Insert local NHS details

$NanO_2$ in Large VessEL Occlusion Stroke (NOVEL): a multicentre single-blind, randomised, placebo-controlled blinded biomarker end-point clinical trial of perfluorocarbon in acute ischaemic stroke due to large vessel occlusion

PARTICIPANT INFORMATION SHEET – SHORT Version for Emergency Care

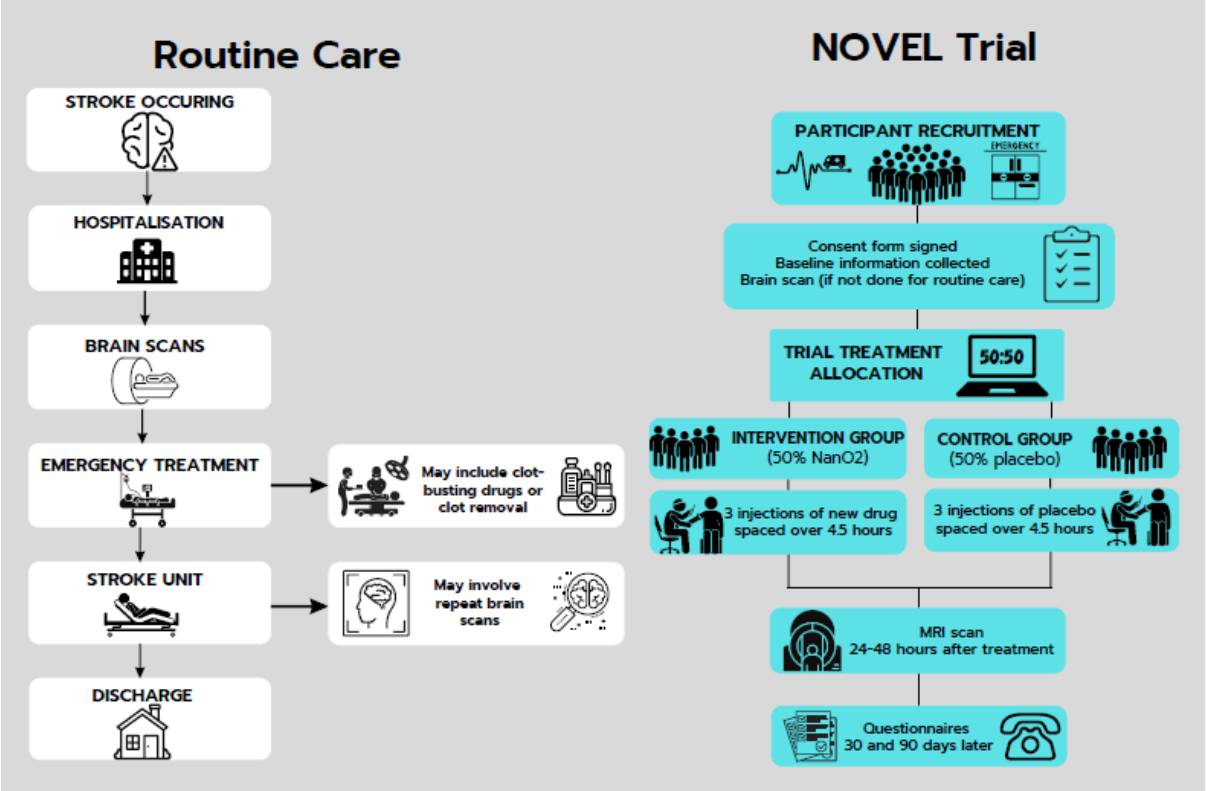
---

Invitation to take part in a research study

You are being invited to take part in this research study because you have been diagnosed with a stroke that has occurred within the past 9 hours. Since treatment decisions in stroke need to be taken quickly, the diagram below and accompanying participant information sheet give the essential details of the research study. Please feel free to ask if you would like more information.

Infographic

The following diagram shows the steps involved in the trial that will occur in parallel to routine care.



What is the purpose of this research?

We are investigating a possible new treatment to limit damage to the brain caused by a stroke, a medicine called $NanO_2$ that carries extra oxygen to brain tissue. We hope this might limit the damage caused by a stroke, particularly if given with other treatments to try and restore the blood supply to the brain.

