the market that are specifically tartgeting vascular inflammation, which is the target of the compound used in this study.

## Study objective

1. The primary objective is to assess the effects of four 250 mg PC-mAB (also referred to as "3G10") once monthly intravenous injections on monocyte function ex vivo.

The secondary objectives are to:

1. assess the functional effects of 3G10 on arterial inflammation in vivo
2. assess the effects of 3G10 on arterial stiffness
3. assess the safety and tolerability of 3G10

## Study design

This is a Phase IIa, prospective, double-blind, randomised, placebo-controlled multicentre study investigating the effects of treatment with PC-mAb (3G10) for four monthly intravenous injections/infusions.

## Intervention

Subjects will be allocated to receive either 250 mg 3G10 or matching placebo, which are both referred to as IMP.
Each subject will receive monthly intravenous injections for four months.

## Study burden and risks

Awaiting the outcome of the study, individual patients might not gain direct "health" benefit from this study.

The results are expected to provide insight into the relation beween Lp(a) and changes in the inflammatory activity in the atherosclerotic arteries. The burden and the risk of participating in this study are estimated to be intermediate. The study requires a maximum of 9 visits to the site and 4 phone consultations. The exposure to radiation related to the PET/CT is 9.4 mSv for the 2 PET/CT scans in this study. Maximum blooddraw in the study is below 450 ml (including clinical laboratory assesments.
Subjects should be in fasting state for 2 visits and should withhold from the use of caffeine, alcohol, energydrinks and nicotine before PET/CT visit.
2 MRI examinations will be performed in a subgroup of the population (optional).
PWV (PulseWaveVelocity) analysis will be performed 6x.

# 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

1. Provision of a signed written informed consent
2. Lp(a) above 50 mg/dL at screening
3. Male or female, >= 50 years of age at screening

## Exclusion criteria

1. History of any clinically significant disease or disorder which, in the opinion of the Investigator, may either put the subject at risk because of participation in the study, or influence the result or the subject*s ability to participate in the study
2. Illness (including common colds) for the last 4 weeks before screening
3. Medical history of myocardial infarction (MI) or stroke within 12 months of screening
4. Ongoing or paroxysmal atrial fibrillation
5. Clinically overt heart failure
6. Hypertension defined as >=180/100 mmHg
7. Diabetes mellitus

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Prevention |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 21-12-2017 |
| Enrollment: | 20 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | PC-mAb |

## Ethics review

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|---|---|
| Approved WMO Date: | 08-08-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 01-09-2017 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 10-10-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-10-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-01-2018 |
| 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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2017-002106-13-NL |
| CCMO | NL62199.018.17 |