A prospective, open, randomized, single center study comparing the effects of duo therapy with Everolimus and steroids versus triple treatment of low dose calcineurin inhibitor, low-dose MMF and steroids at least one year after renal transplantation.
Effects on renal function, tolerability, chronic allograft damage, cardiovascular parameters and malignancies.

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Objective: To investigate the safety and efficacy of a therapy consisting Everolimus and corticosteroids maintenance immunosuppressive regime twelve months after renal transplantation in recipients of donor kidney graft on graft function and acute...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON35450

Source
ToetsingOnline

Brief title
STER

Condition

- Renal disorders (excl nephropathies)

Synonym
acute rejection, renal function

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Centrum heeft de studie opgezet;farmaceutisch bedrijf steunt.,Novartis

Intervention

Keyword: Renal function, Renal transplantation, Tolerability

Outcome measures

Primary outcome

Primary endpoints: Renal function. The percentage of patients that need

reconversion to their original therapy.

Secondary outcome

Secondary endpoints: Cardiovascular incidents and PWV/ AGES, Blood pressure and

the number of antihypertensives. The incidence of malignancies, the incidence

of infections, Haematological and Lipid parameters, Proteinuria.

Study description

Background summary

Rationale: Calcineurin inhibitor-free immunosuppression in kidney transplantation give low rejection rates and excellent graft survival nowadays1. Despite this success, mortality and morbidity in transplant recipients is relatively high due to side effects of our immunosuppressive

strategies. This is one of the reasons for the high cardiovascular mortality in renal transplant recipients. Calcineurin inhibitors may play an important role in the development of chronic allograft nephropathy causing poor kidney function and cardiovascular disease2,3. Also infections and malignancies are the result of immunosuppression in general.
Drugs that might prevent atherosclerosis and malignancies have been developed in the last decade: Everolimus is a promising agent that is known for reduced rates of cytomegalovirus (CMV) infection and of cardiac allograft vasculopathy4. It also carries the promise in a reduced risk for developing cancer.5 By introducing Everolimus twelve months after transplantation while withdrawing the calcineurin inhibitor and the inosine monophosphate inhibitor we expect to achieve a good control of acute rejection, without increasing nephrotoxicity. In a previous study (not published yet) we introduced Everolimus in a dosage of 3 mg two times a day, six months post transplantation. Probably due to that high dose more side effects were seen than expected.
In this present study we will optimize the dose of Everolimus.

Study objective

Objective: To investigate the safety and efficacy of a therapy consisting Everolimus and
corticosteroids maintenance immunosuppressive regime twelve months after renal transplantation
in recipients of donor kidney graft on graft function and acute rejection rates. The other group will
receive a low-dose regimen consisting a low-dose calcineurin inhibitor, low dose MMF and
corticosteroids.

Study design

Study design: Prospective, open, randomized, controlled, single-centre.

Intervention

Intervention: At twelve months those recipients with an acceptable renal function will be randomized to either continue on their calcineurin inhibitor based regime in a lower dose, or convert to Everolimus.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The burden associated with participation consists of more frequently outpatient visits during the conversion period. The amount and number of blood samples,

physical examinations or other tests is the same as in the control group: our standard care after renal transplantation. The risks associated with the investigational product are increase in proteinuria, dyslipidaemia, anaemia, thrombocytopenia, impaired wound healing. The benefits associated with Everolimus are reduced rates of cytomegalovirus (CMV) infection and of cardiac allograft vasculopathy, together with a decreased risk for cardiovascular diseases and malignancies in the long term survival.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
Nederland
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Female or male, aged between 18 and 70 years.
• Recipient of a kidney graft from a deceased donor or living (non-HLA identical) donor.
• The patient understands the purpose and risks of the study and has given written informed

consent to participate in the study.
• Acceptable renal function, eGFR > 40 ml/min, Proteinuria <= 1, 0 g/24hr.

Exclusion criteria

• Patients with multi-organ transplants.
• Patients who have been receiving a second or subsequent transplant.
• Patients with very low function at 1 year post-transplant, GFR < 40.
• Proteinuria > 1, 0 g/24 hr.
• Patients with a screening/baseline total white blood cell count < 2,0 10Eg/l or ANC < 1,0 10Eg/l, platelet count < 100 10Eg/l.
• Patients with baseline fasting triglycerides > 4.5 mmol/l or fasting total cholesterol > 7.8 mmol/l despite optimal lipid-lowering therapy.
• Presence of sub clinical rejection (Borderline or Banff score >1a) in biopsy taken at approximately month 12
• Vascular or Acute rejection (Banff score >= 2a) six months preceding randomization.
• Female patients who are pregnant or unwilling to use adequate contraception during the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2010
Enrollment:	130
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:	Mycofenolaat mofetil
Generic name:	Cellcept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Neoral
Generic name:	Cyclosporine A
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prednisolon
Generic name:	Prednisolon
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prograft
Generic name:	Tacrolimus
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-07-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-09-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-07-2010

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2009-014436-38-NL
CCMO	NL29025.042.09