Inhibition of Mast cell Activation in AtheroScleroTic lesions using an Anti-IgE antibody approach (MAST-trial)

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This study has been transitioned to CTIS with ID 2024-513581-19-00 check the CTIS register for the current data. The primary objective is, to determine whether short term anti-IgE treatment with an anti-IgE monoclonal antibody (omalizumab) can limit...

Ethical review	Approved WMO
Status	Pending
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON54785

Source
ToetsingOnline

Brief title
MAST

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
carotid narrowing; atherosclerotic carotid artery stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW;Dutch Heart Foundation

Intervention

Keyword: Anti-IgE, Atherosclerosis, Mast cell, Omalizumab

Outcome measures

Primary outcome

The primary endpoint is activated mast cell as the percentage of the total mast cell (CD45+CD117+Fc*R+ cells) count, determined by flow cytometry. Normal unactivated mast cells are positive for the markers CD45, CD117 and Fc*R. In addition, activated mast cells are positive for IgE and the activationmarkers CD203c and CD63. The primary study parameter is the % of mast cell activation determined by flow cytometry.

Secondary outcome

Secondary endpoints are (endpoints will be compared between treatment groups and for point 2,3,5 and 6 between baseline and day 3):

(1) Local inflammatory status of atherosclerotic plaque (measuring T-cell subsets, M1/M2 macrophages, neutrophils and B-cells counts)

(2) Plasma tryptase levels

(3) Level of infection parameters (complete blooudcount, hsCRP, IL-1beta and IL-6)

(4) Plaque characterization (using histology)

(5) Serum IgE levels

(6) Basophil activation status

Study description

Background summary

Atherosclerosis, the main underlying pathology of cardiovascular disease is the principal cause of death in the Western society. The mast cell is a prominent immune effector cell, that has been shown to accumulate within atherosclerotic plaques. Mast cells are activated by a various stimuli, of which crosslinking of the Fc*RI via IgE-antigen complexes is most prominent. Previously, we have demonstrated that acute mast cell activation contributes to destabilization of advanced plaques in mice. Moreover, mast cell numbers positively correlate with plaque progression and the mast cell is the only cell type within atherosclerotic plaque that is associated with future acute cardiovascular events (ACE), which is suggestive for a causal relation between mast cells within plaques and disease outcome. This indicates that inhibition of mast cell activation may serve as a novel therapeutic strategy to limit ACE*s. Recently, we have established that anti-IgE treatment in mice results in a reduction in mast cell activation, and subsequently a significant reduction in atherosclerotic plaque size. We hypothesize that in humans anti-IgE treatment with omalizumab can be markedly effective in inhibiting mast cell activation within plaques.

Study objective

This study has been transitioned to CTIS with ID 2024-513581-19-00 check the CTIS register for the current data.

The primary objective is, to determine whether short term anti-IgE treatment with an anti-IgE monoclonal antibody (omalizumab) can limit intraplaque mast cell activation in atherosclerotic plaques.

Study design

Single centre double blind randomized placebo-controlled trial

Intervention

Intervention: a single treatment moment three days before carotid endarterectomy, patients will receive a total of four subcutaneous injections with omalizumab of 150mg (1.2mL) each.

Control intervention: placebo (physiological saline solution) in four subcutaneous injections (1.2mL each).

Study burden and risks

Patients which are scheduled for a CEA based on (a)symptomatic atherosclerotic carotid stenosis, with a suitable timeframe between possible study inclusion

and the scheduled surgery to participate in this study, will be approached. Study participants will be required to make an additional visit to the outpatient clinic for the withdrawal of extra blood samples (total blood volume 9mL: EDTA whole blood 2ml, EDTA 2ml and serum 5ml) through venepuncture, the administration of the study drug and the subsequent observation period of at least two hours after administration of the study drug.

Omalizumab is a FDA and EMA approved anti-IgE antibody which is on the market to treat severe allergic asthma and idiopathic chronic urticaria. The most common adverse events (e.g. injection site reactions, viral infections and upper tract infections) are relatively mild and similar rates of these adverse events were observed in the placebo control groups in studies where patients received omalizumab for asthma, urticaria or other diagnosis. There is a small chance (<0.09%) that patients treated with omalizumab develop an anaphylactic reaction after the administration of omalizumab. To minimize the potential harm of such a reaction, all study participants will be kept under observation for at least two hours after the administration of the study drugs. In the case of an anaphylactic reaction patients will be treated immediately according the local guideline for treating anaphylaxis. As patients will receive the study drug once, we expect that the risk of harmful effects are minimal.

On the day of surgery additional blood (total blood volume 9mL: EDTA whole blood 2ml, EDTA 2ml and serum 5ml) for the study will be drawn through a single venepuncture. During the standard CEA the atherosclerotic plaque will be collected for further processing. We do not know if omalizumab will reduce cardiovascular events in the enrolled patients. However, if omalizumab can indeed limit mast cell activation in atherosclerotic plaque than this finding is potentially of great value for future research and for the non-invasive treatment of patients with atherosclerosis.

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

Patient has a symptomatic or asymptomatic atherosclerotic carotid artery stenosis of at least 50% narrowing of the lumen (calculated by using criteria equivalent to the NASCET method) wherefore revascularisation through carotid endarterectomy is planned routinely.

Exclusion criteria

Any anaphylactic reaction in the medical history

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:	Pending
Start date (anticipated):	01-10-2023
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Xolair
Generic name:	Omalizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-12-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-02-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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: 23598
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2024-513581-19-00
EudraCT	EUCTR2019-002452-16-NL
CCMO	NL70680.041.19