

ROFG meeting

08 October 2024

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 9 trials, which are described in the table below.

Key highlights since previous RINTAG report:

- The PLUS study has entered the data cleaning phase and an NIHR VTC is underway to extend the end date to 28 Feb 2025.
- The protocol and technical documents for the HOPP study (Hypothermic Oxygenated Pancreas Perfusion) are being finalised prior to regulatory submission. Target MHRA submission is Mid-September 2024. HOPP was included in the 02Jul2024 ROFG email round and the project approval letter is awaited shortly.
- The DeFat study opened to recruitment on 23/02/2023, 22 livers have been randomised to the study. Recruitment is currently paused and is due to reopen shortly pending formal TSC approval.
- 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.
- the COBALT study data analysis has been performed. Results have been shared with the Trial Management and Steering Committees. A manuscript for publication will be prepared along with public dissemination of the results. Discussions regarding a potential follow up trial are ongoing.
- The results from the PLUTO trial have now been published in Kidney International <https://doi.org/10.1016/j.kint.2023.09.032>
- The PITHIA analyses have been completed and a draft manuscript has been prepared for publication.
- The NIHR EME grant has been awarded for the CLOTBUST-L trial. The Chief Investigator, Vasilis Kosmoliaptsis, has submitted the trial for review at this ROFG meeting and a draft protocol has been provided to the ODT Research team.

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
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	HOPP was included in the 02Jul2024 ROFG email round and the project approval letter is awaited shortly. Currently finalising documents before MHRA submission (target: Mid-Sep).
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. In early set-up stage. Data sharing to allow identification of QUOD samples completed. An amendment to the data sharing agreement to allow further data sharing with the SIGNET HTA study is in progress.
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 Kosmoliaptis	University of Cambridge and Cambridge University Hospitals NHS Foundation Trust	Grant funding began 1 st September, protocol in progress.
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 paused. The NIHR have just approved a 20-month extension, therefore new end date of November 2025.
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 have opened to recruitment, and 1,271 donors have been recruited to date.
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	Providing administrative support to this study. There are currently 11 centres open to recruitment and recruitment continues.
COBALT	Cardiorespiratory Optimisation By AVF Ligation after Transplantation.	Prof Gavin Pettigrew	Cambridge University Hospitals NHS Foundation Trust & the University of Cambridge	Trial completed and data analysis report completed.
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 recruitment target of 1035 livers was reached in April 2023 and follow-up was completed in April 2024. Data cleaning is ongoing and NIHR VTC is underway to extend end date to 28 Feb 2025.
PITHIA	Pre-Implantation trial of Histopathology In renal Allografts	Prof Gavin Pettigrew	Cambridge University Hospitals NHS Foundation Trust	The NIHR report has been submitted and a manuscript for publication has been written.

Author
CTU team
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