SIGNET

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Statins for Improving orGaN outcomE in Transplantation

The SIGNET study

You are being asked to agree to your relative taking part in the SIGNET study. As you have generously provided consent/authorisation for donation of organs for transplantation, your relative is now in a unique position to be able to participate in this trial which could hopefully make a difference to transplant recipients now and in the future.

The study aims to find out if giving organ donors a single dose of a drug, called a statin, will improve the outcome for the person receiving the organ.

It is entirely up to you whether you wish to consent to/authorise your relative joining the study. The treatment of your relative will be the same whatever you decide. Before you decide we would like to explain why the study is being done and what it would involve for your relative. The specialist nurse in organ donation will discuss this with you, to help you decide whether or not you would provide consent/authorisation for your relative to take part and answer any questions you may have. Please feel free to talk to others about the study if you wish.

Please ask us if there is anything that is not clear or if you would like more information.

What is the study aiming to address?

We wish to find out whether giving organ donors a single dose of Simvastatin, a very widely-used and safe drug, is helpful for the people who will receive the organ.

All donated organs have already suffered some level of damage. This is because as the brain dies, chemicals are released which cause an "inflammation" of the whole body. Measurements of this "inflammation" link to how well the organs will function in the person receiving the organ after the transplant.

Many hearts and other organs are unable to be transplanted due to this reduced function. Hearts are especially affected, and this results in approximately 25% of those that are offered, being used for transplant.

Therefore, whilst everything possible is done to support transplantation, in some cases this may not be possible because of the risk to the recipient. The reason for this is that the most common cause of death after a heart transplant is the donor heart not working properly. Anything we can do prior to transplant which may improve the transplanted heart could have a major benefit to the recipient. This applies to all the other organs transplanted and reduces the chances of an organ not being used.

What are statins?

Statins are cholesterol – lowering drugs that can help many health problems. In particular, statins reduce inflammation in the body and in individual organs. Statins protect the lungs and kidneys in many illnesses.

A recent study carried out by transplant doctors in Finland selected a small number of organ donors to receive a statin. After the transplant the recipients who received a heart from a donor who had statins had less heart damage. The numbers were small and did not show that more survived. It did help lung and liver recipients a little bit. The most important result was it didn't make anyone worse by receiving an organ from a donor who had been given the drug.

Who has reviewed the study?

The study has been reviewed by the London Queen Square Research Ethics Committee.

What are the possible benefits of taking part?

Unfortunately, there will be no benefit to your relative if they take part in the study, but there may be a benefit to the person receiving your relative's organs, if they are transplanted.

People receiving an organ which has been treated with Simvastatin may have better outcomes, and we hope that this will mean we are able to transplant more organs successfully, but we do not know if this will be the case.

What are the possible disadvantages and risks of taking part?

Simvastatin is a licensed drug and one of the most prescribed drugs in the UK. There are some risks associated with taking statins for a long time, however this will be a *single* dose, so these risks are not considered a problem at all for this study.

With any drug there is a risk of allergic reaction. We expect this to be very rare as there has only been one case of this reported.

What does taking part in the study involve?

Before your relative donates their organs, they will be randomly allocated to one of the two groups in the study, to remove any bias. One group will receive 80mg Simvastatin in addition to all of the standard care that they receive, including other usual medications. The other group will receive standard care alone. There is a 50/50 chance of being in either group.

If they are randomised to receive Simvastatin, they will receive a single dose of Simvastatin. The drug will be given to your relative via a tube running into their stomach, as soon as possible after obtaining consent/authorisation. It is likely that your relative already has this tube in place as part of their critical care or because organ donation is planned, but this may need to be placed. This will not cause your relative any distress; it will not be placed until after death has been confirmed.

Some of your relatives medical history will be used as part of the study analysis but you will not need to provide us with this information, the research team will be able to get this from your relatives medical notes and the DonorPath registry DonorPath is used to record the medical history of a donor so that anonymous details can be passed to the doctors looking after potential organ recipients. It is kept as a permanent record, anonymised by NHS Blood and Transplant (NHSBT) We will also need to record your relative's Donor number.

We will follow up with the people that receive your relative's organs to see how they are doing following transplant. To do this we will need to use some of your relative's identifiable data. This is data already collected as part of the organ donation process.

Consent/authorisation – you will decide if you wish for your relative to take part. We will only proceed if you agree.

