Effect of Simvastatin on Bone Metabolism and Arterial Calcification Metabolism: A Sodium Fluoride PET CT Imaging Study

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To determine if Simvastatin can stimulate bone metabolism while simultaneously attenuate vascular calcification metabolism as quantified by Na18F PET CT imaging.

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON38994

Source
ToetsingOnline

Brief title
SIMBA

Condition

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

Synonym
arteriosclerosis, atherosclerosis, osteopenia, osteoporosis

Health condition

Botontkalking (osteoporose)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Bone metabolism, Fluoride PET CT, Simvastatin, Vascular calcification

Outcome measures

Primary outcome

The primary endpoint is the absolute change in fluorine-18 metabolism in the 2nd, 3rd, and 4th lumbar vertebral body (quantified by the volumetric bone metabolic rate; bodyweight corrected standardized uptake value [g/mL] multiplied by the volume of the vertebral body) between baseline and 3 months after baseline.

Secondary outcome

Maximum standardized uptake value in the major arteries (aorta, carotid arteries, coronary arteries) between baseline and three months after baseline.

Study description

Background summary

Remarkably, osteopenia and osteoporosis are often accompanied by ectopic artery calcification, a strong independent risk factor of cardiovascular disease (CVD). This association is known as the calcification paradox. Simvastatin, an HMG-CoA reductase inhibitor, is the first-line drug for the primary prevention of CVD. Recent evidence suggests Simvastatin can also reduce fracture risk in patients with osteopenia / osteoporosis. We hypothesize that Simvastatin achieves the reduction of CVD risk and fracture risk by attenuating vascular calcification metabolism and stimulating bone metabolism, respectively.

Study objective

To determine if Simvastatin can stimulate bone metabolism while simultaneously attenuate vascular calcification metabolism as quantified by Na18F PET CT imaging.

Study design

Case-crossover study

Study burden and risks

Each patient will visit the University Medical Center Utrecht thrice: two weeks before baseline, at baseline, and three months after baseline. At each visit, questionnaires, blood samples, dual-energy X-ray absorptiometry (DXA) of the vertebral bodies, femoral necks, and total hips, and a *whole-body* hybrid sodium fluoride-18 positron emission tomography computed tomography (Na18F PET CT) scan will be acquired. DXA and Na18F PET CT are associated with exposure to ionizing radiation. The effective dosage per DXA and per Na18F PET CT is 0.03 mSv and 5.80 mSv, respectively. For the entire study protocol, the effective dosage is approximately 17.5 mSv. This might marginally increase the lifetime risk of developing cancer. Research participants gain no individual benefit from participating in the study. However the study is expected to open up a promising avenue for the treatment of atherosclerosis, osteopenia, and osteoporosis. Statins do not only attenuate cardiovascular risk, but might possibly reduce fracture risk by increasing bone mineral density. Therefore, evaluating the effect of statins on bone metabolism and vascular calcification metabolism is especially apposite in patients with decreased bone turnover as well as an increased cardiovascular risk profile, as are the patients included in our 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

1. Statin naivety;
2. Age equal to or above 50 years;
3. T-score at inclusion between -1.0 and -2.5;
4. HeartSCORE equal to or above 5% (i.e. clinical indication for Simvastatine 40 mg determined at the discretion of the treating physician).
5. Karnofsky score at inclusion equal to or higher then 90%.

Exclusion criteria

Reduced bone mass due to drugs (i.e., steroids) or a medical condition, such as hyperthyroidism, hyperparathyroidism, renal or liver failure, multiple myeloma, etc.;Current or prior treatment with bisphosphonates, calcium-antagonists, calcium supplements with or without vitamin D, PTH-agonists, and Denosumab.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Medical products/devices used

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

Ethics review

Not approved

Date:	28-01-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2013-003360-32-NL
CCMO	NL45890.041.13