Randomised comparison of two different immunosuppressive regimens on progression of arteriosclerosis in renal transplant patients.
Extension of NOCTX-study: Is progression of arteriosclerosis in ESRD patients inhibited by nocturnal hemodialysis or renal transplantation?

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To compare in a prospective randomised way the effect of two different immunosuppressive regimens - mTOR-based regimen or CNI-based regimen - on the progression of coronary artery calcification in renal transplant patients measured at baseline, 1, 2...

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

Summary

ID

NL-OMON37133

Source
ToetsingOnline

Brief title
Coronary artery calcifications in renal transplantation

Condition

- Coronary artery disorders
- Nephropathies

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
cardiovascular disease in renal transplant patients; vascular calcification in renal transplant patients

Research involving
Human

Sponsors and support

Primary sponsor: Dianet Dialysecentra, lokatie Utrecht
Source(s) of monetary or material Support: Novartis BV

Intervention

Keyword: arterial calcification, everolimus, multi-slice CT, renal transplantation

Outcome measures

Primary outcome

The primary endpoint of the study is:

- change in coronary artery calcification score

Secondary outcome

The secondary endpoints of the study are:

- change in pulse wave velocity

- change in coronary artery stenosis

- association between calcium, phosphate, PTH and change in coronary artery

calcification score

- association between high-sensivitity-CRP, interleukin-6, interleukin-1,

vonWillebrandfactor, myeloperoxidase, and change in coronary artery

calcification score

- association between fetuin A, osteoprotegerin and matrix-Gla protein and

change in coronary artery calcification score

- cardiovascular events and mortality

- renal function

Study description

Background summary

Cardiovascular disease is the leading cause of mortality both in patients with end-stage renal disease (ESRD) as well as in renal transplant patients, during the first 5 years after transplantation. The vascular abnormalities in ESRD are especially characterized by arterial wall calcifications, whereas intimal hyperplasia seen with *classic atherosclerosis* is less pronounced. These calcifications are strongly associated with increased mortality. The exact mechanism by which calcification develops is unknown, but there is a direct relationship with increased serum calcium and serum phosphorus. With long and frequent hemodialysis, such as nocturnal hemodialysis, and with renal transplantation, calcium and phosphate values can be normalized. It is unknown whether these treatments inhibit the progression of arterial calcification or bring about regression of calcification.
Currently, little is known with regard to influences on aortic and coronary calcification progression of different immunosuppressive regimens after transplantation. The mTOR inhibitors are a relatively new class of immunosuppressants, with a possible attenuating effect on intima proliferation and atheroma formation. Furthermore, by their adequate immunosuppressive properties, they allow for early withdrawal of calcineurin-inhibitors, that are known to increase cardiovascular risk factors.
Therefore, as part of a study that compares the progression of coronary calcification in different dialysis modalities in patients with end-stage renal disease, it is of great additional importance also to study the effect of different immunosuppressive regimens on this progression. Therefore we want to compare in a randomised way the effect of a calcineurin-based immunosuppressive regimen with an mTOR-based regimen on progression of coronary calcification on renal transplant patients.
The results of this study will provide more insight in protection against cardiovascular disease in renal transplant patients.

Study objective

To compare in a prospective randomised way the effect of two different immunosuppressive regimens - mTOR-based regimen or CNI-based regimen - on the progression of coronary artery calcification in renal transplant patients measured at baseline, 1, 2, and 3 years after transplantation.

Study design

Prospective randomized study as part of NOCTX-study. This study compares 2 groups of transplant patients, that are randomised at 3 months after renal transplantation to one of two immunosuppressive regimens. Follow-up is identical to the follow-up of the NOCTX-study.

Intervention

Patients with ESRD, 18-75 yr, who undergo a living or postmortal transplant are randomised at 3 months after transplantation to:
A: continuation with CNI-based immunosuppression
B: switch to mTOR-based immunosuppression.

Study burden and risks

The potential value of this study lies in gaining insight in the process of artery calcification in patients with ESRD who undergo renal transplant.. On theoretical grounds, it is plausible that progression is attenuated in patients with a renal transplant, although some immunosuppressive drugs are known to increase cardiovascular risk. However, no long-term data are available about the effect of different immunosuppressive regimens on coronary calcification. Therefore, modern immunosuppressive drugs could offer advantages regarding progression of arteriosclerosis.
The risk and burden to the patient are formed in this study by:
- calcium score MSCT: as described above (7.3 Study procedures) multislice CT is a very short procedure giving a low radiation dose (0.4-1.2 mSv);
- coronary MSCT: as described above (7.3 Study procedures) a coronary CT is also a very short procedure with a low radiation dose (3-4 mSv) (NB for comparison: a diagnostic abdominal CT scan delivers a dose of about 7-10 mSv);
- pulse-wave velocity: non-invasive measurement without risk;
- minor extra blood loss combined with routine venapunction.

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

- age between 18-75 yr
- willingness to provide written informed consent
- ability to understand the study procedures

Exclusion criteria

- life expectancy < 3 months
- claustrofobia
- allergy to iodinated contrast
- treatment incompliance
- pregnancy
- highly HLA-sensitized patients
- severe dyslipidemia or proteinuria
- severe leucopenia or trombocytopenia
- GFR < 30 ml/min

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2010
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Certican
Generic name:	everolimus
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prograf
Generic name:	tacrolimus
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-07-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-02-2012
Application type:	Amendment

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
Other	00950573
EudraCT	EUCTR2009-011605-16-NL
CCMO	NL27323.041.09

Study results

Date completed:	01-06-2012
Actual enrolment:	13

Summary results
Trial is onging in other countries