NHS Blood and Transplant

RINTAG meeting

25th May 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 the NHSBT Clinical Trials Unit is currently managing. There are currently 8 trials in set-up or recruitment., which are described in the table below. A further trial, ITOPS, is currently in close-down prior to data analysis, and there is one additional study for which we are awaiting confirmation of funding.

3. Action Requested

The Committee is asked to:

- Note the contents

4. Current OTDT clinical trials managed by the CTU

Title	Study details	Description	Progress
SONAR-12M **Surveillance Of arterioveNous fistulAe usin g ultrasound – 12 month follow up**	Sponsor: Cambridge University Hospitals NHS Foundation Trust & the University of Cambridge Funder: NIHR Health Technology Assessment Board CTU input: Trial Management, Data Management & Statistics CI: Dr Gavin Pettigrew Sample size: maximum of 311 participants to follow up from the stage 1 observational study	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.	COVID-19 has delayed the set-up of SONAR-12M. HRA approval was received in January 2021, but the first participant was not recruited until 1st April 2021. Currently we have 12 Trust approvals, 10 hospitals open to recruitment and 68 consented participants in the database. We are asking the research teams to provide the data by the end of June and expect to decide in September whether we proceed to Part 2.
SONAR 2nd Phase	Sponsor: Cambridge University Hospitals NHS Foundation Trust & the University of Cambridge Funder: NIHR Health Technology Assessment Board CTU input: Trial Management, Data Management & Statistics CI: Dr Gavin Pettigrew Sample size: 1224 participants	Two stage proposal assessing the utility of Doppler USS to predict AV fistula patency. Part 2 will only occur if part one shows that it is possible to predict failing fistulae. Part 2 would be a randomised interventional study.	In protocol development and study design stage while waiting for results from Part 1.

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. Ther e are currently 9 centres open to recruitment and 130 participants recruited. The trial is currently not on the NIHR portfolio due to being a collaborative study but this is being looked into further as if the trial is in the portfolio, the sites should get support with funding for research staff which may increase the likelihood of new sites joining
PLUS Utilisation of normothermic machine preservation in extended criteria livers – a national threshold-crossing study	Sponsor: University of Oxford Funder: NIHR i4i CTU input: Data Management, Statistics, Trial Management CI: Simon Knight and Peter Friend Sample size: 799 liver offers; 2465 control cohort	Population: Extended criteria (Donor Utilisation Index > 0.27) liver offers made to participating centres through the NHSBT national offering scheme Intervention: Normothermic Machin e 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	In set up - delays due to COVID-19 - expected start date September 2021. To date: Final study protocol and patient information and site documentation completed Ethics pending Data Protection Impact Assessment and Risk Assessment completed OrganOx devices deployed at all sites and sites trained in the use of the OrganOx device Ongoing arrangements with Hub Operations for identification of eligible livers and study enrolment at point of offering.
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.
PLUTO Plasma-Lyte usage and assessment of kidney transplant outcoms 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 6 Trusts set-up and so far, 32 patients have been randomised. The remaining three transplant centres are due to be set-up within the next couple of months.
PITHIA Pre-Implantation Trial of Histopathology In renal Allografts	Sponsor: Cambridge University Hospital Funder: NIHR – Research for Patient Benefit Funding: £350,0 00 CTU input: Trial	Population: Kidneys offered for transplantation from deceased donors (DCD and DBD) aged ≥60 years	PITHIA was paused on 20/03/2020 due to the pandemic and will restart on 01/07/2021. Prior to the pause, a total of 164 PITHIA biopsies had been requested and performed.

A stepped-wedge cluster randomised 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	Intervention: Access to the results of a pre-implantation biopsy of the kidney taken at retrieval. 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	
SIGNET **Statins for Improving orGaN outcomE in Transplantation**	Sponsor: The Newcastle upon Tyne Hospitals NHS Foundation Trust Funder: NIHR – Health Technology Assessment CTU input: Data Management, Statistics, Trial Management CIs: Prof. John Dark and Dr Dan Harvey Sample size: 2600 participants	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 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	The IRAS application has been submitted. The CLODs and research teams at all level 1 and 2 donating hospitals have been contacted, with PI's confirmed at most sites. Training for site teams is due to start in June, pending approvals. Training material for the specialist nurses is currently being drafted.

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