

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

<b>Submission date</b> 05/06/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 03/08/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/01/2025	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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](mailto:cjew2@cam.ac.uk)

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Christopher Watson

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## Additional identifiers

**Integrated Research Application System (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](mailto: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 noradrenaline 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  $\geq 18$  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?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol file</a>	version 1.0	03/08/2021	09/09/2021	No	No
<a href="#">Protocol file</a>	version 3.2	07/05/2022	15/06/2022	No	No
<a href="#">Protocol file</a>	version 5.1	07/02/2023	31/07/2023	No	No