The research team will check brain scans and medical information to see if you are suitable for the study. This may involve an extra scan of brain blood flow. If you are suitable, you will be allocated randomly to injections of either $NanO_2$ or a "dummy" (placebo). A total of three injections into a vein are given within 4½ hours. The first of these will usually be before any other stroke treatments are completed.

Most of your hospital treatment will be identical to routine care of people with a stroke. We will collect information about your routine care from your medical records, including copies of relevant brain scans. In addition, we will undertake a follow-up MRI brain scan between 24 and 48 hours after treatment to measure the amount of brain tissue affected. Brain scans will be sent for analysis at the University of Glasgow after your personal details have been removed. The study involves some additional physical examinations and measurements of blood pressure, heart rate and oxygen levels. You will be contacted by telephone around 30 and 90 days after the stroke to check on your recovery using questionnaires about how you are able to manage day-to-day activities.

What are the risks of taking part in the study?

$NanO_2$ has been given experimentally to more than 2000 people with various medical conditions, including a small trial in 24 people with stroke. Possible side effects were usually mild to moderate and resolved quickly. Symptoms included feeling sick (nausea), vomiting, drowsiness, headache, cough, high and low blood pressure and dizziness. No consistent side effects or safety concerns have been identified when used to treat stroke, but as with all new medicines, experience of $NanO_2$ is limited and we will record information about any unexpected symptoms during the study. There may be other unforeseen risks which are not currently known.

It is not possible to know if you will benefit personally from taking part in the trial even if you are treated with $NanO_2$ and there is no guarantee that you will benefit in any way. The main benefit will be to provide information that may help with treatment of future patients.

Who is organising and funding the research?

The research is funded by the National Institute for Health Research (NIHR). The study is co-sponsored by the University of Glasgow and NHS Greater Glasgow and Clyde. The company that manufactures $NanO_2$ (NuvOx Pharma) is providing the drug free of charge.

If you agree to take part, your personal data will be removed from study documents and scans, other than a separate record of contact details to allow a check on your recovery. You will receive all routine tests and treatments as normal.

If you do not wish to take part, this will not affect your medical care in any way.

Insert local NHS details

Thank you for reading this.

Chief Investigator

Prof Keith Muir
SINAPSE Professor of Clinical Imaging & Consultant Neurologist
University of Glasgow
Queen Elizabeth University Hospital
Glasgow
G51 4TF
Tel: 0141 451 5892

Insert local NHS details

$NanO_2$ in Large VessEL Occlusion Stroke (NOVEL): a multicentre single-blind, randomised, placebo-controlled blinded biomarker end-point clinical trial of perfluorocarbon in acute ischaemic stroke due to large vessel occlusion

PARTICIPANT INFORMATION SHEET (UK)

Invitation to take part in a research study

You are being invited to take part in this research study because you have been diagnosed with a stroke that has occurred within the past 9 hours. Before you decide to take part, please make sure you understand why the research is being done and what it will involve. Please feel free to ask us if there is anything that you find unclear or if you would like more information.

What is the purpose of this research?

We are investigating a possible new medicine to limit damage to the brain caused by a stroke.

Strokes that are caused by a clot blocking an artery in the brain ('ischaemic' strokes) starve brain tissue of oxygen and nutrients. After a short period of time without oxygen, this brain tissue can become permanently damaged. This study is investigating the effects of a drug called $NanO_2$. $NanO_2$ works by picking up some of the oxygen from the air that you breathe. This extra oxygen is then carried in the blood to the area of the brain affected by the stroke. By delivering extra oxygen to the affected brain tissue, it may allow the tissue to survive for longer. It might be especially useful to help prevent further damage happening if treatments to try and open the blocked blood vessel are given. Treatments may include 'clot-busting' drugs, or procedures to physically open a blocked artery. These treatments are very effective, but take time to successfully open the blockage.

The study will involve treating people as soon as possible after they are admitted to hospital with a stroke, and comparing brain scans before and after treatment. Up to 172 patients will take part in this study.

What does the study involve?

Taking part in this study is additional to routine treatment for stroke. Routine tests and treatments, including clot-busting drugs or physical removal of a clot, will be given if required, and done as quickly as possible. Treatment will not be delayed by trial involvement.

Most people who are being considered for these treatments will have scans of the brain and blood vessels, and many also have scans of blood flow in the brain. If you agree to take part and some of these scans have not been done as part of your routine care then they will be done as extra scans to check if you are suitable for the study. It is possible that scans may show that you are not suitable to take part in the study (for example if the area of reduced blood flow is too small), in which case we would not continue with other study procedures and you would not receive the study medicine. If you are not suitable to take part then you will receive the usual care for your condition.

