An integrated immunological-pharmacological approach to improve long-term allograft function

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Ethical review	Approved WMO
Status	Pending
Health condition type	Nephropathies
Study type	Observational invasive

Summary

ID

NL-OMON45414

Source
ToetsingOnline

Brief title
Parameters to improve long-term allograft function

Condition

- Nephropathies

Synonym
graft failure, kidney transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Inwendige Geneeskunde - Nefrologie en Transplantatie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: B-cell memory, kidney transplantation, tacrolimus intra-patient variability, T-cell memory

Outcome measures

Primary outcome

The primary endpoint is donor-specific T-cell and B-cell memory function in

relation to Tac IPV.

Secondary outcome

The secondary endpoints:

- The difference in the development of CRAD between in patients with high IPV

Tac and low IPV Tac. Kidney function and CRAD will be defined by the GFR

determined at 6 months, 1, 3, and 5 years after transplantation.

- The T-cell receptor and B-cell receptor signature in relation to Tac IPV

- Intra-lymphocytic Tac concentrations in relation to Tac IPV and immunologic

parameters

Study description

Background summary

Improving the long-term outcome is the main challenge after kidney transplantation, because 40% of the transplants are lost within 10 years. This may be due to high intra-patient variability (IPV) to tacrolimus (Tac). It is already known that 71% of the patients who lost their graft expressed a high Tac IPV profile. Therefore, optimized exposure to Tac may improve renal function and will inhibit the anti-donor immune response. Remarkably, the connection between high Tac IPV profile and T-cell and B-cell functions leading to graft lost is unknown. We hypothesize that low immunosuppression levels due to high IPV profile triggers the expansion of memory T-cells and memory B-cells resulting in the development of chronic renal allograft dysfunction (CRAD) threatening transplant and patient survival. Identification of patients at risk

for CRAD will enable timely adjustment of immunosuppressive drugs aiming to prevent graft loss after transplantation.

Study objective

The main aims of the present study:
1. Define the causality between low immunosuppression, i.e. high IPV, and anti-donor T-cell and B-cells immune responses
2. Set a robust benchmark for CRAD
3. Improve the knowledge of the biological mechanisms resulting in this CRAD

Study design

This is an investigator-driven, observational study investigating the anti-donor T-cell and B-cell immune response 5-6 years after kidney transplantation in relation to Tac IPV. Tac IPV between 6-12 months after transplantation will be calculated and correlated with graft failure and immunological parameters. The hypothesis is that a high Tac IPV leads to periods of under-immunosuppression which triggers the expansion of donor-specific T-cells and B-cells resulting in CRAD.

Study burden and risks

During a regular follow-up visit at the outpatient clinic between 5 and 6 years after transplantation blood will be drawn to determine kidney function and trough levels of immunosuppressive drugs as part of clinical care. At this same time point additional blood will be sampled for the present study. No risk is involved in participation of the study. The included patients do not benefit from participation, even though they will contribute to identify patients at risk to lose their graft due to CRAD in future.

Contacts

Public
Selecteer

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NL
Scientific
Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Adult recipients (18 years or older) who were 5 to 7 years after kidney transplantation.

Exclusion criteria

ABO-incompatible kidney transplants. Recipients of a non-renal transplant.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2017

Enrollment:	420
Type:	Anticipated

Ethics review

Approved WMO Date:	08-02-2017
Application type:	First submission
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
CCMO	NL59284.078.16