ISRCTN49958194 https://doi.org/10.1186/ISRCTN49958194

An investigation into the treatment of the donor kidney to see if this improves the recovery of the kidney after transplantation

Submission date
15/06/2012

Recruitment status
No longer recruiting

Registration date
03/08/2012

Overall study status
Completed

Last Edited
12/04/2021

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and aims
Before a kidney can be transplanted into a recipient it has to be removed from the donor and transported to the hospital of the recipient. During this period the kidney does not have a blood supply and is stored in a cold solution to minimise damage caused by lack of blood supply. One of the factors that can contribute to the damage of the kidney can potentially be blocked by a drug called Mirococept.
In this study the drug is given to the kidney, after the kidney has been removed from the donor and before it is transplanted into the recipient. The aim of the study is to find out whether damage to the kidney can be prevented and to see if the new treatment improves the function of the kidney and whether this might extend the life of the kidney.

Who can participate?
Patients aged 16 years or older who are on the kidney transplant waiting list and are receiving a kidney from a donor aged 10 or older

What does the study involve:
The study involves a single treatment to the donor kidney before transplantation. After the transplant patients follow their routine transplant assessment and clinic visits. Additional blood and urine samples are collected for the study to assess whether the study drug has worked. Patients are followed up for 1 year.

What are the possible benefits and risks of participating?
The aim of the study is to see if the treatment can reduce the chance of patients needing dialysis after they have had the transplant. By reducing the damage to a kidney during the time it does not have a blood supply the aim is to find out if the treatment can reduce the chance of long-term damage to the kidney. In general, a kidney transplant lasts on average 10 years and one of the aims is to see if the treatment lengthens the lifespan of new kidney transplants. As mirococept (the study drug) is given as a single treatment to the donor kidney before transplant, there is very little risk for it to enter the systemic circulation of the patient. In the first part of this study (in healthy volunteers), doses up to 100 mg given systemically were well tolerated.

Where is the study run from?
The study is taking place at NHS hospitals across the UK

When study starting and how long is it expected to run for?
October 2012 to May 2018

Who is funding the study:
Medical Research Council (UK)

Who is the main contact?
1. Dr Martin Drage (scientific)
2. Miss Laura Nicols (public)

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2011-000958-30

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MD-001

Study information

Scientific Title
An Investigation into the Efficacy of Mirococept (APT070) for Preventing Ischaemia-Reperfusion Injury in the Kidney ALlograft (EMPIRIKAL)

Acronym
EMPIRIKAL

Study objectives
This is a multi-centre double-blind randomized case-control trial, designed to test the superiority of Mirococept in the prevention of Ischaemia-Reperfusion Injury (IRI) in cadaveric renal allografts, as compared to standard cold perfusion fluid (Soltran).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - South East Research Ethics Committee, 22/02/2012, ref: 12/LO/1334

Study design
Multi-centre double-blind randomized case-control trial cumulative cohort design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Ischaemia-reperfusion injury associated with renal transplantation

Interventions
Interventions as of 21/04/2016:
Participants are randomly allocated to Mirococept (Active IMP) or Soltran (Placebo). Randomisation will be carried out in blocks; stratified by centre, type of donor (DCD/Donation after Brain Death (DBD)) and machine pump use. Immunosuppression therapy, antibiotic and antiviral prophylaxis will be administered as per local centre protocols.

Each cohort will be randomised to only two groups, placebo or one dose of Mirococept. As originally planned, the first cohort will be randomised to placebo or 10mg of Mirococept. After the completion of each cohort, an interim analysis will be carried out, which will help to determine the dose allocation for the next cohort. Based on the data from previous studies, 5 possible doses will be used: 5mg; 10mg; 15mg; 20mg and 25mg. The adaptive allocation will be based on a t-test (like) statistic that compares the difference between responses (accumulated) at the current dose, with the mean response at placebo plus our target difference 0.10. Basically, the current dose is repeated if the current estimated difference in responses between dose and placebo (scaled by the variance) is close to the target 0.10, and changed if otherwise.

