Effect of interruption of TNFi on endothelial function in patients with rheumatoid arthritis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON37380

Source
ToetsingOnline

Brief title
POEET- VEF (endothelial substudy)

Condition

- Joint disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
reumatoide artritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Abbott,Abott

Intervention

Keyword: Cardiovascular Diseases, Endothelial function, Rheumatoid Arthritis, Tumor Necrosis Factor alpha

Outcome measures

Primary outcome

The primary endpoint is the interaction between TNFi-withdrawal and the vasodilator response to acetylcholine expressed as difference in FBF between the withdrawal group and the continuing group.

Secondary outcome

Secondary endpoints are the effect of TNFi-withdrawal on circulating VCAM and ICAM

Secondary endpoints are The the interaction between TNFi-withdrawal and the vasodilator response to nitroprusside (expressed as difference in FBF between the withdrawal group and the continuing group). The response to SNP serves as an internal vasodilator control to assess potential endothelium-independent effects of TNFi-withdrawal on the response to acetylcholin.

Study description

Background summary

Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular events. This increased risk is thought to be driven by inflammation-induced endothelial dysfunction, an initial step in atherogenesis. Treatment with TNFalpha inhibitors improve endothelial function in patients with RA. Discontinuation of TNFi could therefore worsen endothelial function even in the absence of recurrence of systemic inflammation or reactivation of arthritis. If stopping TNFi results in worsening of endothelial function this would strongly suggest a higher cardiovascular risk in association with

TNFi-wthdrawal

Study objective

The primary objective of the study is to investigate the effect of interruption of anti-TNF-alpha therapy on endothelium dependent and independent vasodilation and the effect of intra-arterial infusion of infliximab on the endothelium dependent and independent vasodilation.

Study design

This study is a substudy of the POEET (Potential optimalisation of Expediency and Effectiveness of TNF blockers) trial, a open label randomized controlled study design where patients (n=1000) are randomized to discontinue TNF blocking therapy or continue all anti-rheumatic medication including TNF blocking therapy.

In patients included in this substudy, the forearm vasodilator response to acetylcholine and nitroprusside (infused in brachial artery) will be assessed.

During the 6 month follow-up period all patients will be monitored according to the POEET-protocol: recording of concomitant medication, co-morbidity and DAS. In patients who experience exacerbation of RA before the end of the study (6 months) which requires additional disease modifying drugs (including restart of TNFi-therapy) the intra-arterial procedure will be repeated prior to restart of this therapy.

Intervention

Intra-arterial infliximab 20 microgram/dl forearm volume /min during 80 minutes, during venous occlusion plethysmography

Study burden and risks

Patients will not benefit from participating in this study. Plethysmography will cause numbness and discomfort in both hands due to inflation of the wrist-cuffs. This is temporarily and completely reversible. The two experiments will take approximately 4 hours each. Finally, bruising may occur after venapuncture or removal of the intra-arterial 27 G needle. Measures like pressure bandage will be taken to minimize the risk. Sometimes there can be some numbness or tingling of fingers due to a hematoma caused by the intra-arterial cannule for a few weeks after the experiment.No side effects are expected of the infused agents.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Afdeling Reumatologie, Geert Grooteplein Zuid 8
Nijmegen 6500HB
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Afdeling Reumatologie, Geert Grooteplein Zuid 8
Nijmegen 6500HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

a. Informed consent for POEET trial and this additional study;b. On stable medication (except for TNFi-therapy)

Exclusion criteria

a. Uncontrolled hypertension (RR > 140/90 mmHg average of three measurements at screening after 5 minutes of supine rest);b. Diabetes mellitus;c. Heart failure or any other cardiovascular disease that is expected to induce changes in cardiovascular medication during the study period.;d. Expected to start or change medication that can alter endothelial function (lipid lowering drugs, blood pressure lowering drugs, NSAIDs, immunosuppressive therapy other than TNFi drugs)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-02-2013
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO

Date:	09-08-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL40192.091.12