Randomisation – we will randomise your relative to see if they will receive Statin plus all their standard care or standard care only.

80mg Simvastatin plus standard care

- Your relative will be given the statin via a tube into their stomach. This tube is in place for most patients but may be required
- In addition to the Simvastatin, your relative will receive the standard donor care bundle.
- Your relative's organs may be donated, and if so, we will follow up with the people that receive the organs to see how they are doing. If the donation does not proceed your relative will still be in the trial.

Standard Care

- Your relative will receive all their care as standard. As part of the donor care bundle, this may include a tube into their stomach.
- Your relative's organs may be donated, and if so, we will follow up with the people that receive the organs to see how they are doing. If the donation does not proceed your relative will still be in the trial.

Does my relative have to take part?

No, it is your choice whether you decide to allow your relative to take part or not.

If you decide to allow your relative to take part, you will be asked to sign a consent/authorisation form to say that you agree for your relative to take part in the study.

If you do not wish for them to take part, this will not have any impact on your decision to donate your relative's organs. Your decision will not change the care provided to your relative.

You can change your mind and withdraw your relative at any point but any data already collected will be kept.

Who is organising the research?

This study is being run by Professor John Dark at Newcastle University and Dr Dan Harvey at Nottingham University Hospitals and is taking place in hospitals across the UK.

The Sponsor of this study is the Newcastle Upon Tyne Hospitals NHS Foundation Trust. The Sponsor has delegated overall management of this study to the Clinical Trials Unit at NHS Blood and Transplant.

The study is being funded by the National Institute for Health Research.

What if I have a problem?

If you have any concerns regarding your relative's treatment, you can contact the clinical team treating your relative.

If you have concerns and questions about the study, please contact SIGNET@nhsbt.nhs.uk and we can answer any questions or put you in contact with the research team at your hospital.

If you wish to complain about the treatment your relative has received as part of the study, you can contact the hospital's Patient Advice and Liaison Services (PALS).

In the event that something does go wrong and your relative is harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the NHS Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). The University of Newcastle has an insurance policy to cover harm arising as a result of the design of the study.

Please speak to the specialist nurse for organ donation or your local hospital for advice on local support services available to you. There is also support available through the national donor family network, please see the website for more information (https://www.donorfamilynetwork.co.uk/support/).

Will my relative's participation in this study be kept confidential?

We will need to use information from your relative's medical records and DonorPath for the study. All the information about your relative's participation in the study will be kept confidential. The information will be held securely in electronic format under the provisions of the Data Protection Act 2018 and the General Data Protection Regulation.

The Newcastle Upon Tyne Hospitals NHS Foundation Trust is the sponsor for this study based in the United Kingdom. We will be using information from your relative's medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your relative's information and using it properly. NHSBT are the data controller for the UK Transplant Registry.

Your rights to access, change or move your relative's information are limited, as we need to manage your relative's information in specific ways in order for the research to be reliable and accurate. If you withdraw your relative from the study, we will keep the information about your relative that we have already obtained. To safeguard your relative's rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://www.hra.nhs.uk/information-about-patients/ Please let us know if you would like a paper copy of this information.

The research team at your hospital will collect information from your relative's medical records for this research study in accordance with our instructions.

The research team at your hospital will keep your relatives donor number confidential and will not pass this information to The Newcastle Upon Tyne Hospitals NHS Foundation Trust.

NHSBT will collect information about your relative from the DonorPath registry. This will not be shared outside of NHSBT.

The Newcastle Upon Tyne Hospitals NHS Foundation Trust will only receive information without any personal identifiers. The people who analyse the information will not be able to identify your relative.

The research team at your hospital will keep identifiable information about your relative from this study for 5 years after the study has finished (or as required by subsequent clinical trial regulations).

Who to contact for further information

You are encouraged to ask any questions you wish before, during or after your relative's treatment. If you have any questions about the study, please speak to your study doctor/nurse or contact SIGNET@nhsbt.nhs.uk / 01223 588 016.

What will happen to the results of the study?

- The results of this study will be submitted for publication in medical/scientific journals
- Presented at medical/scientific conferences
- To try and improve the care of people undergoing organ transplant in the future the results will be made publicly available

Your relative will not be identifiable in any publications.

Thank you for taking the time to consider participating in the SIGNET study.