Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration (REALIST)

Covering statement, patient information leaflet and consent to continue form
IRAS ID: 227090

A study to determine the effect of a single intravenous infusion of Mesenchymal Stromal Cells (MSCs) in patients with Acute Respiratory Distress Syndrome (ARDS).

You are being invited to continue to take part in a research study called REALIST. The Intensive Care doctors diagnosed you with ARDS while you were in the Intensive Care Unit and your relative/friend/partner or doctor gave consent on your behalf whilst you were not well enough to make the decision for yourself. Before you decide whether you continue taking part it is important for you to understand why the research is being done and what it involves. Therefore we ask if you would read the information sheet carefully and give your opinion as to whether or not you would be willing to continue to participate in this medical research. Please take time to read the following information carefully and discuss it with your doctor and other people if you wish.

If you have any further questions either now or at any time subsequently, please feel free to contact a member of the research team (details at the end of the Information Sheet).

Thank you for your time in considering this request.

Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration (REALIST)

What is the purpose of the study?

For reasons that are unclear when people are critically ill, their lungs often fail which is termed the Acute Respiratory Distress Syndrome (ARDS). ARDs is characterised by widespread inflammation in the lungs which impairs lung function. Patients need to be admitted to the Intensive Care Unit (ICU) and often need to have a breathing machine, or ventilator, to help them breathe and ensure that enough oxygen gets into their blood. Currently, there are no specific drugs or interventions that can be used to treat patients with ARDS.

What are Mesenchymal Stromal Cells (MSCs)?

Mesenchymal Stromal Cells (MSCs) are cells which originate in the human body and can help the body to repair. When MSCs are extracted and used as a treatment, they have been shown to reduce the body's immune response when it is overactive and causing damage.

These MSCs can be found in almost every part of our body, including bone marrow (the tissue inside some of your bones) and umbilical cord tissue (the tube that connects an unborn baby to its mother, through which it receives oxygen and food) after a baby is born. Adults have similar cells present throughout their life but with age are less potent.

Studies have shown that MSCs may be helpful when given to patients with other diseases. These studies to date show that treatment with MSCs is generally well tolerated by patients. The purpose of this study is to investigate if MSCs can improve outcomes in patients with ARDS. We plan to use MSCs obtained from umbilical cords which will be collected from mothers with their consent after childbirth.

Although these cells are from a source other than you there is no clear evidence that they will be rejected or cause any genetic mutations.

We will determine the safety and ability of MSCs to improve lung function in patients with ARDS. We will also take samples of blood, urine and fluid in the lung to allow us to determine the ways in which ARDS develops and how MSCs might work to improve the condition. Records will be kept allowing traceability between the MSC donor and the patient.

Why have you been invited?

The intensive care doctors have found that you were suffering from ARDS and spoke to either your relative/friend/partner or doctor looking after you to explain the study to them and seek their consent for you to participate in the study when you were not well enough to make this decision yourself. Neither the researchers nor the intensive care doctors know whether MSCs will help you recover more quickly. Therefore, we are inviting you to give consent for you to continue to take part in this study to help us find out if MSCs are beneficial for patients with ARDS. We plan to recruit up to 78 patients to join the study. Patients from several ICUs will take part.

Do I have to take part?

No. It is up to you to decide whether or not you continue to take part in the study. If you do decide to continue you will be given this information sheet to keep and will be asked to sign a study consent to continue form. You are still free to withdraw at any time and without giving a reason. If you decide not to take part the standard of care you receive will not be affected.

What will happen to me if I continue to take part?

The study is being carried out in 2 parts, you will only have been enrolled in either part 1 or part 2.

Part 1 of the trial is to determine the best dose to use for the second part of the trial. Part 1 will involve 3 groups of patients, consisting of 3-6 patients in each group. The first group will receive a low dose of MSCs. If the dose is well tolerated, the following

group will receive a higher dose of MSCs and if this dose is well tolerated, then the final group will receive the highest dose, which is the dose we aim to use in part 2 of the trial.

Patients who are enrolled in part 2 of the trial will be put into one of two groups. It is not possible to know which group you are in; this will be decided by chance. One group receives the MSCs once only and one group receives a dummy infusion (placebo). Both the MSCs and placebo will have a similar appearance and it will not be possible to determine which treatment the patient is receiving. Patients have a 1:1 chance of receiving MSCs or placebo; 30 patients will receive MSCs and 30 will receive the placebo, totalling 60 patients to complete the study. When you received the study treatment, neither you, nor your relative/friend/partner nor the doctors and nurses knew which group you are in, although the doctors can find out if they need to. This type of study is called a randomized, double-blind, placebo-controlled trial and it ensures that the treatment is tested fairly.

The medical notes will be reviewed by the doctors and nurses, to find out if the treatment that you have received has had any effect. The study team reviewed your progress on a daily basis whilst a patient in ICU.

