Prevention of rheumatoid arthritis by atorvastatin in seropositive arthralgia patients: a multi-center doubleblind randomized placebo-controlled trial

Published: 20-03-2014
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To investigate whether statin treatment can prevent or delay the development of RA in persons at increased risk of RA.

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

Summary

ID

NL-OMON44914

Source
ToetsingOnline

Brief title
STAtins to Prevent Rheumatoid Arthritis (STAPRA)

Condition

- Autoimmune disorders

Synonym
arthritis, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Reade
Source(s) of monetary or material Support: Reumafonds

Intervention

Keyword: Atorvastatin, Preclinical rheumatoid artrhtitis, Prevention

Outcome measures

Primary outcome

The development of arthritis (*1 swollen joint) is the primary outcome measure.

Secondary outcome

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 description

Background summary

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 RA in persons at increased risk for RA.

Study objective

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

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.

Study burden and risks

Participants will be evaluated before initiation of therapy or placebo, every 3 months thereafter in the first year and every 6 months thereafter until a total of three years, with additional consultations by telephone at the three-month time points in between. At all visits there will be a questionnaire and physical examination (including a 44 joint examination). At each visit there will be drug dispension, and check of adverse events and compliance of drug therapy (pill count). Additional blood collection and carotid ultrasonography (cIMT arterial stiffness measurements) will be performed each year in Reade and in a part of the participating centers (at 0, 12, 24, and 36 months and the ultrasonography at 0 and 36 months).

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

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
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, hematologic disease, gastrointestinal disease, (diabetes with a serum glucose >7.0 mmol/L), pulmonary, cardiac, neurologic, or cerebral disease.
10) Subjects who are pregnant or who are breastfeeding or wish to become pregnant.
11) Subjects who currently abuse recreational drugs
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 phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-10-2015
Enrollment:	220
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	20-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2015
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-12-2017
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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: 19910
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-005524-42-NL
CCMO	NL47550.048.13
OMON	NL-OMON19910

Study results

Results posted:	04-01-2021
Actual enrolment:	0

First publication
04-01-2021