NHS
Blood and Transplant

RINTAG meeting

3rd November 2021

NHSBT Clinical Trials Unit

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 in set-up or recruitment, which are described in the table below. A key highlight of recent activity is the SIGNET Study which has now opened to recruitment. The study will involve 80 Trusts, and SNOD teams recruiting 2600 donors over 4 years.

3. Action Requested

The Committee is asked to:

- Note the contents

Table 1. Current OTDT studies managed by the CTU

Title	Study details	Description	Progress
SONAR-12M Surveillance Of arterioveNous fistulAe using ultrasound – 12 month follow up	Sponsor: Cambridge University Hospitals & the University of Cambridge Funder: NIHR Health Technology Assessment Board CTU input: Trial Management, Data Management & Statistics CI: Dr Gavin Pettigrew Sample size: 311	Two stage proposal assessing the utility of Doppler USS to predict AV fistula patency. SONAR-12M is a follow-up of the observational study which forms Part 1. SONAR-12M will provide additional data to either support or halt progression to Part 2, dependent upon whether part one shows that it is possible to predict failing fistulae.	Recruitment completed in June 2021. Data has been analysed, which did not support progression to Stage 2 of the project.
TWIST Multicentre, Open-label Randomised Trial of Superficial Wound Drain on Surgical Site Infection in high Body Mass Index (BMI) Kidney Transplant Recipients.	Sponsor: Oxford University Hospital Funder: Herrick Trust CTU input: Administrative support CI: Dr James Hunter Sample size: 360 participants	This study is being managed by surgical trainees under the supervision of Dr Hunter. The surgical trainees are responsible for recruiting, consenting and following up patients. Population: obese (BMI >30) transplant recipients Intervention: Wound drain Comparator: No drain Outcome: Surgical site infection at 30 days	The CTU are providing administrative support to CI to open participating centres. There are currently 10 centres open to recruitment and 160 participants recruited to the trial. Recruitment is expected to continue at a positive rate with the support from participating sites.
PLUS Utilisation of normothermic machine preservation in	Sponsor: University of Oxford Funder: NIHR i4i	Population: Extended criteria (Donor Utilisation Index > 0.27) liver offers made to participating centres	In set up - Waiting for REC approval. Expected start date end Nov 2021 Site Initiation Visits

