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A trial of a clot-busting treatment in livers before transplantation

Submission date 05/06/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 03/08/2021	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 15/01/2025	**Condition category** Surgery	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Transplanted livers are susceptible to develop scarring in the bile ducts due to blockage of the blood supply to the wall of the bile duct around the time of transplant. These blocks are thought to be caused by blood clots developing as the liver recovers from a period of storage outside the body. The walls of bile ducts that have had their blood supply blocked heal by scarring, causing narrowed areas in the duct (strictures). Livers from donors donating after circulatory death, as opposed to brain dead donors, are particularly prone to develop this problem.

This study will place a liver on a perfusion machine outside the body and use a clot busting treatment that has been shown to work in non-transplanted livers to break down any clots that form before the liver is transplanted. This clot busting treatment cannot be given after a transplant because of the risk of bleeding in the recipient, something that is not a problem on a perfusion machine.

This study will look at the incidence of bile duct scarring, but the main aim is verify the safety of this approach looking at the incidence of bleeding post-transplant intraoperatively

Who can participate?

Patients having a liver transplant in the participating centres

What does the study involve?

The liver is treated with a clot-busting treatment while it is being perfused on a machine before transplantation

What are the possible benefits and risks of participating?

Benefits: There may be a reduced chance of developing bile duct strictures

Risks: Bleeding post-transplant

Where is the study being run from?

Cambridge University (UK)

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

June 2021 to December 2024

Who is funding the study?
Investigator initiated and funded

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

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
297403

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 297403

Study information

Scientific Title
A pilot study of thrombolysis during machine perfusion of circulatory death donor livers to prevent biliary strictures

Study objectives
Thrombolytic treatment to livers undergoing machine perfusion reduces cholangiopathy

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/12/2021, East of England - Cambridge East Research Ethics Committee (Currently being held remotely via Teleconference/ZOOM, The Fulbourn Centre, Home End, Fulbourn, Cambridgeshire, CB21 5BS; +44 (0)207 104 8102, +44 (0)207 104 8102, +44 (0)207 104 8134; cambridgeeast.rec@hra.nhs.uk), ref: 21/EE/0237

Study design
Interventional open label safety and feasibility study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Livers from donors dying following circulatory arrest (DCD donors) undergoing normothermic perfusion will receive a bolus of 10 mg alteplase and 50 ml fresh frozen plasma at the start of perfusion, followed by an infusion of 40 ml alteplase and 200 ml fresh frozen plasma over the next 80 min. A minimum of 100 min perfusion will follow before the liver can be considered for transplantation.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Alteplase

Primary outcome(s)
Post reperfusion intra-operative blood loss. These data will be obtained from the anaesthetic records and are recored realtime on the electronic patient record

Key secondary outcome(s))
1. Total and post reperfusion intra-operative blood transfusion and blood loss measured using recorded values on electronic anaesthetic record
2. Proportion of liver perfusions resulting in a transplant measured using aptient records at the end of the study
3. Incidence of symptomatic anastomotic and non-anastomotic strictures at 6 months post-transplant determined at cholangiography; symptomatic meaning associated with raised bilirubin or ALP or cholangitis.
4. Incidence of any anastomotic or non-anastomotic stricture excluding those related to hepatic artery thrombosis determined at cholangiography

5. Incidence of “clinically relevant” non-anastomotic strictures, using the van Rijn definition (associated with raised bilirubin or ALP or cholangitis.) at 6 months
6. Incidence of post reperfusion syndrome: 30% fall in systolic BP lasting at least a minute in the first 5 minutes post reperfusion in the recipient or the need for adrenaline or doubling of noradenaline to support the circulation
7. Early allograft function (Olthoff criteria and model for early allograft function score) at 7 days
8. Incidence of hepatic artery thrombosis in the first 6 months post transplant: determined by CT or angiography
9. Incidence of acute kidney injury (RIFLE criteria) (increase in recipient serum creatinine on days 1 to 7 post transplant compared to the baseline creatinine

Completion date
29/04/2024

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Patient requiring a liver transplant under the care of the participating hospitals

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
80

Key exclusion criteria
1. Inability to give consent
2. Recipient of a brain dead donor liver

Date of first enrolment
01/08/2021

Date of final enrolment
01/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.0	03/08/2021	09/09/2021	No	No
Protocol file	version 3.2	07/05/2022	15/06/2022	No	No
Protocol file	version 5.1	07/02/2023	31/07/2023	No	No