

ROFG meeting

08 April 2025

Clinical Trials Unit Update**1. Status – Public****2. Executive Summary**

This paper provides an update on the clinical trials in organ donation and transplantation that NHSBT Clinical Trials Unit (CTU) are currently managing. There are currently 11 trials, which are described in the table below.

Key highlights since previous ROFG report:

- The ASK Trial: new trial in living-donor Kidney transplantation started 01 Nov 2025.
- The OrQA-UK Trial: new trial in liver donation/transplantation with start date of 01 May 2025.
- The HOPP Study: regulatory submission package is complete, however the MHRA will not permit submission until the Field Safety Notice for Belzer MPS is lifted. All actions have been completed by the Manufacturer but MHRA will not provide timeline to approval of Belzer MPS to be made available on UK market. CTU activity is paused until regulatory submission can be made.
- CLOTBUST-L: confirmed to be a medical device trial by the MHRA, therefore increased regulatory requirements and complexity. is had increased the regulatory, which has increased regulatory oversight of the trial. Current target recruitment start date of July 2025.
- The DeFat Study: opened to recruitment on 23/02/2023, 22 livers have been randomised to the study. Recruitment is currently halted:
 - o CI paused study as a precaution in May 2024 after a fatal SAE
 - o Event was reviewed by DMC and no safety concerns raised, recommended re-opening recruitment
 - o Non-fatal SUSAR (later confirmed not related) occurred in April 2024
 - o Reported by manufacturer (OrganOx) to MHRA
 - o MHRA halted recruitment in Aug 2024 until a notice of No Objection is received for the study
 - o MHRA submission made and currently awaiting final response from MHRA
- The PLUS Study: all final analyses have been performed. The results were presented at the BTS conference in March 2025 and there are 3 publications intended; study results, health economics and Donor Utilisation Index (DUI) paper.
- The SIGNET Study: is continuing to open sites to recruitment. All of the planned 92 Trusts are now open, with 1,271 organ donors randomised so far.
- TWIST: now closed.
- COBALT: Trial completed and final ad-hoc analysis completed. Publication upcoming.
- PITHIA: Trial now closed. Publication is pending

3. Action Requested

The Committee is asked to:

- Note the contents

Table 1. Current OTDT studies managed by the CTU
(in **set-up**, **recruitment**, or **follow-up/analysis**)

Trial Name	Trial Summary	Chief Investigator(s)	Sponsor	Progress
ASK	Trial of a patient and family outreach service to improve access to living-donor Kidney transplantation.	Dr Phillippa Bailey	University of Bristol	NIHR contract signed in Nov 2024. Submission to REC expected April with recruitment to begin July 2025. Currently have 10 sites on board to be participating sites with a further 5 in discussions.
OrQA-UK	Organ Quality Assessment: AI enabled liver photograph assessment tool to improve organ utilisation	Prof Colin Wilson	The Newcastle upon Tyne Hospitals NHS Foundation Trust	Project start date 01 May 2025. Sample size is 1,970 liver image sets and no participating sites. Expected to be a medical device trial but confirmation from MHRA is upcoming.
HOPP	Investigate the feasibility and safety of Oxygenated Hypothermic Machine Perfusion of pancreas grafts prior to transplantation in clinical practice.	Prof James Hunter	University of Oxford	Regulatory submission package is complete, however the MHRA will not permit submission until FSN of Belzer MPS is lifted. All actions have been completed by the Manufacturer but MHRA will not provide timeline of Belzer MPS to be back on UK market. CTU activity is paused until regulatory submission can be made.
CLOTBUST-L	An open-label, multicentre, randomised controlled trial to evaluate the efficacy of ex situ fibrinolysis during normothermic perfusion in liver transplantation from donation after circulatory death donors	Dr Vasilis Kosmoliaptsis	University of Cambridge and Cambridge University Hospitals NHS Foundation Trust	The MHRA has confirmed this is a medical device trial, which has increased regulatory oversight of the trial. This has increased the complexity of set up which continues with a target recruitment start date of July 2025.
SIGNET-EME	Examine the mechanisms in the potential down regulation of brain stem death induced proinflammatory responses by Simvastatin	Prof Simi Ali	The Newcastle upon Tyne Hospitals NHS Foundation Trust	A mechanistic sub-study of SIGNET, using QUOD samples. Recruitment has started. An amendment to the data sharing agreement to allow further data sharing with the SIGNET HTA study is in progress. Extension to the project has been requested.
DeFat	Delivery of Ex-situ deFattening Agents during normothermic liver perfusion for Transplantation– a randomised clinical trial.	Prof Peter Friend Mr Simon Knight Mr Syed Hussain Abbas	University of Oxford	Open to recruitment since February 2023, 22 livers have been enrolled to the study. Recruitment is currently halted as requested by MHRA. Submission to MHRA has been made and awaiting final approval.
SIGNET	Statins for Improving orGaN outcomE in Transplantation.	Prof John Dark Prof Dan Harvey	The Newcastle upon Tyne Hospitals NHS Foundation Trust	SIGNET opened to recruitment in September 2021. To date, 92 Trusts (150 sites) have opened to recruitment, and 1,507 donors have been recruited to date.

COBALT	Cardiorespiratory Optimisation By AVF Ligation after Transplantation.	Prof Gavin Pettigrew	Cambridge University Hospitals NHS Foundation Trust & the University of Cambridge	Trial completed and final ad-hoc analysis completed. Publication upcoming.
PLUS	Utilisation of normothermic machine preservation in extended criteria livers – a national threshold-crossing study.	Prof Peter Friend Mr Simon Knight	University of Oxford	The project end date was extended to 28 Feb 2025 and all analyses have been performed. The results were presented at the BTS conference in March 2025 and the final NIHR report will be submitted shortly. There are 3 publications intended; study results, health economics and Donor Utilisation Index (DUI) paper.
PITHIA	Pre-Implantation trial of Histopathology In renal Allografts	Prof Gavin Pettigrew	Cambridge University Hospitals NHS Foundation Trust & the University of Cambridge	Trial now closed. Publication is pending in Lancet Regional Health Europe.
TWIST	Multicentre, Open-label Randomised Trial of Superficial Wound Drain on Surgical Site Infection in high Body Mass Index (BMI) Kidney Transplant Recipients.	Mr James Hunter	Oxford University Hospitals NHS Foundation Trust	Trial now closed, results were presented at BTS conference.

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