Minutes of Cardiothoracic Transplant Clinical Trials Meeting

Research Board Room, Royal College of Surgeons of England
30 June 2016 11:00-14:30

Attendees: Nawwar Al-Attar, Glasgow
David Quinn, Birmingham
Chris Bowles, Harefield
Jenny Mehew, NHSBT Statistics and Clinical Studies
Steven Tsui, Papworth
Nagarajan Muthialu , Great Ormond Street
John Dark, Newcastle
Andrew Fisher, Newcastle
Sanjeet Singh, Glasgow
Owais Dar, Harefield

1. Declarations of interest in relation to agenda
None

2. Welcome and introductions

3. Minutes of the meeting held on 2nd November 2015 - CTAG(16)S7
Agreed

4. Project Updates:

a) Post-conditioning using cyclosporine for mitochondria protection.
Study focuses on DBD hearts. A rodent model is currently being developed to help define dosage for future clinical trials, involving Professor Peter MacDonald.. This will be a feasibility investigation. No collaboration required for this initial animal study. It was discussed that the use of cyclosporine is similar to ischaemic preconditioning in that it provides protection to the heart. Cyclosporine can be used either pre or post ischaemia. The group discussed previous studies from which this project has stemmed from, one of which used an NSTEMI population but it was noted that this population is very different to a heart transplant cohort so results are not entirely translatable. It was also felt that the sample size required may be large, in particular Bob Bonser had previously found that approximately 1,400 patients would be required for a similar ischaemic pre-conditioning study.

b) Glasgow Transplant Score
S Singh presented the latest developments with this observation study (not a clinical trial). First step is to develop a recipient score which is illustrated through a polygon for recipient-only risk factors to aid MDT decisions. The number of parameters presented has now been reduced from 25 to 8, including pre-op and post-op factors. Muscular strength (frailty) is an important factor to include. The impact of these factors upon 30 day mortality was considered. The ultimate aim would be to develop donor polygons and to

merge these on to the recipient polygon in order to decide how best to allocation organs. The group agreed that statistical modelling is required to inform the weighting criteria for each axis. A clinical trial would not be needed as observational retrospective/prospective data is suitable. Data collection on ischaemia time is being done and used in this project, as defined by the fields recently agreed by CTAG.

c) Randomised trial of LVAD verses OMM.
NHS England have submitted an application for destination therapy funding. A paper will be submitted to a Clinical Panel in September 2016 for Commissioning Through Evaluation. Therefore, this project will be put on hold until the outcome of the submission has been reached.

d) The role of T3 in marginal heart donors.
R Venkataswaran was not present to discuss progress with this project. However, the group noted that the definition of marginal donors is difficult. OCS usage should be factored in to account for cold storage and warm storage. It was suggested that donors that are not used due to functional reasons should be used for this study, although this would not therefore be a clinical trial.

e) The use of real time imaging to aid donor organ assessment.
J Parmar was not present to discuss progress with this project.

f) Markers for aspiration in lung donors.
J Parmar was not present to discuss progress with this project.

g) Up-regulation of endothelial nitric oxide synthase (eNOS).
No progress since last meeting.

h) Circulating donor-derived DNA
Animal study at present. Grant has been received for a prospective study. Single centre at GOSH at present for validation cohort as proof of concept..

i) Cardiac allograft protection study.
Approximately 200 patients are required. Most centres have formally agreed to participate. BHF grant of £700k has been applied for.

Post-meeting note: centre contacts for this study are:
Birmingham – S Lim
Glasgow – M Petrie
Harefield – O Dar
Manchester – S Shaw
Newcastle – G Parry
Papworth - S Pettit

5 New Project Ideas

a) QUOD Initiative

J Dark introduced the ideas behind the QUOD initiative and how this works. The QUOD biobank is in Oxford and currently hold blood and urine samples from more than 1000 donors including those taken when in ITU. Blood and urine samples are stored and liver and kidney biopsies are taken from all abdominal retrievals. It is funded to collect, process and store samples. Anyone wishing to obtain samples from the biobank need to pay a fee and must apply to the QUOD committee to do so. QUOD does not do culture.
J Dark suggested that the group may wish to collect samples for cardiothoracic retrievals. The first proposal was to carry out routine research BAL of lungs wherever thoracic retrieval team is present (60mL of sterile saline) in addition to BAL for culture (clinical use). The group were supportive of this proposal.
J Dark to take a protocol to the next CTAG centre directors telecon.
The second proposal was to take biopsies for the left ventricle for all cardiac donors in the UK. This was not thought to be a priority for DCD hearts due to time constraints. The risk of taking a biopsy and recipient consent were discussed. Most delegates were not keen to biopsy the donor heart just to bank samples but were supportive in principle if there is an actual research proposal tabled..

b) CT scans
J Dark presented a proposal to use CT on lung donors to identify cases of emphysema as this cannot be detected through standard chest xrays. The group agreed that a pilot would be required which would need to be a blinded study as the lungs may not be used if the CT scan shows some emphysema. J Dark to table proposal.

6. Next meeting
The group agreed that a face to face meeting in 6 months time should take place.