A randomised, double blind, parallel-group study of the oxidative stress lowering effect of simvastatin and atorvastatin.

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To compare the rapidity of onset and the extent of oxidative stress lowering of atorvastatin with that of an (in terms of LDL lowering) equipotent dosage of simvastatin.

Ethical review	Approved WMO
Status	Pending
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON30464

Source
ToetsingOnline

Brief title
The oxidative stress lowering effects of statins

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arteriosclerosis, Atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Pfizer,Pfizer Netherlands BV

Intervention

Keyword: Atherosclerosis, Lipids, Oxidative stress, Statins

Outcome measures

Primary outcome

Considering that there is no gold standard to measure effect on oxidative stress, established parameters of oxidative stress such as oxidized LDL, malondealdehyde and isoprostane will be measured in plasma and urine. All parameters of oxidative stress before and during treatment with one of both statins will be compared to determine whether atorvastatin causes a stronger and quicker reduction of oxidative stress than simvastatin.

Secondary outcome

Niet van toepassing

Study description

Background summary

HMG-CoA reductase inhibitors (statins) are effective lipid-lowering agents and are known to reduce cardiovascular events. Beneficial effects of statins seem to occur very early in the course of their therapy and subgroup analysis of large trials indicates that subjects in statin-treated arms have less cardiovascular events than subjects in placebo-controlled arm with comparable serum cholesterol levels. Therefore, it has been suggested that statins may have antiatherogenic effects beyond their cholesterol lowering effect. Many studies have demonstrated a rapid improvement in vascular function with atorvastatine which cannot solely be accounted for by achieved lipid reduction. A rapid oxidative stress lowering effect of atorvastatin has been proposed as the probable mechanism of this action. Whether atorvastatine has stronger antioxidant effect and whether atorvastatin lowers oxidative stress earlier in the course of therapy than other statins has not been studied yet.

Study objective

To compare the rapidity of onset and the extent of oxidative stress lowering of atorvastatin with that of an (in terms of LDL lowering) equipotent dosage of simvastatin.

Study design

A randomised, double blind, parallel-group study design.

Intervention

All included patients are randomized to treatment with simvastatin 40 mg daily or atorvastatin 10 mg daily to achieve a comparable lipid reduction.

Study burden and risks

After inclusion, all patients visit our oupatient clinic four times. Before each visit a 24 hours urine sample is collected and during each visit blood will be drawn.
Myopathy is a potential harmful side effect. In 1-7% of statin users muscle complaints can appear due to myotoxicity and following myopathy. When myopathy is not recognised in time, rhabdomyolysis may develop. In case of rhabdomyolysis muscle damage can be so severe that in exeptional cases damage to kidneys and other organs may develop with acute renal failure that could be fatal.
During the visits a sample of blood will be drawn (total of 150 ml). This can be inconvenient or painful and could result in haemorrage, swelling or local inflammation.

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

Patients in the age between 18 and 70 years, with diabetes mellitus type 2 and/or hypertension (RR > 140/90 mmHg) and/or obesity (BMI >25) and LDL > 2,5 mmol/l.

Exclusion criteria

Stage 5 chronic kidney disease
Use of an ACE inhibitor
Statin use in three months prior to inclusion
LDL cholesterol < 2,5 mmol/L

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2006
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lipitor
Generic name:	atorvastatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zocor
Generic name:	simvastatin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	03-04-2007
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
Other	00404599
EudraCT	EUCTR2007-000608-34-NL
CCMO	NL15330.029.06