ISRCTN76326553 https://doi.org/10.1186/ISRCTN76326553

The DRIP Study: desensitisation of highly pre-sensitised dialysis patients waiting for kidney transplantation by Rituximab, Intravenous Immunoglobulin-L (IVIG-L) and rescue Plasmapheresis (AMC-DRIP)

Submission date 16/07/2007	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 16/07/2007	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 17/09/2008	**Condition category** Surgery	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Ajda T Rowshani

Contact details
Academic Medical Centre
Department of Internal Medicine, F4-215
P.O. Box 22700
Amsterdam
Netherlands
100 DE
+31 (0)20 566 3365 page 58816
T.Rowshani@amc.nl

Additional identifiers

Protocol serial number
NTR1000

Study information

Scientific Title

Acronym
AMC-DRIP

Study objectives
Donor-specific antibodies form a significant barrier in transplantation of highly pre-sensitised dialysis patients. Increased waiting time is associated with increased morbidity and mortality among these patients. Thus, there is a need to further develop desensitising therapies not only to make transplantation for this group of patients feasible, but also to reduce the occurrence of acute and chronic antibody-mediated graft damage caused by human leukocyte antigen (HLA) or non-HLA specific antibodies. Acute and chronic antibody-mediated graft damage is increasingly associated with decreased graft function and survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the Medical Ethics Committee of the Academic Medical Centre on the 15th February 2007 (ref: MEC 07/017# 07.17.0262).

Study design
A prospective, open, observational multi-centre clinical trial

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Highly sensitised renal transplant recipients

Interventions
In vivo administration of Rituximab (two doses):
The first dose of Rituximab (MabThera®, Roche) 375 mg/m^2 will be administered intravenously five months prior to the transplantation. The second and last dose will be administered before transplantation and after the completion of a successful treatment course with four doses of monthly IVIG administrations. The changes in the acceptable mismatch antigens will be analysed after each IVIG treatment course and the then extended profile of acceptable mismatches will be adjusted in the AM program. We expect that the patient can then be transplanted immediately or maximally up to six weeks thereafter.

Initial infusion: Start rate of 50 mg/hour; if there are no adverse side effects; increase the rate 50 mg/hour every 30 minutes, to a maximum of 400 mg/hour.

Subsequent infusions: Start at 100 mg/hour; if it is safe; increase the rate 100 mg/hour every 30 minutes, to a maximum of 400 mg/hour. All recipients will be given acetaminophen (1000 mg) and Di-adresoneF (25 mg), tavegil (2 mg), 30 minutes before the infusion.

In vivo administration of IVIG:
Intravenous administration of IVIG (IVIG-L, Nanogam, Sanquin) in a dose of 2 g/kg with a maximum of 140 gram, in a dilute, low-osmolaric solution. IVIG-L administration will be started at a speed of 30 ml/hr during the first 15 minutes. IVIG-L can be infused with infusion rates up to 8 ml/min (7 ml/kg/hr) without occurrence of severe side effects (Sanquin Clinical Study Report KB 97003B). In case of minor side effects, infusion will be withheld and after full clinical recovery of symptoms restarted at 50% of the original speed. To avoid the risk of over-hydration in dialysis patients, IVIG-L has to be given during dialysis in a 4-hour period and if necessary continued thereafter (dependent on the total dose which has to be infused), or otherwise IVIG-L infusion can be started on a not-dialysis day (dependent on the cardiovascular status of the patient and under clinical surveillance) followed by dialysis thereafter. No High Flux kidneys will be used in order to preserve and not to filter the administered IVIG.

Briefly, IVIG-L (2 g/kg; maximum dose: 140 g) will be administered, on dialysis or the day after, monthly maximally for 4 months with the last course one month before transplantation. If the patient who has completed the full desensitising treatment course has to wait longer than 4 weeks on the AM list in order to find a cross match negative organ, then another IVIG-L dose should be administered. The number of IVIG-L infusions depends on the results of the in vitro tests (PRA and CMX against unacceptable antigens) after each dose.

Plasmapheresis (PP):
If treatment consisting of the first dose of Rituximab and the full IVIG-L course of four monthly doses fail to achieve an acceptable low PRA and a negative cross-match (CMX) against the primarily unacceptable antigens, transplantation cannot take place. In this case we will institute a rescue plasmapheresis protocol encompassing maximal seven courses of daily large volume pheresis (40 ml/kg body weight) substituting plasma with saline/albumin solution in order to remove the antibodies, as it is known that a part of these patients can still respond to PP. If this occurs and the patient is eligible for transplantation, the second dose of Rituximab will be administered according to the protocol. After each third pheresis, plasma will be substituted with fresh frozen plasma (FFPs) in order to prevent and minimise the risk of bleeding.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Rituximab, intravenous immunoglobulin-L

Primary outcome(s)
Primary end-point is achievement of a negative cross-match test with the donor kidney and transplantability.

Key secondary outcome(s))
1. Patient and graft survival
2. Graft function as assessed by:

2.1. Calculated creatinine clearance
2.2. Proteinuria
2.3. The number and severity of acute (antibody mediated) rejections
2.4. Blood pressure (antihypertensive treatment)
2.5. Monitoring of infections
2.6. Occurrence of malignancies

Outcomes measured at six months after staring therapy and one year after transplantation.

Completion date
15/01/2010

Eligibility

Key inclusion criteria
Patients older than 18 years with end stage renal failure and a current plasma renin activity (PRA) higher than 80% who are for more than two years on the waiting list for a cadaveric donor kidney, and included in the AM program. Only heart beating donors will be accepted.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Complete Immunoglobulin-A (IgA) deficiency
2. Over-hydration
3. History of anaphylaxis against blood/plasma products
4. Significant cardiac or pulmonary disease, hepatitis C or human immunodeficiency virus (HIV) infection, or malignancy within the last five years

Date of first enrolment
15/07/2007

Date of final enrolment
15/01/2010

Locations

Countries of recruitment

Netherlands

Study participating centre
Academic Medical Centre
Amsterdam
Netherlands
100 DE

Sponsor information

Organisation
Academic Medical Centre (AMC) (The Netherlands)

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Academic Medical Centre (AMC) (The Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration