SIGNET Study Update May 2022

Background

You may remember a presentation on this study to your Advisory Group in the autumn of 2020. Funding had been confirmed but there were Covid-related delays so the study recruitment commenced in September 2021.

The background is the anti inflammatory, pleiotropic effect of statins, in the setting of brain stem death. A small study in Finland had shown reduction in liver and heart injury after transplant with an organ from a statin-treated donor, and no deleterious effects in any organ group. On this basis we made an application to NIHR for a four year study randomising adult brain dead donors to single dose of simvastatin across the UK. There will be 2600 donors in all, with half receiving just a standard care. We believe it is the largest donor intervention study in the world. Detailed information can be found on the study website - https://www.nhsbt.nhs.uk/clinical-trials-unit/current-trials-and-studies/signet/
No concerns were raised at any of the advisory groups on the initial presentation. We have a range of primary (cardiac) endpoints, and secondary endpoints across all organ types.

Progress

The study is run by the NHSBT Clinical Trials Unit in Cambridge and donors will be recruited at 78 Level 1 and Level 2 donor hospitals. So far we have 33 of the 35 Level 1 Trusts, and 41 of the 43 Level 2 Trusts open to recruitment. We have randomised, by May 9, 179 donors. There have been no serious adverse effect events in either donors or recipients; the worst that has happened is that a donor was given atorvastatin rather than simvastatin.

Co-Enrollment

Retrieval teams and in particular implanting centres will be blind to the allocation of a particular donor, whether to receive Simvastatin or best standard care. This study will run four years and so include a high proportion of adult brain dead donors. It clearly has implications for other research studies that might affect the early outcomes after organ transplantation.

We have a mechanism to communicate with other studies, with a co-enrollment process, in particular to be able to show that there is no confounding effect of the statin on those studies and conversely those studies have no confounding effect on our outcomes. But it is very important that you communicate with us so the process can be established. We have done this for a number of studies already, but it is crucial that we learn about other studies. In addition, we would like to be in touch with teams doing Service Evaluations, which fall-short of full-blooded research but might affect early outcomes. We would emphasis that SIGNET involves only DBD, adult donors

If you have started, or plan to start, other research studies during or early after transplantation, or plan new service evaluations, please can you contact us so we can discuss if there are reasons to exchange information and establish co-enrollment. Best contacts are directly to the CTU at SIGNET@nhsbt.nhs.uk, or to one of the co-CI's, John Dark, john.dark@newcastle.ac.uk, or Dan Harvey, Dan.Harvey@nhsbt.nhs.uk