Samples were also taken whilst you were in ICU to allow the study team to determine the ways in which ARDS develops and by which MSCs might work to improve their condition. We may share these samples, which will be anonymised, with investigators in the UK or internationally for more specialised tests to help us understand ARDS.

A procedure called a bronchoalveolar lavage (BAL) may have been performed at the start of the study and on the fourth day of the study. BAL involves the passage of a flexible tube (bronchoscope) with a light and video camera, which sends pictures to a television screen in the room. The bronchoscope is passed through a tube already in your throat and down into a lung. Some salty water is flushed into a small part of the lung and drawn back up again then the bronchoscope is removed. This is a well-

recognised safe procedure often undertaken often in ICU to look at lung inflammation. If the procedure was performed, you would have already been sedated but extra sedation may have been used if needed and some local anaesthetic may have been used to make the procedure comfortable for you. This procedure can rarely be associated with a fall in oxygen levels. Prior to inserting the bronchoscope, the amount of oxygen will have been increased and we closely monitored these levels during the test. The test would have been stopped if the oxygen level fell significantly. This procedure would not have been performed if the consultant in charge of the ICU had any concerns whatsoever.

We will contact your GP to let them know of your participation in the study. After discharge from hospital we will follow-up on your medical status either by telephone, contact with the GP or review of your health care record to 2 years following treatment. We may also use NHS Digital if available in your region to confirm contact details and medical status. Where possible, participants in the trial will have blood samples taken at 1 and 2 years following treatment. A member of the trial team will contact you and if it is possible to do so, arrangements will be made for you to attend a suitable healthcare facility to have samples taken.

Storage of Samples

The samples taken will be stored in anonymised format in Queen's University Belfast. Samples are always stored according to appropriate regulations. We would like to store your samples indefinitely, however if you do not want this it does not affect your participation in the study and any samples will be disposed of when the study analyses are completed. The reason we want to store samples is that if new information or techniques are discovered in the future this will allow us to use the samples stored to investigate if this new information is important for patients who have ARDS. Future tests may involve genetic analysis. We may share samples with other investigators or commercial organisations in the UK or internationally, to help further understanding of ARDS. If this is happens, the samples shared would be anonymous and external investigators or organisations would not be able to identify you. The anonymized data collected as part of the study may also be used to understand the sample analyses. If future studies are to be carried out on the stored

samples the investigators will first obtain an Ethics Committee approval, if additional to the analyses planned as part of this trial.

What are the possible benefits and disadvantages of taking part?

Taking part in this study may contribute to improved treatment of patients with ARDS in the future. The treatment may have side effects that no one knows about yet and this is the reason for follow up over 2 years. Many patients have been treated with MSCs for a variety of conditions and to date no long-term harms including cancer have been reported. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

What if something goes wrong?

If you have any concerns about any aspect of this study, you should contact the local Principal Investigator (contact details below), who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the normal NHS Complaints Procedure.

If something does go wrong and you are harmed due to someone's negligence, then you may have grounds for a legal action against your NHS Trust, but you may have to pay their legal costs.

Would your taking part in this study be kept confidential?

Any information which is collected about you during the course of the study will be kept strictly confidential and will only be seen by staff involved in the study from the NHS Trust, Trial Co-ordinating centre, Belfast Health and Social Care Trust and people from regulatory authorities who ensure that studies such as this are carried out correctly. All of them will have a duty of confidentiality to you as a research participant.

In addition, information held and maintained by central UK NHS bodies, and organisations contracted to provide services to the NHS, may be used to access data collected routinely during your stay in hospital and to ascertain your long term health status. In this instance only your NHS number/hospital number and date of

birth will be used and held by the Trial Co-ordinating Centre, all other personal data will remain anonymised. This information will be used only for this study and will not be given to anyone else.

Because we may need to contact you after you leave hospital, the Trial Co-ordinating Centre will need to keep records of your name, address and other contact details.

You have the right to see your personal health information related to the research study, but you will not be able to review some parts of the information until after the study has finished. When any information from the study is published it will contain no personal information and it will not be possible to identify any individual.

The data from this study will be kept for at least thirty years after its conclusion and may be used in other research studies and data may be retained by Belfast Health and Social Care Trust and Queens University of Belfast. If it is used in this way all personal identifiers will be removed and it will not be possible to identify any individual.

What will happen to the results of the research study?

The study is expected to take 2-3 years, commencing in March 2018. It is envisaged that publication of the results will follow shortly after this, through medical publications, websites and press releases. At this point we will be happy to forward a summarised version of the principle findings of the results of the study at your request. This can be requested through the Northern Ireland Clinical Trial Unit (NICTU), contact details can be found at the end of this leaflet.

Who is organising and funding the study?