Previous interventions:
Mirococept (Active IMP) or Soltran (Placebo) perfused through donor kidney via the renal artery, under 1 meter hydrostatic pressure prior to transplantation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Mirococept, Soltran

Primary outcome measure
Outcome measure as of 21/04/2016:
Delayed graft function measured by recording the need for dialysis in the first 7 days following transplantation.

Previous primary outcome measure:
To reduce Delayed Graft Function (DGF) as estimated by the number of patients requiring dialysis in the first week.

Secondary outcome measures
Secondary outcome measures as of 21/04/2016:
1. Duration of delayed graft function is measured by recording the need for dialysis at all follow up assessments (up to 12 months)
2. Mean calculated GFR measured using MDRD at 12 months
3. Mean calculated GFR measured using Cockcroft-Gault at 12 months
4. Functional delayed graft function is measured by the absence of decrease in serum creatinine of at least 10% per day for at least 3 consecutive days in first week post-transplant

Previous secondary outcome measures:
1. To include reducing the delay of recovery in those grafts with immediate function independent of dialysis
2. To determine if treatment influences renal function/histology at 12 months (a surrogate of long term graft outcome) and acute rejection episodes during this time

Overall study start date
18/10/2012

Completion date
30/05/2018

Eligibility

Key inclusion criteria
Inclusion criteria as of 21/04/2016:
1. Aged 16 years or older
2. Registered on the kidney transplant list
3. Willing to participate in the study and provide written informed consent
4. Must have the ability to comply with the study requirements
5. Patient is on dialysis
6. Receiving kidney from a donor over 10 years of age

Original inclusion criteria:
1. Patient must be 16 years of age or older
2. Patient must be willing to participate in the study & provide written informed consent
3. Patient must have the ability to comply with the study requirements
4. Donor must be older than 10 years of age

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
560

Key exclusion criteria
Exclusion criteria as of 21/04/2016:
1. Patient is recipient of a living-donor kidney
2. Patient is a recipient of a DCD kidney Maastricht category 1 or 2
3. Patient has evidence of current infection with HIV, HBV or HCV
4. Patient is recipient of a paediatric en bloc or a adult double renal transplant
5. Any recipient of a multi-organ transplant or a previous recipient of a non-renal solid organ transplant

6. Females who are pregnant or lactating
7. Male and Female patients not willing to use contraception for at least one month post-transplant
8. Any planned ABO blood group or HLA antibody incompatible transplant
9. Patient is involved in other experimental drug trials

Original exclusion criteria:
1. Patient is recipient of a living-donor kidney
2. Patient is not yet on dialysis
3. Patient is a recipient of a Donation after Cardiac Death (DCD) kidney Maastricht category 1 or 2
4. Patient has evidence of current or previous infection of human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV)
5. Patient is recipient of an en bloc double renal transplant
6. The donor kidney has more than 2 renal arteries, unless the artery is small enough to be ligated and not perfused.
7. Any ABO or HLA incompatible transplant
8. Patients receiving donor organs with a cold ischaemic time >30 hours
9. Any recipient of a multi-organ transplant or a previous recipient of a non-renal solid organ transplant
10. Females who are pregnant or lactating
11. Patients not willing to use contraception for at least one month post transplant
12. Patients with a history of malignancy within the last 5 years, except adequately treated squamous or basal cell carcinomas of the skin or cervical intraepithelial neoplasia
13. Patients involved in other experimental drug trials
14. Patients who might be expected to have an allergic response to the molecule

Date of first enrolment
29/10/2015

Date of final enrolment
01/05/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Guy's Hospital
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) grant ref: G1001197/1

Results and Publications

Publication and dissemination plan
Planned publication of study protocol and results papers.

Intention to publish date
30/05/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	06/06/2017		Yes	No

Results article	01/03/2021	12/04/2021	Yes	No
HRA research summary		28/06/2023	No	No