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Calcineurin Inhibitor Minimisation in Renal Transplant recipients with Stable allograft function: A prospective randomised controlled trial

Submission date	Recruitment status	[ ] Prospectively registered
16/07/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
22/08/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
26/02/2019	Injury, Occupational Diseases, Poisoning	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00541814

Protocol serial number
RRK3367

Study information

Scientific Title
Calcineurin Inhibitor Minimisation in Renal Transplant recipients with Stable allograft function: A prospective randomised controlled trial

Acronym
CNIM-SRT

Study objectives
Calcineurin Inhibitor minimisation is effective in protecting renal transplants from chronic allograft nephropathy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North Staffordshire Local research Ethics Committee gave approval on the 20th September 2007 (ref: 07/H1204/103)

Study design
Prospective randomised controlled open-label parallel-group trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Renal transplantation; chronic allograft nephropathy

Interventions
Patients who fullfill the study entry criteria will require a renal allograft biopsy prior to randomisation to exclude acute rejection, recurrent disease or de novo glomerulonephritis. Those patients with an acceptable biopsy will proceed to randomisation on a 1:1 basis into 2 groups:

Group 1: Cyclosporin minimisation
Group 2: Cyclosporin withdrawal

At this point paticipants will undergo assessment of the primary and secondary outcome measures. The treatment period comprises three stages:

Stage 1: A 2 week period during which the patient will be stabilised on mycophenolate sodium 720 mg twice daily (in place of azathioprine).
Stage 2: A 3 month period during which the calcineurin inhibitor will be either targeted to a specified low blood level of 50-100 ng/ml, or withdrawn completely (depending on randomisation).
Stage 3: A 12 month maintenance period on the new immunosuppression regimen.

During the first two stages, patients will be reviewed every 2 weeks. This 2-weekly follow-up will continue for the first two months of the third stage of the study, and then visits will be reduced to monthly. At these visits routine blood and urine analysis will be performed as per routine clinical practice.

At the end of the third stage of the study (i.e. 16 months after randomisation) the participants will undergo the second assessment of the primary and secondary outcome measures. This will signify study end for the individual study participant.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Cicolsporin

Primary outcome(s)
To compare renal allograft markers of damage and evolving injury in biopsies immediately pre study and at the end of the study. The primary tissue assessments will comprise:
1. Index of chronic damage (an objective measure of the amount of chronic damage, shown to be a powerful indicator of prognosis in non-allograft renal biopsies)
2. Interstitial fibrosis quantification by Sirius Red staining
3. TGF-Beta expression
4. P-selectin expression and leukocyte infiltration (macrophage)
5. Fibroblast function
6. Epithelial mesenchymal transformation markers
7. Markers of apoptosis
8. Electron microscopy

Key secondary outcome(s))
The following will also be assessed immediately pre study and at the end of the study:
1. Renal:
1.1. Serum creatinine
1.2. Estimated Glomerular Filtration Rate (GFR)
1.3. Isotopic GFR
1.4. Urinary Albumin : Creatinine Ratio (ACR)
1.5. Graft loss

2. Immunological:
2.1. Acute clinical rejection episodes between both groups
2.2. Sub-clinical rejection on month exit biopsy
2.3. Donor specific and non-donor specific anti-HLA antibody formation
2.4. T cell responses

3. Infection:
3.1. Cytomegalovirus (CMV) PCR
3.2. BK polyoma virus PCR
3.3. Bacterial (fever, with identification of an organism by culture)

4. Cardiovascular:
4.1. Fasting lipid profile
4.2. Serum uric acid
4.3. Serum C-Reactive Protein (CRP)
4.4. Serum fibrinogen
4.5. Asymmetric Dimethylarginine (ADMA) levels
4.6. Ambulatory blood pressure
4.7. Arterial stiffness
4.8. Left ventricular mass on echocardiography

5. Malignancy

6. Patient Survival

Completion date
01/12/2009

Eligibility

Key inclusion criteria
1. Adult recipients of a first kidney transplant
2. A functioning kidney allograft (with estimated Glomerular Filtration Rate [eGFR] by Modification of Diet in Renal Disease [MDRD] >30 ml/min/1.73m^ 2) and be between 1 and 5 years post transplantation
3. Stable allograft function, as defined by no greater than 10% rise in serum creatinine in the preceding 6 months, on ciclosporin and azathioprine based immunosuppression
4. Minimal proteinuria, evidenced as urine albumin:creatinine ratio <50mg/mmol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. <18 years of age
2. Pregnancy or suspicion of pregnancy confirmed by positive b-HCG pregnancy test
3. Female patients unwilling to take effective contraception for study duration
4. Untreated ureteric obstruction on ultrasound of allograft
5. Recurrent urosepsis
6. Severe systemic infection
7. Untreated significant (>50%) renal artery stenosis on magnetic resonance angiography performed prior to study
8. History of acute allograft rejection

9. History of myocardial infarction
10. History of malignancy in previous 5 years (excluding non-melanomatous tumours limited to skin)
11. Symptomatic ischaemic heart disease
12. Hepatitis B surface antigen positive, hepatitis C positive or HIV positive
13. Recipient of combined organ transplantation (e.g. pancreas / kidney; liver / kidney)
14. Recipient of ABO-incompatible kidney
15. Greater than 1 HLA mismatch at either the B or DR locus
16. Peak HLA antibody Panel Reactivity (PRA) greater than 10%
17. Recipient who underwent HLA desensitisation procedure prior to transplantation

Date of first enrolment
01/08/2007

Date of final enrolment
01/12/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Sponsor information

Organisation
University Hospital Birmingham NHS Foundation Trust (UK)

ROR
https://ror.org/014ja3n03

Funder(s)

Funder type
Industry

Funder Name
University Hospital Birmingham Renal Research Fund supported by an unrestricted grant form Novartis Pharmaceuticals (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration