A multi-center, randomized, controlled trial with programmed introduction of Sirolimus-based, Calcineurin inhibitor free immunosuppression in recipients of non-heart-beating donor kidney grafts.

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To investigate the safety and efficacy of a programmed introduction of a sirolimus based calcineurin inhibitor free maintenance immunosuppressive regime three months after renal transplantation in recipients of a non-heart-beating donor kidney graft...

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

Summary

ID

NL-OMON31753

Source
ToetsingOnline

Brief title
PRINS study

Condition

- Renal disorders (excl nephropathies)

Synonym
kidney transplant function

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Wyeth

Intervention

Keyword: calcineurin inhibitor free, kidney / renal transplantation, non-heart-beating donor, sirolimus

Outcome measures

Primary outcome

eGFR as determined by Nankivell at month 12 post randomization.

Secondary outcome

Biopsy proven acute rejection rate at month 12 post randomization

eGFR as determined by Cockroft Gault and MDRD methods at month 12 post

randomization

Suspected, treated and confirmed combined rejection rate

Graft survival

Patient survival

Rate of infection-viral,fungal,bacterial at 12 months post-randomisation

Rate of malignancy at 12 months post-randomisation

Dyslipidaemia at 3, 6 and12 months post-randomisation

Rate of proteinuria- mean increase in protein excretion by group and number of

patients, increasing protein excretion by > 0.5g/24hr and > 1g/24hr at 3, 6 and

12 months post-randomisation

Change in selectivity index of proteinuria at 3, 6 and 12 months

post-randomisation

Number of antihypertensive drugs at 3, 6 and 12 months post-randomisation

Rate of Serious Adverse Events at 12 months post-randomisation

Rate of treatment associated Adverse Events at 12 months post-randomisation

Rate of Cardiovascular events at 3 and12 months post-randomisation

Discontinuation rate at 6 and12 months post-randomisation

Mycophenolate area under the curve at randomisation

Study description

Background summary

Organ shortage requires extension of donor criteria, including accepting non-heart-beating donors. To extend kidney graft half-life in this group research into non-nephrotoxic immunosuppressive regimens is necessary. To date most renal transplant centres prescribe a regimen combining calcineurin inhibitor, inosine monophosphate inhibitor and corticosteroids. This is highly efficacious in preventing acute rejection, but calcineurin inhibitors are nephrotoxic. Introducing sirolimus three months after transplantation while withdrawing the calcineurin inhibitor we expect to achieve a good control of acute rejection, without increasing nephrotoxicity and impairing wound healing.

Study objective

To investigate the safety and efficacy of a programmed introduction of a sirolimus based calcineurin inhibitor free maintenance immunosuppressive regime three months after renal transplantation in recipients of a non-heart-beating donor kidney graft on graft function and biopsy proven acute rejection rates.

Study design

Randomized, controlled, multi-center.

Intervention

At 3 months those recipients with an acceptable renal function will be randomized to either continue on their calcineurin inhibitor based regime or convert to sirolimus.

Study burden and risks

The burden associated with participation consists of weekly outpatient department visits during the conversion period (from tacrolimus to sirolimus). 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 and development of lymphoceles.

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: at least 18 years
Acceptable renal function (eGFR Nankivell > 30 ml/min, proteinuria < 1.0 g/day)

3 - 4 months post renal transplantation with non-heart-beating donor graft

Exclusion criteria

Banff grade > 2 acute or vascular rejection at any time during this transplant pre-randomization
Multiple organ transplants (i.e., prior or concurrent transplantation of any organs other than renal transplant)..
Evidence of active systemic or localized major infection.
Planned use of agents with a known interaction with any of the following: sirolimus or its derivatives, macrolide antibiotics, corticosteroids, tacrolimus, or IMPDH inhibitor.
Immunosuppressive therapies other than those described above
Subjects with a screening/baseline total white blood cell count < 2,000/mm3 or ANC < 1000, platelet count < 100,000/mm3.
Fasting triglycerides > 400 mg/dL (> 4.5 mmol/L) or fasting total cholesterol > 300 mg/dL (> 7.8 mmol/L) despite optimal lipid-lowering therapy.
Subjects who are known to be HIV positive and/or subjects with active Hepatitis B or active Hepatitis C.

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-10-2007
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prograf
Generic name:	Tacrolimus
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rapamune
Generic name:	Sirolimus
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-09-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-09-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-02-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2007-002763-27-NL
CCMO	NL18145.078.07