Tacrolimus monotherapy in low-risk kidney transplant recipients.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26543

Source
NTR

Brief title
TACmono

Health condition

kidney transplantation/ niertransplantatie
rejection/ rejectie
immunologic profiling/ immunologisch risico
tacrolimus
advagraf
infectious compications/ infectieuze complicaties

Sponsors and support

Primary sponsor: Erasmus Medical Center, Rotterdam, The Netherlands
Source(s) of monetary or material Support: investigator-driven

Intervention

Outcome measures

Primary outcome

Feasibility objectives are consent rate, BPAR-rate and biological plausibility.

The primary objective of the pilot study consists of the following immunological markers:

I. Number of cytokine-producing alloreactive CD137+ T cells.

II. Total number of infectious episodes.

III. Vaccination response score.

Eight secondary objectives are described in the protocol.

Criteria for success of pilot study:

1. A total of 100 patients is recruited within three years.

2. Consent is given in 70% of eligible patients.

3. The descriptive outcomes in general immune responses provide for a biological plausible benefit of TACmono over dual therapy.

Secondary outcome

1. BPAR rate 15 months after kidney transplantation.

2. Assessment of de novo (complement-fixating) alloantibody formation as detected by Luminex.

3. Kidney allograft function (eGFR with MDRD formula and proteinuria expressed in urine protein/creatinine ratio).

4. Detection of donor-specific CD137+ T cells.

5. Composition of leucocyte subsets.

6. Blood pressure levels and number of antihypertensive drugs after discontinuation of MMF as compared to continuation with dual TAC/MMF therapy.

7. Histological findings in renal transplant biopsy at time of randomisation (6 months) and its correlation with BPAR-rate 15 months after transplantation.

8. Gastrointestinal symptom score and quality of life outcomes.

Study description

Background summary

Rationale: Kidney transplant recipients with a favorable immunological profile, such as less than four HLA mismatches and less than five per cent panel reactive antibodies have a low risk of rejection. Therefore standard immunosuppressive therapy after kidney transplantation might expose them to a higher than necessary risk of infectious diseases and malignancies.

Objective: The objective of this pilot study is to determine the feasibility of a larger non-inferiority trial investigating the safety of tacrolimus monotherapy (TACmono) in terms of rejection rate after kidney transplantation. Feasibility objectives are consent rate, BPAR-rate and biological plausibility. This biological plausibility will be the primary endpoint of the pilot study and includes immunological parameters as surrogate markers for infectious disease and malignancy.

Study-design: This is a randomized, investigator-driven, open-label, single centre pilot study. The pilot is conducted to assess the feasibility of a larger non-inferiority study. The follow-up will be 15 months for the primary and secondary outcomes. The aim is to recruit 100 patients.

Study population: Adult patients (18 years and older) receiving a deceased or living donor kidney transplant in the Erasmus Medical Center Rotterdam, and historical panel reactive antibodies of less than five per cent and less than four HLA mismatches on A, B and DR loci, are eligible for this study.

Intervention: Participants are converted from Prograft to Advagraf one week after kidney transplantation. Six months after transplantation participants with stable renal function (eGFR >30 ml/min and proteinuria ≤0.5 gram per 10 mmol creatinin in spot urine) are randomized to either continue standard therapy with Advagraf and Cellcept or gradually decrease the Cellcept, to Advagraf monotherapy at 9 months. A renal transplant biopsy is performed at randomisation, 6 months after transplantation. One year after kidney transplantation participants are vaccinated against pneumococcus and DTP (Diphteria, tetanus and poliomyelitis). Depending on the season also the influenza vaccine is administered. Participants are asked to fill in questionnaires about gastrointestinal symptoms and quality of life at 6, 12 and 15 months after transplantation.

Main study parameters: Feasibility objectives are consent rate, BPAR-rate and biological plausibility.
The primary objective of the pilot study consists of the following immunological markers:

I. Number of cytokine-producing alloreactive CD137+ T cells.

II. Total number of infectious episodes.

III. Vaccination response score.

Eight secondary objectives are described in the protocol.

Criteria for success of pilot study:

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2. Consent is given in 70% of eligible patients.

3. The descriptive outcomes in general immune responses provide for a biological plausible benefit of TACmono over dual therapy.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Extra blood tubes are taken at time points when blood is already drawn, except for the blood drawn to measure vaccination responses. The main risk of vaccination is the rare incidence of anaphylactic reactions. Norepinephrine will be present during administration of the vaccine. Mild side effects occur in the majority of patients and are self-limiting (local redness, itching, pain, headaches and malaise). A renal transplant biopsy has a small risk (<2%) of clinically relevant bleeding. Protocol biopsies are standard of care in many transplant centers. Treatment by TACmono has theoretically a greater risk of rejection. Therefore a time window for discontinuation at nine months has been chosen. The investigators and the DSMB will closely monitor rejection rates. The potential benefit of treatment by TACmono consists of fewer infections and less malignancies. In the intervention group participants have a more patient-friendly medication regime with only once daily an immunosuppressive tablet, enhancing compliance.

Study objective

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Study design

Pre-transplantation and 6, 9, 12 and 15 months after kidney transplantation.

Intervention

Participants are converted from Prograft to Advagraf one week after kidney transplantation. Six months after transplantation participants with stable renal function (eGFR >30 ml/min and proteinuria ≤0.5 gram per 10 mmol creatinin in spot urine) are randomized to either continue standard therapy with Advagraf and Cellcept or gradually decrease the Cellcept, to Advagraf monotherapy at 9 months. A renal transplant biopsy is performed at randomisation, 6 months after transplantation. One year after kidney transplantation participants are

vaccinated against pneumococcus and DTP (Diphteria, tetanus and poliomyelitis). Depending on the season also the influenza vaccine is administered. Participants are asked to fill in questionnaires about gastrointestinal symptoms and quality of life at 6, 12 and 15 months after transplantation.

Contacts

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Eligibility criteria

Inclusion criteria

- Adult patients receiving a deceased or living kidney transplant in the Erasmus Medical Center Rotterdam, The Netherlands and:

- Historical PRA <5% and

- HLA MM <4.

Re-transplantation are allowed when meeting the before mentioned criteria.

Patients have to give written informed consent to participate in the study.

Before randomization at 6 months, renal function should be stable with eGFR (MDRD formula) >30 in mL/min with proteinuria ≤0.5 gram per 10 mmol creatinin in spot urine.

Exclusion criteria

- HLA identical living-related transplant recipients.

- Patients with an indication to continue MMF or other immunosuppressive drugs, e.g. vasculitis, SLE etc. (according to judgement of treating physician).

- Recipient of an ABO-incompatible allograft or with a positive crossmatch (complement-dependent cytotoxicity or flow cytometry).

- Biopsy proven rejection three months and later after transplantation.

- Recipient of multiple organ transplants.

- Females of childbearing potential who are planning to become pregnant, who are pregnant and/or lactating or who are unwilling to use effective means of contraception.

- T-cell depleting therapy (anti-thymocyte globulin and alemtuzumab) after transplantation.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-09-2014
Enrollment:	100
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-09-2014
Application type:	First submission

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
NTR-new	NL4672
NTR-old	NTR4824
Other	: MEC-2014-318 / NL48634.078.14.

Study results