ISRCTN55817881 https://doi.org/10.1186/ISRCTN55817881

CAlciNeurin-inhibitor Nephrotoxicity and Efficacy Study

Submission date	Recruitment status
19/12/2005	No longer recruiting
Registration date	**Overall study status**
19/12/2005	Completed
Last Edited	**Condition category**
23/10/2008	Injury, Occupational Diseases, Poisoning

- [ ] Prospectively registered
- [ ] Protocol
- [ ] Statistical analysis plan
- [ ] Results
- [ ] 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 J W de Fijter

Contact details
Leiden University Medical Centre
Department of Nephrology, C3-P22
P.O. Box 9600
Leiden
Netherlands
2300 RC
+31 (0)71 5262169
jwdefijter@lumc.nl

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR390

Study information

Scientific Title
A prospective, open, randomised, multicentre study comparing once-daily versus twice-daily dosing of cyclosporin A (Neoral®) or tacrolimus (Prograf®) on renal graft structure and function at 6 and 12 months

Acronym
CANNES

Study objectives
We believe that a routine graft biopsy at 6 and 12 months together with graft function represents the best surrogate marker for late graft loss.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Received from the local medical ethics committee

Study design
Multicentre, randomised, active controlled factorial trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Renal transplant

Interventions
Before transplantation, patients will be randomised 1:1 to receive either a standard CsA-based or tacrolimus-based immunosuppressive regimen and either a twice daily (bid) or once daily (od) dosing schedule.

In the first four days after implantation Neoral or Prograft will be given twice daily schedule at approximately 12 hours intervals starting before surgery. The initial target 12 hours trough level (= C0) in these first days will be aimed at 225 ng/ml (range 200 to 250) and 12.5 ng/ml (range 10 to 15) for Neoral and Prograft respectively.

On day 4, in patients assigned to the once daily schedule the total bid dose of CsA or tacrolimus will be given once daily in the morning. At the end of the first week CsA or tacrolimus full 'area under the concentration curves' (AUCs) will be studied to assess true drug-exposure. Subsequent dose-adjustments will be made to achieve the defined AUCs for Neoral (AUC12 = 5400 ng*h/ml) and Prograft (AUC12 = 210 ng*h/ml) using a three-point sampling method (at C0, C2, C3). Such an approach is required since CsA trough levels do not predict drug exposure 6,9 while the experience with tacrolimus pharmacokinetics is limited.

AUCs will be calculated with an algorithm based on three-point sampling. After the first 6 post-transplant weeks the defined AUC for Neoral (AUC12) is 3250 ng*h/ml) and for Prograft (AUC12) 125 ng*h/ml. In the first 6 weeks after transplantation C0, C2 and C3 hour levels will be assessed weekly.

Thereafter these levels will be assessed at the regular visits to the out-patient clinic. Dose-adjustment in each patient will be guided by computer-assisted AUC extrapolation based on C0, C2, C3 drug levels.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. To investigate which drug regimen is associated with the best graft structure and function at 6 and 12 months
2. Degree of inflammation and fibrosis in renal biopsies taken at 6 and 12 months after implantation. Biopsies will be evaluated according to the Banff '97 Criteria for Renal Allograft Biopsy Interpretation and morphometric analysis of the interstitial fibrous tissue will be performed using the digital image analysis technique available in our department.
3. Graft function will be assessed by measuring glomerular filtration rate (GFR) using 125I-iothalamate and protein excretion rate

Secondary outcome measures
1. Patient and graft survival
2. Rejection episodes: number of (biopsy-proven) acute rejection episodes, their severity, histopathological pattern and time to first rejection episode
3. Side effect profile: blood pressure, cholesterol, fasting glucose, HbA1c, uric acid, need for supportive treatment, infectious complications, lymphoproliferative disorders
4. Calcineurin inhibition
5. Plasma levels of TGF-b
6. MPA-levels and IMPDH activity over time
7. mRNA expression of collagen in biopsies
8. Functional analysis of T lymphocytes. Assessment of the CMV-specific CD4+ T cell proliferation

Overall study start date
29/09/2000

Completion date
21/10/2002

Eligibility

Key inclusion criteria
1. Female or male, aged between 18 and 70 years
2. Recipient of a kidney graft (first or second) from a cadaveric donor or living (non-human leukocyte antigen [HLA] identical) donor
3. The patient understands the purpose and risks of the study and has given written informed consent to participate in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
126

Key exclusion criteria
1. Patients who are receiving a simultaneous pancreas kidney transplant or a double kidney transplant
2. Patients who are receiving a third or fourth transplant
3. Patients who have greater than 50% (current or historic) panel reactive antibodies
4. Female patients who are pregnant or unwilling to use adequate contraception during the study
5. Patients on other investigational drugs
6. Patients who are unable to take medication orally
7. Patients with a life expectancy less than 1 year

Date of first enrolment
29/09/2000

Date of final enrolment
21/10/2002

Locations

Countries of recruitment
Netherlands

Study participating centre

Leiden University Medical Centre
Leiden
Netherlands
2300 RC

Sponsor information

Organisation
Leiden University Medical Centre (LUMC) (The Netherlands)

Sponsor details
Albinusdreef 2
P.O. Box 9600
Leiden
Netherlands
2300 RC

Sponsor type
Hospital/treatment centre

Website
http://www.lumc.nl/english/start_english.html

ROR
https://ror.org/027bh9e22

Funder(s)

Funder type
Not defined

Funder Name
Not provided at time of registration

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration