ISRCTN95769119 https://doi.org/10.1186/ISRCTN95769119

RituxiMab in INDuction therapy for living donor renal transplantation

Submission date	Recruitment status	[X] Prospectively registered
01/10/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
15/12/2009	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
27/01/2023	Surgery	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Kidney transplantation is the best treatment for end stage kidney disease. Immunosuppression (reducing the strength of the body's immune system) prevents rejection and prolongs the life of a transplant. However, long-term graft loss remains a problem with an incidence of up to 20%. This is mainly due to immune system cells called B cells and the side effects of immunosuppression. Rituximab is a drug that targets B cells, reducing their numbers, and there is evidence that it reduces rejection. The aim of this study is to determine whether rituximab in combination with reduced immunosuppression can be used in kidney transplants to reduce the side effects of immunosuppression.

Who can participate?
Patients aged over 18 receiving their first living donor kidney transplant, or their second if the first was not lost from acute rejection

What does the study involve?
Participants are randomly allocated to either receive rituximab or to not receive rituximab 2 - 4 weeks before receiving their kidney transplant.

What are the possible benefits and risks of participating?
The potential benefits are significant. If rituximab is effective, patients could be safely managed with a reduced immunosuppressive treatment, which would lead to better graft function, lower rates of post-transplant diabetes, heart complications and infections, and potentially less rejection. This could result in improved long-term graft and patient survival: this would profoundly affect the approach to immunosuppression in kidney transplantation. There are two potential risks for participants: side effects due to rituximab administration, and the risks of rejection related to a reduced immunosuppressive treatment. These will be closely monitored during the study.

Where is the study run from?
Guy’s Hospital, Derriford Hospital, Glasgow Renal and Transplant Unit, Queen Elizabeth Hospital Birmingham, Sheffield Kidney Institute and Manchester Renal Transplant Unit (UK).

When is the study starting and how long is it expected to run for?
November 2010 to November 2021

Who is funding the study?
Astellas Pharma and Guy's Hospital Transplant Surgical Research Fund (UK)

Who is the main contact?
Nizam Mamode
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01095172

Protocol serial number
Study ID: 9154

Study information

Scientific Title
A phase IV open label randomised controlled trial of rituximab in induction therapy for living donor renal transplantation

Acronym
ReMIND

Study objectives
Can the use of a single dose of rituximab at induction allow a maintenance regimen of low dose tacrolimus and mycophenylate alone?

Ethics approval required

Old ethics approval format

Ethics approval(s)
Guy's Research Ethics Committee, 25/01/2010, ref: 09/H0804/110

Study design
Phase IV open-label randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Live donor renal transplantation

Interventions
Pre-medication with paracetamol 1 g orally (PO), hydrocortisone 100 mg intravenously (IV) and chlorphenamine 10 mg IV is provided 30 minutes before start of rituximab infusion. A single dose of rituximab 375 mg/m^2 administered via a dedicated IV line is given 2 - 4 weeks prior to transplantation. The dose should be rounded to the nearest 100 mg unless the difference comprises more than 5% of calculated dose, in which case the dose should be rounded up to the nearest 10 mg.

Patients then receive the medications as below:
1. Basiliximab (Simulect®): 20 mg IV 1 hour prior to induction of anaesthesia, and a further 20 mg IV dose on day 4 post-transplant
2. Tacrolimus: dose calculated to give levels of 3 - 7 ng/ml
3. Mycophenylate mofetil: 2 g/day in divided doses
4. Prednisolone: all patients will be given 1 g methylprednisolone at induction of anaesthesia. Patients receiving rituximab will be given 100 mg hydrocortisone twice daily (bd) on day 1 after transplantation, then prednisolone at 0.3 mg/kg on day 2, 0.25 mg/kg on day 3, 0.2 mg/kg on day 4 and 0.16 mg/kg on day 5. On day 6 they will receive 5 mg prednisolone, and on day 7 none. For patients not receiving rituximab, our current protocol will be followed. Prednisolone will continue at 0.3 mg/kg for the first month after transplantation, 0.25 mg/kg for months 2 and 3, and 0.16 mg/kg for months 4 to 6. Subsequent steroid maintenance or withdrawal will be at the discretion of the patient's clinician.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Rituximab, tacrolimus, mycophenylate

Primary outcome(s)
Glomerular filtration rate (GFR) (Modification of Diet in Renal Disease [MDRD] study calculation) at 12 months

Key secondary outcome(s))
1. Biopsy proven acute rejection, graft and patient survival at 1 year
2. Infections
3. Post-transplant lymphoproliferative disorder (PTLD)

Completion date
16/11/2021

Eligibility

Key inclusion criteria
1. Adult patients aged over 18 years, either sex
2. Receiving their first living donor renal transplant, or their second if the first was not lost from acute rejection
3. Have given written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Amendments as of 22/12/2010:
Point 8 of the below exclusion criteria has been amended to read as follows:
8. Patients who have been involved in any other investigational trial or non protocol immunosuppressive regimen in the previous 90 days prior to transplant

Initial information at time of registration:
1. Previous other organ transplants lost through acute rejection
2. Patients undergoing antibody removal
3. Patients with other organ transplants
4. Patients previously treated with cylophosphamide, ATG, OKT3 or rituximab
5. Patients with white cell count below 4,500/mm^3
6. Patients with platelet count below 1,500/mm^3
7. Patients who are treated with drugs that are strong inhibitors or inducers of cytochrome P450, or treated with terfenadine, astemizole, cisapride or lovastatin
8. Patients who have been involved in any other investigational trial or non protocol immunosuppressive regimen in the previous 30 days prior to transplant
9. Pregnant or breastfeeding women
10. Patients with a documented history of malignancy and its origins and treatment in the last

five years. Localised basal cell carcinoma of the skin is permitted
11. Patients known to be human immunodeficiency virus (HIV), hepatitis B or C surface antigen positive
12. Patients who in the opinion of the Investigator would not be a suitable candidate for study participation

Date of first enrolment
16/11/2010

Date of final enrolment
30/11/2018

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Guy's Hospital
London
United Kingdom
SE1 9RT

Study participating centre
Derriford Hospital
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Glasgow Renal and Transplant Unit
Greater Glasgow & Clyde NHS trust
Western Infirmary
Dumbarton Road
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G11 6NT

Study participating centre
Renal Transplant Unit
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
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B15 2WB

Study participating centre
Sheffield Kidney Institute
Northern General Hospital
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S5 7AU

Study participating centre
Manchester Renal Transplant Unit
Central Manchester University Hospitals
Manchester Royal Infirmary
Oxford Road
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M13 9WL

Sponsor information

Organisation
Guy's and St Thomas' Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name

Guy's Hospital Transplant Surgical Research Fund (UK)

Funder Name
Astellas Pharma Europe

Alternative Name(s)
Astellas Pharma Europe Ltd

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
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IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No