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An investigation into how well Mirococept (APT070) works in preventing injury to the kidney during transplant

Submission date
28/03/2024

Recruitment status
No longer recruiting

Registration date
04/07/2024

Overall study status
Ongoing

Last Edited
13/09/2024

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Up to half of kidney transplant patients are diagnosed with delayed graft function (DGF). DGF is when a donor kidney does not work straight away after the transplant. The donor organ undergoes a lack of blood supply after organ retrieval. Following the reintroduction of blood flow upon transplantation the local complement system reacts. This is a set of inflammatory proteins that play a critical role in the development of DGF. Patients who develop DGF are more likely to reject the transplanted kidney. DGF can also contribute to reduced kidney transplant survival and to prolonged hospitalisation. Thus, a treatment that can help prevent DGF is important. The EMPIRIKAL-2 trial is evaluating the effect of a drug called Mirococept. The study aims to identify the best dose for the drug to help protect against DGF. Treatment of the donor kidney with Mirococept will occur before transplantation. Mirococept is retained in the donor kidney where it targets the complement system. So, the systemic impact of the drug is expected to be limited.

Who can participate?
Eligible patients aged ≥ 16 years old and over on the kidney transplant register

What does the study involve?
Recruitment will take place at NHS hospital centres in the UK. Initially, 9 participants will be recruited to assess preliminary safety. Three different doses will be tested. If successful, the enrolment of a further 144 participants will be undertaken. Allocation to one of four different treatment groups will be at random. They will receive a kidney treated with Mirococept at one of three doses or with a standard solution. There will be blinding (concealment) of treatment allocation during this stage. Participant follow-up is for 12 months after transplantation. This will be during routine clinical follow-up (no extra appointments). There will be some collection of research blood and optional tissue samples. All other tests/procedures will be as per routine care.

What are the possible benefits and risks of participating?
Mirococept may help the recovery of kidney function following a kidney transplant. However,

this cannot be stated for certain until this and future studies have been completed. There may be no direct benefit from participating in this study. Still, the information gained from participation may help improve the treatment of patients with this condition in the future.

Where is the study run from?
King’s College London and Guy's Hospital

When is the study starting and how long is it expected to run for?
March 2024 to August 2026

Who is funding the study?
Medical Research Council (MRC)

Who is the main contact?
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Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008476

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
3639, EMPIRIKAL-2, IRAS 1008476, CPMS 63808

Study information

Scientific Title
A multi-centre, multi-arm, double-blind randomised placebo-controlled dose finding trial investigating the safety and Efficacy of MirococePt (APT070) In Reducing delayed graft function In the Kidney ALlograft

Acronym
EMPIRIKAL-2

Study objectives
Primary objective:
To identify the most safe and efficacious dose of Mirococept to reduce delayed graft function (DGF) rate in deceased-donor renal transplantation so this can be taken forward in a pivotal Phase III study

Secondary objectives:
1. Evaluate the efficacy of Mirococept to improve the rate of recovery in grafts with DGF or immediate graft function (IGF) independent of dialysis.
2. Determine if treatment influences renal function at 12 months (a surrogate of long-term graft outcome) and the incidence of acute rejection episodes during this time.
3. Estimate more accurately effect size, currently estimated conservatively at 20%. This will also allow the correct powering of the phase III pivotal study.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 13/05/2024, North East - Newcastle & North Tyneside 2 Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8086, (0)207 104 8140, (0)207 104 8016; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 24/NE/0071

Study design
Randomized placebo-controlled double-blind parallel-group study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Kidney failure

Interventions
Mirococept is perfused as a single dose of 60mg, 120mg, 180mg or placebo (vehicle solution), mixed with a cold storage solution to the explanted donor kidney via the renal artery(s) before transplantation.

Initial Safety Run
9 participants will be enrolled into the safety run at Guy's Hospital, assigned to one of the three treatment doses (60, 120 or 180mg) and followed up for 12 months. Participants 1-3 will receive kidneys treated with 60mg of Mirococept; participants 4-6 will receive kidneys treated with 120mg; and participants 7-9 will receive kidneys treated with 180mg. Recruitment within each dosing group will be staggered so that the interval between participants will be a minimum of 48 hours and up to two weeks, to allow a full safety assessment for each participant. In between the dosing groups, there will be a review of safety data before dose escalation to the next level.