The research team will make sure that all of the necessary scans of the brain and blood supply have been done. If these confirm that you are suitable for the study, you will be allocated to receive injections of either $NanO_2$ or a "dummy" treatment (placebo). This is done randomly by a computer (like tossing a coin) to ensure that the results are unbiased. You will have a 50:50 chance of being in the group that receives $NanO_2$. You or the doctors will not be able to decide which treatment you are given and you will not be told what treatment you will receive.

$NanO_2$ (or the placebo) will be given as an injection over 3-5 minutes into a plastic tube placed in a vein. There will be three injections in total. The first dose will usually be given either before, or shortly after the start of other treatments (clot-busting drug treatment or a procedure to remove a clot) that are planned. Two further doses will be given in the next 4½ hours.

We will collect important information about your stroke from your medical records including copies of relevant brain scans, medical background, and details of the stroke and any routine treatments.

In addition, we will collect some details that are extra to your routine care including questionnaires and checks on your recovery, some measurements of basic body functions such as blood pressure and heart rate, and an additional brain scan to check on the outcome of the stroke.

What will happen if I decide to take part?

If you agree to take part in this study, you will be given this information sheet to keep and once the study has been explained to you and any questions answered, you will be asked to sign and date a consent form. Most of the study activities will happen in the first few days in hospital, but in total you will be involved in the study for around 90 days (depending on the date your final check is scheduled). Your personal involvement will stop after this time. You will also be asked to give permission for us to record details from your medical records relating to your medical history, other treatments, details of the stroke itself, and your recovery over this period.

Many of the tests and medical checks for this study are part of routine care for people with stroke. The research team will check the following from your medical records:

Routine care

- Your medical history, including medications
- Details about the stroke (for example the time symptoms started, and what symptoms were experienced), treatment, and findings from neurological examination.
- Results and copies of scans related to the stroke, usually CT or MRI scans of the head, the blood vessels and the blood supply to the brain before and after treatment.
- Results of blood tests including blood count, kidney function and blood sugar.
- Recordings of your blood pressure, heart rate, temperature and oxygen levels.

Extra things that are done for the study

- You will already have had scans of the brain and the blood vessels supplying the brain as part of your routine care. If you have not had a scan of blood flow to the brain as part of your routine care, then this will be done as an extra scan. It involves an injection of a contrast agent into a vein, the same as done for the scan of your blood vessels. The CT scanner takes a series of scans over about 1 minute from which we can calculate the blood flow. This scan allows us to see how much tissue has poor blood flow.
- If you are suitable for the study you will be given injections of either $NanO_2$ or placebo. There will be three doses in total, spread over 4½ hours.
- You will undergo an MRI scan of the head between 24 and 48 hours after the stroke to check how much tissue has been affected. If an MRI scan cannot be done then an extra CT scan might be done as an alternative.
- Some extra recordings of your blood pressure, heart rate and oxygen levels may be done in the first 24 hours.
- The research team will undertake an extra check on the effects of the stroke on your day-to-day function (using questionnaires) approximately 30 and again at 90 days after the stroke. This involves questions about activities such as washing, dressing, eating, walking and whether there are any restrictions on your activities. To do these checks, a member of the research team based in Glasgow will contact you by phone. Depending on your health at that time, we may also need to speak to your GP, a relative, or other healthcare staff to answer any questions

What is involved in an MRI scan?

MRI scans are routinely used for scanning the brain and do not involve radiation. MRI scanning uses a strong magnet, so you or a relative will be asked to complete a checklist to make sure that you have no metal implants, heart pacemakers or other devices that would not allow scanning.

The research study involves a routine MRI scan and will usually take 30 minutes or less. The scanner itself is noisy and some people feel claustrophobic, but scanning staff will check on you during the scan and you will have ear protection. The scan can be stopped at any time.

What is involved in a CT scan?

CT scanning is a routine scan that uses X-rays. If MRI is not possible for follow-up scanning then a repeat CT scan of the head can be done as an alternative. Scanning is routine as part of follow-up in many patients, and if a scan has been done as part of your routine care in the right time frame then we will use this for the study and will not need to do any extra scans.

