Towards a further extension of the potential donor pool for highly sensitized patients.

Published: 13-08-2007
Last updated: 08-05-2024

The aim of this project is to enhance transplantation prospects of highly sensitized patients who are waiting for a long time for a suitable kidney graft. Despite their inclusion in the Acceptable Mismatch (AM) program (initiated in The Netherlands...

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

Summary

ID

NL-OMON30695

Source
ToetsingOnline

Brief title
Extension of the potential donor pool for highly sensitized patients.

Condition

- Renal disorders (excl nephropathies)

Synonym
Kidney transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Nierstichting Nederland

Intervention

Keyword: HLA antibodies, Kidney, Patients, Transplantation

Outcome measures

Primary outcome

Finding new Acceptable HLA mismatches and leading to an increased chance to get an organ offer.

Secondary outcome

Secondary objectives are patient and graft survival, graft function as assessed by calculated creatinine clearance, proteinuria, the number and severity of acute (antibody mediated) rejections, blood pressure (antihypertensive treatment), monitoring of infections and the occurrence of malignancies.

Study description

Background summary

The prospects for highly sensitized patients to receive a donor organ are grim. This is due to policies that share the assumption that contact with foreign HLA antigens causes priming of the immune system of the recipient. However, not every confrontation with foreign HLA antigens will lead to sensitization or to diminished graft survival. Studies have shown that not all patients transplanted across a positive historical crossmatch reject their kidney grafts. Furthermore, transplantation with donor kidneys harbouring HLA mismatches that are shared by previous blood transfusions, pregnancies and/or failed transplants is often successful. Today, serological crossmatching is a routine procedure in clinical organ transplantation. In contrast, T cell alloreactivity has never been used as parameter for organ allocation. In a pilot study we have shown that the presence of a naive in vitro T cell allorepertoire at the day of transplantation in patients with a historical positive crossmatch is associated with good graft function. For this purpose we designed a limiting dilution assay that distinguishes naive from primed donor specific T lymphocytes.

Study objective

The aim of this project is to enhance transplantation prospects of highly sensitized patients who are waiting for a long time for a suitable kidney graft. Despite their inclusion in the Acceptable Mismatch (AM) program (initiated in The Netherlands with support of the Dutch Kidney Foundation), it is estimated that a mere 60 % of these highly sensitized patients benefit from this program when studied in a two years period. We hypothesize that there is room for improvement. We will focus on those patients that are highly sensitized in historical sera only. In these patients we will analyze the presence of primed or naïve (or both) CTL against frequently occurring HLA antigens. HLA antigens for which only naïve CTLs are present will be classified as AM in the program. This approach will lead to an extension of the potential donor pool for highly immunized recipients and will enhance transplantation of this group of difficult patients.

Study design

From the patients blood will be drawn in order to check the presence of antibodies against the most frequent HLA antigens. Against those antigens towards no antibodies are present analysis for the presence of primed or naïve (or both) CTL will be carried out. After consultation with the nephrologist and transplantation immunologist dealing with specific patient the newly found HLA antigens will be added to the Acceptable Mismatches of this patient.

In case the patient has not been transplanted within 6 months after the first blood sample the second blood sample has to be taken and analysed.

Intervention

Mainly the selection of suitable donors will change for a certain patient. The medical procedure of the transplantation will not differ from that of other renal transplant recipients besides the fact that the patients will receive a mild induction therapy with ATG as described in Brennon et al. Treatment with antithymocyte globulin was initiated intraoperatively, before graft reperfusion. Subsequent doses were given daily through day 4, for a total dose of 7.5 mg per kilogram.

Study burden and risks

Burden is minimal: blood will be drawn from a vene in the arm. The risk is to experience a rejection of the graft which can be treated adequately in most cases by the current rejection treatment therapies.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
2333 ZA Leiden
Nederland
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
2333 ZA Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Older than 18 years.
Patients with renal failure on the Eurotransplant kidney waiting list.
PRA in historical sera higher than 85%.
More than 1 year on the AM list.
A signed "informed consent" form.

Exclusion criteria

1) Patients with severe gastrointestinal disorders, that interfere with their ability to receive or absorb oral medication and patients with severe diarrhea.
2) Patients with active peptic ulcer disease.

3) Patients or their donors with serologic evidence of HIV, HCV or HBsAg in the past.
4) Patients with malignancies (current or history within last 5 years) except non metastatic basal or squamous cell carcinoma of the skin that has been treated successfully.
5) Patients with systemic infection requiring therapy at the time of entry in the study.
6) Patients with any form of substance abuse or psychiatric disorder which in the opinion of the investigator might invalidate patients communication with the clinician.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2007
Enrollment:	21
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL14100.058.07