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A randomised controlled trial comparing the use of sirolimus based biphasic immunosuppression with myfortic to allow early CalciNeurin Inhibitor (CNI) withdrawal in renal transplantation

Submission date	Recruitment status	[ ] Prospectively registered
29/08/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
16/10/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/08/2012	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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RMRCTV1

Study information

Scientific Title

Study objectives
Most renal transplants last between 8-10 years. The commonest cause of their failure is chronic allograft nephropathy - a pathological process where the kidney becomes fibrotic. This fibrosis is partly due to calcineurin inhibitors- the immunosupressants which protect the transplant.

The hypothesis to be tested in this study is that a combination of Myfortic and Sirolimus can be used to eliminate the calcineurin inhibitor Tacrolimus at 3 months post renal transplantation, thereby avoiding the long term detrimental effects of Tacrolimus on the development of renal allograft fibrosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. UK Medicines and Healthcare products Regulatory Agency (MHRA) approval obtained on 01/08/2007
2. The Central Office for Research Ethics Committees (COREC) approval pending minor changes to study literature as of 15/08/2007. (Nottingham Research Ethics Committee 2, 1 Standard Court, Park Row, Nottingham, NG1 6GN, UK). We will submit to local ethics review body (Leicester General Hospital) when central ethics approval has been gained.

Study design
A single-centre open randomised controlled trial.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Not Specified

Participant information sheet

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

Interventions
Patients will be randomised to one of two drug regimens at three months post transplantation:

Regimen 1:
Tacrolimus: Twice daily oral doses as specified by attending physician to obtain trough levels of 5-15 ng/ml
Prednisolone: Once daily 20 mg oral dose. This will be reduced to 5 mg daily over two months.
Myfortic: Twice daily 720 mg oral dose

Regimen 2:
Sirolimus: Once daily oral dose as specified by attending physician to obtain trough levels of 10-15 ng/ml
Prednisolone: Once daily 20 mg oral dose. This will be reduced to 5 mg daily over two months.
Myfortic: Thrice daily 360 mg oral dose

Duration of interventions: 2 years

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. Renal allograft fibrosis at 6 months post-trial entry
2. Renal function as measured by change in the slope of the eGFR over a period of at least 2 years (least squares method)

Secondary outcome measures
1. Change in cystatin C concentrations at 6 and 12 months compared to baseline
2. Incidence of biopsy proven acute rejection. The diagnosis and graded severity of acute renal allograft rejection will be made by employing the 1997 Banff criteria
3. Renal allograft profibrotic gene expression determined by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)
4. Patient and graft survival at 6, 12 and 24 months post-trial entry
5. Comparison of blood pressure and the requirements for anti hypertensive therapy
6. Comparison of hyperlipidaemia (to include cholesterol, triglycerides, Low Density Lipoprotein [LDL] and High Density Lipoproteins [HDL]) and the requirement for treatment of elevated lipids
7. Proteinuria assessed by 24 hour urinary protein at 3, 6 and 12 months
8. Quality of life differences on the 36-item Short Form health survey (SF-36) at 6 and 12 months compared to baseline

Overall study start date
01/10/2007

Completion date
01/10/2009

Eligibility

Key inclusion criteria
Patients will be eligible for the trial if all of the following criteria are met:
1. Age greater than or equal to 18 years
2. Patients receiving a primary or secondary renal allograft from a living related, living unrelated or heart-beating cadaveric donor
3. Patients with second transplants must have maintained their primary graft for at least six months after transplantation (with the exception of graft failure due to technical reasons)
4. Stable renal allograft function over the first 3 months post transplant
5. An absence of subclinical rejection on the 3 month protocol biopsy
6. A negative pregnancy test pre-protocol biopsy
7. Signed written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
42

Key exclusion criteria
Patients will not be eligible for the trial if any of the following criteria apply:
1. Kidney transplantation from a non heart-beating donor
2. Patients suffering an acute rejection episode in the first 3 months post transplant with a Banff classification of 1b or above
3. Sub-clinical rejection seen in the 3-month protocol biopsy
4. Proteinuria >500 mg/24 hours
5. Estimated Glomerular Filtration Rate (eGFR) <40 mls/min (Cockcroft-Gault formula)
6. Evidence of active systemic or localised major infection at study entry
7. Known hypersensitivity to Tacrolimus, macrolide antibiotics or Myfortic
8. Use of any investigational drug or treatments within 28 days before study entry
9. Known or suspected malignancy within five years before study entry
10. Any condition which in the opinion of the investigator makes the patient unsuitable for entry into the study

Date of first enrolment
01/10/2007

Date of final enrolment
01/10/2009

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Renal Transplantation
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Sponsor information

Organisation
University Hospitals of Leicester NHS Trust (UK)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Government

Funder Name
University Hospitals of Leicester NHS Trust (UK)

Funder Name
Funding is also being sought from Wyeth Pharma and Novartis

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