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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23598

Source
Nationaal Trial Register

Brief title
MAST

Health condition

Atherosclerotic narrowing of the carotid artery

Sponsors and support

Primary sponsor: ZonMW, Dutch Heart Foundation
Source(s) of monetary or material Support: ZonMW, Dutch Heart Foundation

Intervention

Outcome measures

Primary outcome

Primary outcome: The extent of mast cell activation in atherosclerotic plaque after administration of the study drugs (either omalizumab or placebo) measured by flow cytometry

Secondary outcome

Secondary outcomes:
The effect of administration of the study drugs (either omalizumab or placebo):
- Other inflammatory cells in the plaque (T-cell subsets, M1/M2 macrophages, neutrophils and B-cells)
- Circulating IgE
- Tryptase levels in blood
- Activation status of basophils
- Inflammatory markers such as: white blood cell count, hsCRP, IL-1beta and IL-6
- Tryptase and chymase levels in plaque
- Plaque phenotype (histology)

Secondary safety parameter:
- The onset of arterial thromboembolic events during follow-up

Study description

Background summary

Background: Destabilization and subsequent rupture of atherosclerotic plaque is a crucial underlying mechanism of ischemic cardiovascular events. After the activation of mast cells, various cytokines and proteases such as tryptase and chymase are released which contribute to the progression and destabilization of atherosclerotic plaque. This occurs due to the accumulation of lipids, the influx of pro-inflammatory immune cells, apoptosis of macrophages, endothelial cells and smooth muscle cells, matrix degradation and the occurrence of intraplaque hemorrhage. Mast cells accumulate during the progression of atherosclerosis. The number of mast cells in atherosclerotic plaque is associated with an increase in the microvessel density and intraplaque hemorrhage, moreover the number of mast cells are associated with future cardiovascular events. Mast cells can be activated by various stimuli, of which crosslinking of the FcεRI with IgE-antigen complexes is most prominent. Recent animal studies have demonstrated that treatment with anti-IgE can inhibit mast cell activation and effectively reduce plaque size.

Aim: Does single treatment with an anti-IgE monoclonal antibody (omalizumab) affect the degree of mast cell activation in atherosclerotic plaques?

Method: Patients with (a)symptomatic carotid stenosis which will undergo a carotid endarterectomy will be treated with the study medication (omalizumab or placebo) prior to surgery. The study medication will be administrated with subcutaneous injections. During the surgery the plaque will be collected. With the use of flowcytometry the primary endpoint, the degree of mast cell activation, will be determined. Furthermore, individual subsets of other immune cells will be studied with the use of flowcytometry and mast cell activation markers will be determined in blood and atherosclerotic plaque samples.

Hypothesis: We assume that single treatment with an anti-IgE monoclonal antibody can inhibit the degree of mast cell activation in atherosclerotic plaque. In the future, further research will have to show whether the inhibition of mast cell activation is a potential new therapy to prevent atherosclerotic plaque destabilization and ultimately acute cardiovascular events.

Study objective

We assume that single treatment with an anti-IgE monoclonal antibody can inhibit the degree of mast cell activation in atherosclerotic plaque

Study design

Screening, day 0, day 3 and 3 months

Intervention

Single treatment with Omalizumab 600mg s.c. or placebo

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Patient is 18 years of age or older
• Patient is able and willing to give their consent and sign an informed consent
• 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

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Previous anaphylactic reaction (e.g. food allergy, medication such as antibiotics etc.)
• Previous CEA or CAS in the ipsilateral artery
• Patients with severe asthma or chronic urticaria which are treated or have been treated with omalizumab s.c.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-12-2019
Enrollment:	80
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion
Date: 13-01-2020
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 54785
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8294
CCMO	NL70680.041.19
OMON	NL-OMON54785

Study results

Summary results
N/A