REALIST is being organised by a group of doctors and scientists led by Professor Danny McAuley, who is a consultant in Intensive Care Medicine at the Royal Hospitals, Belfast, Northern Ireland. It is funded by the Wellcome Trust Health Innovation Challenge Fund. The sponsor of the study is the Belfast Health and Social Care Trust.

Who has reviewed the study?

This research has been reviewed and given a favourable opinion by an independent group of people, called a Research Ethics Committee (REC), to protect your safety, rights, wellbeing and dignity. The Ethics Committee is completely independent from the trial. The study has also been reviewed by the regulatory body, the Medicines and Healthcare Products Regulatory Agency (MHRA).

What happens if I have any questions, concerns or complaints about the study?

If you have any questions about your participation in this study or concerns about the way it has been carried out, you should contact the local Principal Investigator, member of the research team or for independent advice [insert local name] (contact details below).

What happens if I don't want to carry on with the study?

You are free to withdraw your consent to participate at any time and without giving a reason. This will not affect the standard of care you receive. You have the right to request samples collected as part of this study to be destroyed and no further laboratory analysis to be performed. Your study doctor can take you out of the study at any time if it is in your best medical interests to stop your participation.

If you have any questions that remain unanswered, the study doctor or research nurse will be happy to answer these for you. If you require any further information you may contact the local Principal Investigator or the co-ordinating centre as below.

Thank you for taking the time to read this Information Sheet.

Contact details:

Chief Investigator:

Name: Prof Danny McAuley

Address: Regional Intensive Care Unit

Royal Hospitals

Grosvenor Road

Belfast, BT12 6BA

Telephone: 028 961 50690

Principal Investigator:

Name: «name»

Address: «address»

Telephone: «telephone»

REALIST Co-ordinating Centre:

Address: NI Clinical Trials Unit

1st Floor Elliott Dynes Building

Royal Hospitals

Grosvenor Road

Belfast, BT12 6BA

Telephone: 028 96151447

Complaints/concerns:

Name: «name»

Address: «address»

Telephone: «telephone»

Belfast Health and Social Care Trust is the sponsor for this study.

How will we use information about you?

We will need to use information from you, from your medical records, your GP, NHS Digital, national clinical audit databases, central UK NHS bodies and organisations contracted to provide services for the NHS for this research project.

This information will include your initials/ NHS Number/ Hospital number/ name/ contact details/ national clinical audit database number. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records/ your hospital/ your GP/ national clinical audit databases. If you do not want this to happen, tell us and we will stop.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. We can provide a list of the type of information we are collecting, upon request.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/

- our leaflet available from www.belfasttrust.hscni.net/about/DataProtection.htm
- by asking one of the research team
- by sending an email to [**email**], or
- by ringing us on [**phone number**].

NOTE: At least one of these sources must be able to point people directly to the sponsor's Data Protection Officer.

Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration (REALIST)

Regarding patient (please write patients name here): _____

Please initial each box

1. I confirm that I have received a personal copy of, and have read and understood the information sheet for the above study and have had the opportunity to ask questions and discuss the study. ☐

2. I understand that my participation is voluntary and that I am free to withdraw my consent at any time, without giving any reason and without my medical care or legal rights being affected. ☐

3. I understand that sections of my medical notes may be inspected by responsible individuals from the NHS Trust, Trial Co-ordinating Centre, Belfast Health and Social Care Trust or regulatory authorities, where it is relevant to taking part in this research. I give permission for these individuals to have access to my records. I agree to information related to this research being retained at the NHS Trust, Trial Co-ordinating Centre, Belfast Health and Social Care Trust and the Queen's University of Belfast. ☐

4. I understand that the Trial Co-ordinating Centre will keep records of my name and contact details and may access information held by other central UK NHS bodies and organisations contracted to provide services to the NHS to access data collected routinely during my hospital stay, to facilitate follow up and to ascertain my long term health status. ☐

5. I agree to any biological samples that have been already collected to be analysed and the data generated from these analysis to be used. ☐

6. I agree to my samples being stored indefinitely so they can be used in future research in the event of new scientific research or techniques becoming available with regards to ARDS. ☐

7. I agree to my anonymised data being kept for at least 30 years after the study conclusion and it being used in other research studies, and I understand that they will not be personally identified. ☐

8. I understand the samples taken during this study may be shared with external non-NHS organisations to undertake the planned and future analyses, including genetic analysis, transfer abroad and commercial research. ☐

9. I understand that my data will be shared in an anonymised format in publications, at conferences, and in research data-sharing repositories, and I understand that I will not be personally identified. ☐

10. I agree to being followed-up by the research team to assess my medical status ☐

11. I agree to continue taking part in this study. ☐

Name of Patient	**Signature**	**Date (dd/mm/yy)**
Name of person taking consent	**Signature**	**Date (dd/mm/yy)**