extended criteria livers – a national threshold-crossing study	CTU input: Data Management, Statistics, Trial Management CI: Simon Knight and Peter Friend Sample size: 799 liver offers; 2465 control cohort	through the NHSBT national offering scheme Intervention: Normothermic Machine Preservation (NMP) with oxygenated blood using the OrganOx metra Control: Static cold storage A priori defined real-world cohort identified from NHSBT UK Transplant Registry. Outcome measures: Functional utilisation – transplantation of the liver with 12-month graft and patient survival	Site R&D approvals pending following REC approval
DeFat Delivery of Ex-situ deFatting Agents during normothermic liver perfusion for Transplantation– a randomised clinical trial	Sponsor: Oxford University Hospital Funder: NIHR EME CTU input: Data Management, Statistics, Trial Management CI: Peter Friend, Co-CI Simon Knight, Co-investigator, Syed Hussain Abbas. Sample size: 60 liver offers	Population: Livers from donors with a fatty liver index (FLI) threshold value of >80 considered for enrolment into the trial. Intervention: Normothermic Machine Preservation (NMP) with oxygenated blood using the OrganOx metra with the following adjuncts to the preservation system: Lipoprotein apheresis filtration, L-carnitine, Forskolin, Insulin and Glucose: Control: Normothermic Machine Perfusion (NMP) with oxygenated blood using the OrganOx Metra, Outcome measures: The proportion of fatty livers that achieve all transplantability criteria (based on adequate liver function during NMP).	In protocol development and set up stage. There are 4 participating sites. All documents nearly completed for REC submission end Oc 2021. Expected start date Jan 2021
PLUTO PlasmaLyte usage and assessment of kidney transplant outcomes in children.	Sponsor: Great Ormond Street Hospital (GOSH) Funder: NIHR – Research for Patient Benefit Funding: £350,000 CTU input: Data Management, Statistics, Trial Management CI: Dr Wesley Hayes Sample size: 144 participants	A multi-centre, open-label randomised controlled trial, to determine whether the incidence of clinically significantly abnormal plasma electrolyte levels will be different with the use of Plasma-Lyte 148 compared to standard intravenous fluid in children following kidney transplant. Primary endpoint: Acute hyponatraemia in the first 72 hours post kidney transplant.	There are 7 Trusts open to recrutiment and so far, 70 patients have been randomised.
PITHIA Pre-Implantation Trial of Histopathology In renal Allografts. A stepped-wedge cluster randomised trial.	Sponsor: Cambridge University Hospital Funder: NIHR – Research for Patient Benefit Funding: £350,000 CTU input: Trial Management, Data Management & Statistics CI: Mr Gavin Pettigrew Sample size: N/A– there are 22 participating centres (all UK kidney transplant centres). The use of the biopsy service and any resulting effect on transplant numbers will be monitored throughout the 2-year trial period.	Population: Kidneys offered for transplantation from deceased donors (DCD and DBD) aged ≥60 years Intervention: Access to a pre-implantation biopsy service for kidneys. Comparator: Usual care (no biopsy service). 4-5 centres will be given access to the biopsy service every 4 months until all centres have access. Each centre is one cluster Outcome: 1. Proportion of kidneys that are transplanted on first offer. 2. Estimated glomerular filtration rate (eGFR) measured at 12-15 months after transplant	PITHIA was paused in March 2020 due to the pandemic and restarted on 01/07/2021. A total of 205 PITHIA biopsies have been requested and processed.
SIGNET Statins for Improving orGaN outcomE in Transplantation	Sponsor: The Newcastle upon Tyne Hospitals NHS Foundation Trust Funder: NIHR – Health Technology Assessment	A multi-centre, single blind, prospective randomised controlled trial to evaluate the benefits of a single dose of Simvastatin given to potential organ donors declared	SIGNET opened to recruitment on 14th September 2021. To date, 20 Trusts (Level 1&2 donor hospitals) have opened to recruitment, and 5 donors have been recruited to

	CTU input: Data Management, Statistics, Trial Management CIs: Prof. John Dark and Dr Dan Harvey Sample size: 2600 participants	dead by neurological criteria on outcomes in organ recipients. Primary outcome: Composite of death, mechanical circulatory support or renal replacement therapy within the first 30 days post heart transplant. All level 1 and 2 ICUs will be involved. SNODs will recruit and consent the donors and their families. This is being funded by NIHR service support funding via the clinical research networks	date. The remaining 58 Trusts will be opening to recruitment over the next two months.
COBALT Cardiorespiratory Optimisation By AVF Ligation after Transplantation	Sponsor: Cambridge University Hospitals & the University of Cambridge Funder: NIHR – Research for Patient Benefit Funding: £350,000 CTU input: Data Management, Statistics, Trial Management CI: Mr Gavin Pettigrew Sample size: 40 participants.	Should we ligate haemodialysis fistulas in patients once they have been transplanted successfully? A randomised, interventional feasibility study for a proposed multi-centre randomised controlled trial.	Protocol and study documents are being prepared, for submission to the HRA/REC in November 2021.
ITOPS Improving Transplant Opportunities for patients who are Sensitised	Sponsor: Cardiff and Vale University Health Board. Funder: Kidney Research UK. Funding: £500,000 CTU input: Trial and data management and statistics. CI: Dr Sian Griffin Sample Size: 38	This is multi-center, randomised controlled feasibility trial, which aims to assess the efficacy of a combination of B cell depletion and proteasome inhibition, together with antibody removal and steroids, to reduce HLA antibodies in Highly Sentisised Patients, predictive to improve rates of transplantation, and to determine the feasibility of conducting a future definitive trial.	The trial has completed recruitment and data collection stage. Although recruitment was ended prematurely due to COVID19, and 25 participants were randomised in total. Currently the trial team is in the process of data cleaning. Analysis will commence in January 2022.

Author
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