After completion of the safety run, a DMC meeting will be convened to review the safety data before progression to the randomised controlled trial is permitted. It will be considered successful if the DMC consider at least one dose can be taken forward for comparison to placebo. This will provide a go/no go gate to the main recruitment of the multi-centre randomised controlled trial (RCT).

Multi-arm randomised placebo-controlled trial
If safety is met, 144 participants (36 per arm) (allowing for a 10% dropout rate) will be randomised at multi-centres via an online randomisation system to one of the three treatment doses of Mirococept (60, 120 or 180mg) or placebo on a 1:1:1:1 basis, stratified by centre and donor type. 90 participants (30 per arm) will be required if 2 of the proposed doses are well-tolerated and 40 participants (20 per arm) if only one dose is well-tolerated in the safety run. Participants will be followed up for 12 months.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Mirococept [MIrococept]

Primary outcome(s)
Delayed graft function (DGF) – the requirement for dialysis during week 1 post-transplantation

Key secondary outcome(s))
1. Functional DGF – failure of serum creatinine to decrease by at least 10% daily on 3 consecutive days in week 1 post-transplantation (excludes patients with biopsy-proven rejection or calcineurin inhibitor (CNI) toxicity in week 1 post-transplantation)
2. Number of dialysis sessions during the first 30 days post-transplantation

3. Duration of DGF
4. Mean calculated GFR (CKD-EPI) at 12 months post-transplantation
5. Mean calculated creatinine clearance (Cockcroft-Gault) at 12 months post-transplantation
6. Primary non-function – permanent lack of graft function for 3 months post-transplantation
7. AUC of serum creatinine on days 1-14 post-transplantation
8. Biopsy-proven acute rejection at 6 and 12 months post-transplantation
9. Biopsy-proven calcineurin (CNI) toxicity within 12 months post-transplantation
10. Duration of post-transplantation hospital stay
11. Number and duration of any hospital admissions during the first 12 months post-transplantation
12. 1-year graft survival (censored and uncensored for death with functioning allograft)
13. 1-year patient survival

Completion date
13/08/2026

Eligibility

Key inclusion criteria
1. Male or female patients aged ≥ 16 years old and over at the date of consent
2. Registered on the kidney transplant list
3. Recipient of a deceased donor kidney only
4. Able and willing to provide written informed consent
5. Able to comply with study requirements
6. On Dialysis at the date of consent
7. Donor age > 10 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Sex
All

Key exclusion criteria
1. Evidence of HIV, HCV or current HBV infection at screening
2. Multi-organ transplant or a previous non-renal transplant
3. Planned ABO- or HLA-antibody-incompatible transplant or patients with delisted HLA specificities
4. Recipient of a living-donor kidney
5. Recipient of a DCD kidney Maastricht category 1 or 2
6. Paediatric-en-bloc or an adult double-renal transplant

7. Kidneys undergoing machine perfusion both ex-vivo and Normothermic Regional Perfusion (NRP)
8. Pregnant or lactating patients (females of childbearing potential with a positive serum pregnancy test at screening)
9. Female patients of childbearing potential who are not willing to use a highly effective method of contraception for at least 1-month post-transplantation to prevent pregnancy, or abstain from heterosexual activity
10. Male patients who are not willing to use an effective method of contraception (condoms), at least 1 month post-transplantation, when engaging in sexual activity with a female of childbearing potential
11. Involvement in other interventional trials from the date of consent until completion of visit week 52
12. Known hypersensitivity to Mirococept and/or its excipients
13. Receiving treatment with a systemically administered complement inhibitor

Date of first enrolment
07/10/2024

Date of final enrolment
12/08/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
The Royal London Hospital
Alexandra House
London
United Kingdom
E1 1BB

Study participating centre
St Georges Hospital
Blackshaw Road

Tooting
London
United Kingdom
SW17 0QT

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Kings College Hospital
Mapother House
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Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Kent and Canterbury Hospital
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date