Geriatric anti-donor T-cell activity and development of alloreactive long-term hypo-responsive T cell function (GANDALF); Post-transplant development of anti-donor-specific hypo-responsiveness; Lessons to be learned from older kidney transplant recipients

Published: 27-03-2018
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To identify the mechanism(s) of DSH by analysis of post-transplant kinetics of phenotype and function of alloreactive CD4+ and CD8+ T cells.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON48839

Source
ToetsingOnline

Brief title
GANDALF

Condition

- Other condition

Synonym
anti-donor immunity, post-transplant anti-donor reactivity

Health condition

orgaantransplantatie

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

Intervention

Keyword: anti-donor hypo-responsiveness, kidney transplantation, older kidney transplant recipient

Outcome measures

Primary outcome

The primary study parameter comprises of a detailed characterization of

anti-donor reactivity at different time-points following kidney transplantation

to identify the mechanism(s) of DSH.

Secondary outcome

not applicable

Study description

Background summary

In the majority of kidney transplant recipients with stable graft function, anti-donor T-cell reactivity is absent long after transplantation (>5 years) as reflected by a decreased proliferative response of recipient T cells to donor antigen presenting cells, a phenomenon referred to as donor-specific hypo-responsiveness (DSH). The mechanism(s) underlying this phenomenon are unclear and may involve deletion of anti-donor reactive T cells, active suppression of anti-donor reactive T cells by regulatory T cells or induction of anergy in these anti-donor reactive T cells. Kidney transplant recipients on the waiting list for kidney transplantation have a prematurely aged T cell

compartment accompanied by a compromised T cell-mediated immunity. This may partly explain the clinical observation that older recipients (> or equal to 55 yrs) are more prone to develop DSH relatively early after transplantation. We hypothesize that a general principle of DSH development is operative in recipients of a donor kidney which can be revealed by studying the phenotype and function of alloreactive T cells of recipients at different time-points after transplantation, comparing the elderly with young recipients.

Study objective

To identify the mechanism(s) of DSH by analysis of post-transplant kinetics of phenotype and function of alloreactive CD4+ and CD8+ T cells.

Study design

This is an investigator-driven, observational (cross-sectional and longitudinal) study comparing features of anti-donor T-cell reactivity at different time-points after transplantation.

Study burden and risks

Participation in the cross-sectional part of the trial consists of one additional blood donation (7 heparin tubes a 7 mL blood= 49 mL of blood) at the time of routine blood withdrawal prior to, 3-5, 5-10, 10-15, 15-20 or >20 years following transplantation. The biobank *Niertransplantatie (versie 2, 29 februari 2012)* contains material of both the recipient as well as the donor prior to transplantation for which we have obtained permission to use for this research purpose.

Participation in the longitudinal part of the trial consists of 5 blood donations (5 times 7 heparin tubes a 7 mL blood= 245 mL) prior to and at different intervals after transplantation, i.e. 3 and 6 months and 1 and 3 years after transplantation during a regular visit at the outpatient clinic. The corresponding donor will be asked to participate at the time of donation of the kidney and blood (7 heparin tubes a 7 mL blood=49 mL) will be drawn at the time of routine blood withdrawal. The burden for the patient (and donor) is minimal and no additional risks are involved when participating in this study. Participation in this study does not compose of a direct advantage for this patient but contributes to the increased knowledge obtained with respect to kinetics of donor-specific hypo-responsiveness following transplantation. Furthermore, this may facilitate individualizing immunosuppressive regimes thereby minimizing adverse effects of long term use and prolonging graft and patient survival.

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

-18 years or older; i.e. between 18-45 years and >54 years
-kidney transplant recipient who is supervised at the Erasmus University Medical Center in Rotterdam
-recipient of a living or post mortal donor kidney
-stable graft function (defined as absence of recurrence disease and chronic rejection) 3-5
or 5-10, 10-15, 15-20 and >20 years after transplantation (cross-sectional sub-study)

Exclusion criteria

age<18 years and 46-54 years

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-06-2018
Enrollment:	540
Type:	Actual

Ethics review

Approved WMO Date:	27-03-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2019
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
CCMO	NL62179.078.18