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A trial of different treatments on livers before transplantation

Submission date	Recruitment status	[_] Prospectively registered
05/06/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
07/09/2021	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
15/01/2025	Surgery	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
A recent innovation in liver transplantation is the ability to store livers outside the body for a period of time before implantation. This involves restoring an artificial blood supply to the livers (perfusion), which typically includes red calls in a plasma substitute with some additional chemicals which either help the liver during this period of storage or are believed to improve the way the liver will work after transplantation.
The aim of this study is to explore variations in both the plasma substitute and the additional chemicals to see which is associated with a better outcome. Outcome in this study will be determined by the expression of genes related to liver function and the immune response.

Who can participate?
Any adult at our centre undergoing a liver transplant.

What does the study involve?
The study involves altering the composition of the perfusate and measuring the outcomes in terms of gene expression, but also other markers such as the perfusion parameters, and chemical markers of looking at the injury occurring in the livers when the perfusion begins

What are the possible benefits and risks of participating?
The possible benefits are an improvement in the quality and initial function of the liver following transplantation. Conversely, the risks are that it may be worse.

Where is the study run from?
Cambridge University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2021 to December 2026

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Prof Chris Watson, cjew2@cam.ac.uk

Contact information

Type(s)
Public

Contact name
Prof Chris Watson

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
295373

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 295373

Study information

Scientific Title
A study to evaluate the effects of different perfusion conditions during ex situ liver perfusion

Study objectives
Transcriptomics will differentiate between the effects of different perfusates during ex situ perfusion

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 17/09/2021, Cambridge South REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8104; cambridgesouth.rec@hra.nhs.uk), ref: 21/EE/0177

Study design
Interventional randomized single-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Liver transplantation

Interventions
This is a study of isolated livers undergoing normothermic perfusion ex situ (ex vivo). There are additional readouts for some groups)
Study groups (n=6 to 10) will undergo incremental changes before proceeding to the next group.

Intervention arms include:
1. Comparing starting perfusate pHs of 7.2 and 7.6
2. Addition of a leucocyte filter into the circuit vs. none
3. Addition of a cytokine filter into the circuit vs. none
4. Addition of a thrombolytic agent (TPA) into the perfusate
5. Use of Gelofusin, human albumin, or fresh frozen plasma as plasma substitute
6. Use of an amino acid (Aminoven) infusion, or L-arginine infusion, vs a one off loading dose at the start of perfusion (additional readout: pefusate amino acid concentrations)
7. Exclusion of insulin from the perfusate vs its inclusion
8. Addition of 100mg hydrocortisone vs 3.3mg dexamethasone vs no steroid in perfusate
9. Addition of 4mg ciclosporin to perfusate vs no ciclosporin
10. Addition of allopurinol to perfusate vs none
11. Addition of vitamins C and E to perfusate vs none

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Organox metra liver perfusion device, alteplase, Gelofusine, human albumin solution, fresh frozen plasma

Primary outcome measure
Transcriptomic profile measured using liver biopsies collected into RNA Later before and after 4 hours and at the end of liver perfusion and after reperfusion in the recipient

Secondary outcome measures
1. Transcriptomic signature measured using DESeq on biopsies of the liver taken pre-perfusion and after 4h, and at the end of perfusion and following reperfusion
2. Post transplant function:
2.1. Post reperfusion syndrome measured using mean blood pressure measured using an invasive arterial pressure monitor recording for the five minutes before and after reperfusion of the liver
2.2. Early allograft function measured using the model for early allograft function score which looks at recipient biochemical and haematological variables over the first 3 days post transplant
2.3. Early allograft function measured using L-GraFT7 score which looks at recipient biochemical and haematological variables over the first 7 days post transplant
2.4. Early allograft function measured using Olthoff score which looks at recipient biochemical and haematological variables over the first 7 days post transplant
2.5. Incidence of anastomotic and non-anastomotic structures in DCD livers measured using MRCP in the first 6 months post transplant
2.6. Peak creatinine d1-7 measured using serum creatinine measurements at baseline and the first 7 days post transplant
3. Perfusate chemistry:
3.1. TBARS measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
3.2. HMGB-1 measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
3.3. Hyaluronic acid levels measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
3.4. Uric acid measured using the Piccolo Express near patient analyser at 1, 2 and 4 hours
3.5. D-dimer concentration (thrombolysis group) measured on perfusate taken after 30mins and 4 hours of perfusion using a commercial assay kit

Early allograft function and cholangiopathy are based on tests in the recipient post transplant; one post transplant biopsy for transcriptomics will be done post transplant

Overall study start date
04/06/2021

Completion date
31/12/2026

Eligibility

Key inclusion criteria

1. Aged ≥18 years
2. Requiring a liver transplant

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
150 to 250

Key exclusion criteria
1. Lack of consent
2. Inability to comprehend the information

Date of first enrolment
01/08/2021

Date of final enrolment
01/07/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
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Sponsor information

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Sponsor type
Research organisation

Website
http://www.cam.ac.uk/

ROR
https://ror.org/013meh722

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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/07/2027

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 3.1	07/03/2023	31/07/2023	No	No