Statins to Prevent Rheumatoid Arthritis (STAPRA)

Published: 26-06-2015
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The use of atorvastatin in persons at high risk of RA is associated with a reduction in de development of arthritis

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

Summary

ID

NL-OMON19910

Source
Nationaal Trial Register

Brief title
STAPRA

Health condition

Rheumatoid arthritis, RA, Arthralgia, Atorvastatin, seropositive, ACPA, RF, prevention reumatoide arthritis, artralgie, atorvastatine, seropositief, preventie

Sponsors and support

Primary sponsor: Amsterdam Rheumatology & immunology Center | Reade
Source(s) of monetary or material Support: Reumafonds
Amsterdam Rheumatology & immunology Center | Reade

Intervention

Outcome measures

Primary outcome

The occurrence of clinical arthritis confirmed by a rheumatologist participating in the study.

Secondary outcome

Effect on improvement of lipid profile, (sub)clinical CV risk, inflammatory parameters and changes in cIMT and arterial stiffness.

Study description

Background summary

Background and hypothesis
Rheumatoid arthritis (RA) affects the joints and can lead to serious disability. In RA, a preclinical phase is often present, in which patients do not have arthritis, but do exhibit specific antibodies, often accompanied by vague joint symptoms and general symptoms. The existence of an at-risk phase enables us to investigate interventions with the goal of preventing the development of RA. One of the major complications of RA is cardiovascular (CV) disease, which is doubled in comparison to the general population. Inflammation is thought to play an important role in this increased risk. Dyslipidaemia is also present, many years before RA becomes clinically apparent. Therefore, we hypothesize that statin therapy, due to its combined lipid-lowering and anti-inflammatory effects, may be able to prevent the development of clinical arthritis in persons at increased risk for RA.

Study objective
To investigate whether statin treatment can prevent or delay the development of clinical arthritis in persons at increased risk of RA.

Study population
Persons aged 18 years and older, who are either IgM-RF and ACPA positive or have a high ACPA titer (>3x ULN).

Study design
Multicenter double-blind randomized placebo-controlled trial.

Intervention
Atorvastatin 40 mg or placebo OD will be given to 110 seropositive arthralgia patients in each arm during three years.

Main study parameters
The development of arthritis (¡Ý1 swollen joint) is the primary outcome measure. Serum lipids, calculated 10-year risk of cardiovascular events (in participants aged 40 years and over), changes in cIMT and arterial stiffness are secondary outcome measures.

Study objective

The use of atorvastatin in persons at high risk of RA is associated with a reduction in de development of arthritis

Study design

After inclusion at baseline patients will be monitored every 3 months for 3 years (in the outpatient clinic or by telephone). Then they will stop taking the medication and will receive one more visit after 1 year.

Intervention

Patients will be randomized for atorvastatin 40 mg or placebo tablets. Patients will be taken their medication for 3 years or until they develop arthritis

Contacts

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Eligibility criteria

Inclusion criteria

1) Age >= 18 years
2) Seropositive
-IgM-RF and ACPA positive OR
-High ACPA titer (>3x cut-off)

3) With or without current joint pain, but without current clinical synovitis (ultrasound exam should not be performed in case of doubt, since US was shown to be often false-positive in this patient group)
4) Written informed consent

Exclusion criteria

1) Patients with synovitis during clinical examination (any of 44 joints of DAS) at inclusion or synovitis in the past during clinical examination by a rheumatologist.
2) Patients with typical RA erosions on X-rays of hand and feet.
3) In case of inclusion depending on the presence of RF, the presence of situations with possible false-positive RF: known active infection with hepatitis C or Ebstein-Barr virus or recent radiotherapy.
4) Use of statins or other lipid-lowering agents within the last three months.
5) A history of previous use of statins discontinued due to side effects.
6) Patients with an indication for statin therapy according to local guidelines. All patients will be screened pior to randomisation, patients who fall into this category (SBD>180 mmHg, TC/HDL> 8.0 or have a cardiovasculair risk ¡Ã20% (only for patients between 40-70 years old) with SBD>140 mmHg and/ or LDL>2,5 mmol/L (see appendix H)) will be referred to the general practitioner with treatment advice).
7) Previous use of DMARDs other than hydroxychloroquine, or use of hydroxychloroquine within the last three months.
8) A history of oral or parenteral use of corticosteroids within the last 12 weeks used to treat the current episode of musculoskeletal symptoms.
9) Subjects with current severe, progressive, or uncontrolled hepatic disease (ALT>3x ULN), CK >3x ULN, hematologic disease, gastrointestinal disease, (diabetes with a serum glucose >7.0 mmol/L), pulmonary, cardiac, neurologic, or cerebral disease which, in the opinion of the investigator, might place a subject at unacceptable risk when participating in the study.
10) Subjects who are pregnant or who are breastfeeding or wish to become pregnant.
11) Subjects who currently abuse recreational drugs, or drink alcohol in excess (defined for the purposes of this trial as ¡Ã 21 units of alcohol per week; one unit = 1 glass of wine (125 mL) = 1 measure of spirits = ¡§ö pint of beer).
12) Subjects who have a limited life expectancy.
13) Subjects who are unable to fill out the questionnaires.
14) Subjects who are using ciclosporin (which interacts with statins).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2015
Enrollment:	220
Type:	Anticipated

Ethics review

Positive opinion

Date:	26-06-2015
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 44914
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5036
NTR-old	NTR5265
CCMO	NL47550.048.13
OMON	NL-OMON44914

Study results

Summary results
N/A