A phase IIa, placebo-controlled, double blind, randomised multicentre pilot study to investigate the efficacy, safety and tolerability of the monoclonal antibody ATH3G10 in patients with ST-elevation myocardial infarction

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

Summary

ID

NL-OMON48214

Source
ToetsingOnline

Brief title
ATH3G10 in patients with STEMI

Condition

- Coronary artery disorders

Synonym
Acute Heart Infarct, ST elevation Myocardial infarction

Research involving

Human

Sponsors and support

Primary sponsor: Athera Biotechnologies AB
Source(s) of monetary or material Support: Athera Biotechnologie

Intervention

Keyword: Myocardial Infarction, PCI

Outcome measures

Primary outcome

Primary endpoint: Left Ventricular End-Diastolic Volume index (LV EDVi) change

from Visit 2 to Visit 3.

Safety endpoints: Safety and tolerability: AEs/SAEs, blood pressure, physical

examination, ECG and laboratory assessments including clinical chemistry,

haematology and coagulation.

Secondary outcome

Secondary endpoints: Myocardial Salvage index (MSi) at Visit 2.

Study description

Background summary

The present study ATH3G10-006 aims to investigate efficacy and safety in patients that have suffered a STEMI. The current experimental data suggest that ATH3G10 may reduce infarct size and left ventricular remodelling. Thus, ATH3G10 may reduce risk for heart failure development if it can be administered to STEMI patients that has suffered a major anterior wall infarction or where coronary blood flow is less than normal in spite of successful PCI. These patients are at high risk for later complications and there are today no medical treatments that specifically reduce risk in these patients. The acute inflammatory reaction in conjunction with a STEMI and reperfusion by PCI has an acute onset and last for several weeks. The signals leading to the final size of the infarction and to left ventricular remodelling is established during

this time. Therapies aiming to block these reactions should thus last over this period. ATH3G10 is an IgG1 antibody, and its pharmacokinetic properties are such that a single dose will lead to a relevant exposure over the entire period of interest. To cover the entire period of post-infarction inflammation, the drug should be given as soon as possible when reduced TIMI flow has been noted.

Study objective

The main goal of this study is to evaluate efficacy of a single administration of ATH3G10 in patients presenting with an acute STEMI undergoing PCI.
The primary objective is to investigate effects on left ventricular remodelling as measured by the change in end diastolic volume measured by MRI.
The safety objectives are to investigate the safety and tolerability of ATH3G10.
The secondary objective is to investigate effects on myocardial salvage index (MSi) measured by MRI

Study design

Phase IIa, placebo-controlled, double-blind, randomized multicenter pilot study

Intervention

Patients will be allocated to receive either 250mg ATH3G10 or matching placebo given as a single dose within 120 minutes of the start of the PCI procedure.

Study burden and risks

Potential study patients will be identified in the hospital catheterisation laboratory at the study sites where PCI procedure is performed. In connection with PCI procedure, the patients will be informed about the study. The patients need to consent to study participation before any study specific assessments are performed.

After confirmation of fulfilled eligibility criteria, the patient will be randomised to treatment with 250 mg of ATH3G10 (corresponding to approximately 2-4 mg/kg) or placebo and the study medication will be administered as soon as possible after randomisation and within 120 minutes of start of the PCI procedure. Blood samples for safety (clinical chemistry, haematology and coagulation), drug concentration analysis, immunogenicity, cardiac samples (TnT, BNP and CRP) and protein biomarkers will be drawn pre-dose. Blood pressure and ECG will be assessed pre-dose and through-out the visit. Blood samples for safety will be drawn at 8, 16 and 24 hours post-dose.

At Visit 2, within 24-72 hours of performed PCI procedure, an MRI examination will be performed and again blood will be drawn. The patients will then be monitored for adverse events and otherwise treated in hospital according to

clinical practice until discharged.

An outpatient 3-month follow-up visit will be performed with clinical and adverse event evaluation and blood will be drawn, and a second MRI examination will be performed. The patient will answer a quality of life questionnaire in connection with the visit.

The patients will be contacted by telephone at 6 and 12 months(last visit) for adverse event reporting including cardiovascular events of special interest and concomitant medication. The patient will also answer a quality of life questionnaire in connection with the 12-month follow-up visit.

The current study is designed to be a well-controlled study investigating efficacy of ATH3G10 in patients suffering poor perfusion at PCI for STEMI and to further evaluate safety and tolerability of the drug. The study will be double blind to minimize bias.
The single dose slow intravenous injection of 250 mg ATH3G10 is expected to result in relevant plasma levels in patients in the planned study. The dose is selected based on pharmacokinetic data from previous studies in healthy volunteers and patients.

The exposure in the planned clinical study (250 mg given as a single dose IV injection), will be lower than in the medium dose group in the toxicity studies, conservatively estimated to approximately 1/5 .

All patients will be carefully monitored to ensure that potential risks are minimized. The risk/benefit balance using a single dose of ATH3G10 in patients suffering a STEMI with ST elevation remaining despite PCI, is therefore considered acceptable.

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

Patients must fulfil all of the following criteria to be included in the study:
1. Provision of informed consent
2. Symptoms and signs consistent with acute MI and ST elevation at the J-point in two contiguous leads (cut-points: >0.2mV in men and >0.15 mV in women in leads V2-V3 and/or >0.1 mV in other leads)
3. Start of PCI, defined as when the guide wire is passed through the stenosis, less than 4 hours after symptom onset
4. TIMI flow grade 0 at angiography before PCI in left anterior descending coronary artery (segment 6 or 7) without collaterals OR TIMI flow grade less than 3 in any infarct related main coronary arteries after PCI
5. Age 40-85, inclusive
--Females must be of non-childbearing potential at screening confirmed by fulfilling one of the following criteria a) postmenopausal defined as amenorrhea for at least 12 months, or b) documentation of irreversible surgical sterilization.

Exclusion criteria

1. Cardiogenic chock, non-compensated acute heart failure and/or pulmonary oedema.
2. Previous major vascular intervention within the last 4 weeks.
3. History of an infarct in the same artery that is currently affected.
4. Thrombolysis prior to admission.
5. Previous treatment with ATH3G10
6. Weight of less than 63 kg at screening (results in dose more than 4 mg/kg body weight)7.
8. Recent (<1 month prior to screening) or current treatment with methotrexate

and/or tumour necrosis factor alpha (TNF*) inhibitors such as infliximab.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-10-2019
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ATH3G10
Generic name:	na

Ethics review

Approved WMO Date:	01-07-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	22-07-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2019
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-003676-12-NL
CCMO	NL70235.100.19

Study results

Date completed: 31-03-2021

Actual enrolment: 16

Summary results
Trial is onging in other countries