# Short term statin treatment and endothelial dysfunction due to ischemia and reperfusion injury

Published: 07-08-2009 Last updated: 04-05-2024

To study the protective effect of pretreatment (both 3 day and 7 day) with rosuvastatin and atorvastatin on flow mediated dilation after 15 minutes ischemia and 15 minutes reperfusion.

**Ethical review** Approved WMO **Status** Recruitment stopped

**Health condition type** Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Study type Interventional

## **Summary**

#### ID

NL-OMON33420

Source

ToetsingOnline

**Brief title** 

Statins-IRI-FMD

#### **Condition**

Arteriosclerosis, stenosis, vascular insufficiency and necrosis

#### Synonym

ischemia and reperfusion injury, myocardial infarction

#### Research involving

Human

# **Sponsors and support**

**Primary sponsor:** Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W

#### Intervention

**Keyword:** flow mediated dilation, ischemia reperfusion injury, statin

#### **Outcome measures**

#### **Primary outcome**

Difference in flow mediated dilation before and after 15 minutes ischemia.

#### **Secondary outcome**

ecto-5\*-nucleotidase activity after rosuvastatin and atorvastatin treatment (3 day and 7 day)

# **Study description**

#### **Background summary**

Apart from their cholesterol lowering effects, statins have cholesterol-independent pleiotropic actions, such as upregulation of 5\*-ectonucleotidase and up-regulation of NO-synthase that may increase tolerance against ischemia-reperfusion injury (IR-injury). Several animal studies have shown reduction of IR-injury as a result of statin treatment in both the heart and the kidney. Recently we have shown, using Annexin A5 targeting after voluntary ischemic exercise to assess IR-injury, a protective effect of a 7 day oral rosuvastatin treatment. A three day treatment with atorvastatin however failed to reduce annexin targeting.

Assessment of the flow mediated dilation of the brachial artery as measure of endothelial (dys)function, is a validated model to research effects of possible protective strategies and perform mechanistic experiments on IR-injury in humans in vivo.

We hypothesize that pretreatment with statins can increase endothelial tolerance against ischemia and reperfusion injury.

#### **Study objective**

To study the protective effect of pretreatment (both 3 day and 7 day) with rosuvastatin and atorvastatin on flow mediated dilation after 15 minutes ischemia and 15 minutes reperfusion.

#### Study design

placebo-controlled randomised double-blind trial

#### Intervention

Treatment with either rosuvastatin 20 mg, atorvastatin 80mg or placebo during either 3 or 7 days

#### Study burden and risks

Treatment with rosuvastatin or atorvastatin is not expected to harm the volunteers. Most reported side effects of rosuvastatin and atorvastatin are gastro-intestinal complains and myalgia. The volunteers will not benefit directly from participating in this study.

## **Contacts**

#### **Public**

Universitair Medisch Centrum Sint Radboud

postbus 9101 6500 HB Nijmegen Nederland

#### **Scientific**

Universitair Medisch Centrum Sint Radboud

postbus 9101 6500 HB Nijmegen Nederland

## **Trial sites**

#### **Listed location countries**

**Netherlands** 

# **Eligibility criteria**

#### Age

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

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#### Inclusion criteria

- Age 18-50
- Written informed consent

#### **Exclusion criteria**

- Smoking
- History of any cardiovascular disease
- Hypertension (in supine position: systole >140 mmHg, diastole >90 mmHg)
- Diabetes Mellitus (fasting glucose >7.0 mmol/L or random glucose >11.0 mmol/L)
- Hyperlipidemia (fasting total cholesterol >5.5 mmol/L or random cholesterol >6.5 mmol/L)
- Alanine amino transferase >90 U/L
- Creatine kinase >440 U/L
- Raised rabdomyolysis risk
- o GFR <60 ml/min
- o Overt clinical signs of hypothyroidism
- o Myopathy in family history
- o Alcohol abuse
- Concomitant chronic use of medication
- Participation to any drug-investigation during the previous 60 days as checked with VIP check.

# Study design

## **Design**

Study phase: 4

Study type: Interventional

Intervention model: Parallel

Allocation: Randomized controlled trial

Masking: Double blinded (masking used)

Control: Placebo

Primary purpose: Prevention

#### Recruitment

NL

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Recruitment status: Recruitment stopped

Start date (anticipated): 05-10-2009

Enrollment: 48

Type: Actual

### Medical products/devices used

Registration: No

Product type: Medicine

Brand name: crestor

Generic name: rosuvastatin

Registration: Yes - NL outside intended use

Product type: Medicine

Brand name: lipitor

Generic name: atorvastatin

Registration: Yes - NL outside intended use

## **Ethics review**

Approved WMO

Date: 07-08-2009

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 25-09-2009

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

EudraCT EUCTR2009-014831-18-NL

CCMO NL29271.091.09