# Is augmentation of PORH by rosuvastatin adenosine-receptor mediated?

Published: 14-11-2008
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To study the influence of caffeine on post occlusive reactive hyperaemia before and after 7 days treatment with rosuvastatin.

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON32791

**Source**
ToetsingOnline

**Brief title**
rosucaf2

### Condition

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

**Synonym**
Heart infarction, Ischaemia

**Health condition**

ischemie

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Sint Radboud
**Source(s) of monetary or material Support:** Ministerie van OC&W,NWO

## Intervention

**Keyword:** adenosine, ischemia, PORH, rosuvastatine

## Outcome measures

### Primary outcome

Forearm blood flow (FBF) will be measured as an indicator for post occlusive

reactive hyperaemia (PORH).

### Secondary outcome

effect of 7 day treatment with rosuvastatin on lipid profile

# Study description

### Background summary

Statins form a class of drugs that is widely prescribed for hypercholesterolaemia, specifically to reduce the risk on atherosclerosis by lowering LDL-cholesterol. Next to the effect for which the drug was originally developed, it became obvious that statins have several other beneficial effects. Such pleiotropic effects include the activation of ecto-5*-nucleotidase which can increase endogenous adenosine production (by dephosphorylation adenosine monophosphate into adenosine) and subsequently cause vasodilation. A recent study of Meijer et al (not yet published) showed that rosuvastatin significantly augments vasodilation after a brief period of ischemia (post occlusive reactive hyperaemia). However, it is not yet verified whether this increase in post occlusive reactive hyperaemia is truly caused by a rise of extracellular adenosine and subsequent adenosine receptor stimulation. In this study, the mechanism by which rosuvastatin augments post occlusive reactive hyperaemia will be investigated by blocking adenosine receptors with caffeine, a competitive A1 and A2 adenosine receptor antagonist. Caffeine is a medium that can be safely used in normal concentrations to block the adenosine receptor. Thus, if the augmenting effect of rosuvastatin on PORH is caused by an increase of extracellular adenosine formation, this effect can

be diminished by blocking the adenosine receptor using caffeine.

### Study objective

To study the influence of caffeine on post occlusive reactive hyperaemia before and after 7 days treatment with rosuvastatin.

### Study design

open label cross-over

### Intervention

Eight volunteers will receive a 7 day treatment with rosuvastatin 20 mg daily.

### Study burden and risks

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

## 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

Healthy volunteers, 18-50 years of age

### Exclusion criteria

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 total cholesterol >6.5 mmol/L)
Alanine amino transferase >90 U/L
Creatin kinase >440 U/L
Raised rabdomyolysis risk
GFR <80 ml/min
overt clinical signs of hypothyroidism
Myopathy in family history
Alcohol abuse
Concomitant chronic use of medication
Participation to any drug-investigation during the previous 60 days as checked with VIP check according to CRCN standard procedures.

## Study design

### Design

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|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |

| | |
|---|---|
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 02-03-2009 |
| Enrollment: | 8 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Crestor |
| Generic name: | rosuvastatin |
| Registration: | Yes - NL outside intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 14-11-2008 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 22-01-2009 |
| 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 | EUCTR2008-005985-30-NL |
| CCMO | NL25101.091.08 |