If an extra scan of brain blood flow is needed for the study then this will also involve an injection of a "dye" also known as a contrast agent. The contrast agent is usually well tolerated and is washed out of the body through your kidneys. Side effects include headache, feeling sick, and flushing. Rarely (may affect up to 1 in 1000 patients) low blood pressure and light-headedness and allergic reactions including rash, which can be serious, can occur.

What are the risks of taking part in the study?

As with all new medicines, there is **limited experience** of $NanO_2$ and it is not currently approved for the treatment of any condition. $NanO_2$ was first developed in the early 1990s as a possible aid to ultrasound scanning, where it was given experimentally to more than 2000 people. Possible side-effects when used as an aid to ultrasound were mild to moderate in intensity and included feeling sick (nausea), vomiting, drowsiness, headache, high and low blood pressure and dizziness. Side-effects usually resolved quickly.

Like all medicines $NanO_2$ may cause side effects although not everyone will be affected. In theory, larger bubbles of $NanO_2$ could form in the lungs which could be harmful but this has not been seen in studies with patients and measures have been put in place to minimise the risk. In a small trial involving 24 people with stroke in the USA, patients were found to have high blood pressure and reported cough, headache and muscle pain but as yet no consistent side effects or safety concerns have been identified when used to treat stroke. There may be other unforeseen risks which are not currently known. Throughout the study we will monitor you carefully and record information about any possible symptoms related to your involvement in the study. You should also tell the research team about any symptoms you experience.

We do not expect side-effects to occur due to placebo treatment.

CT scans involve radiation. Some of these scans may be extra to those that you would have if you did not take part in this study. These procedures use ionising radiation to form images of your body. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study may increase the chances of this happening to you to about 50.1%.

Extra considerations about pregnancy (relevant for both women and men)

Since there is no information yet about the safety of $NanO_2$ in an unborn child, you will not be able to take part in this study if you are **pregnant** or breast-feeding. If you could become pregnant, you will be required to have a pregnancy test before proceeding with the study. This is not necessary if you are post-menopausal (your regular menstrual periods have

stopped for a minimum of 12 consecutive months with no other cause), have been permanently sterilised (including hysterectomy), or have medically confirmed ovarian failure.

Once given, $NanO_2$ is quickly removed from the body so there are no special contraception measures required for men with female partners who could have a child or for women who could have a child.

If you think your partner may have become pregnant, please tell the study team immediately. With your partner's consent the study doctors would like to collect information about your partner's pregnancy and the health of your partner and their baby.

Will my treatment be affected?

You will continue to receive all treatment or tests that your doctors think are required. No routine treatment or tests will be delayed or left out if you take part in the study. If clot-busting drugs or procedures to remove a clot physically are needed, then you will receive this treatment. All routine scans will be done as deemed necessary by your clinical care doctor.

Will I benefit from the study?

It is not possible to know if you will benefit personally from taking part in the trial even if you are treated with $NanO_2$ and there is no guarantee that you will benefit in any way. The main benefit will be to provide information that may help with treatment of future patients.

Who is organising and funding the research?

The study is being led by Professor Keith Muir (University of Glasgow) and is taking place in hospitals across the UK. The Principal Investigator (PI) at this site is *<NAME>*

The study is co-sponsored by the University of Glasgow and NHS Greater Glasgow and Clyde.

The research is funded by the National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation programme.

The US company that manufactures $NanO_2$ (NuvOx Pharma) is providing the medicine free of charge.

No member of the research team is being directly paid or given incentives for including you in the study.

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to your study doctor who will do their best to answer your questions.

In the event that something does go wrong, there are no special compensation arrangements. NHS Greater Glasgow and Clyde is a member of the Clinical Negligence and Other Risks Indemnity Scheme (CNORIS) which covers the Sponsor's legal liability in

relation to clinical trials; this includes clinical negligence. Clinical negligence is also covered by the participating sites' own insurance schemes.

Harm from study design is covered by the University of Glasgow's clinical trials insurance. If you are harmed due to someone's negligence, or your participation in the study, you may have grounds for legal action for compensation, but you may have to pay your legal costs.

The normal National Health Service complaints mechanisms are available if you wish to complain or have any concerns *[insert local hospital complaints phone number].*

What information will be used for the study?

We wish to record details of relevant medical conditions, information about the stroke itself (for example the time symptoms first appeared, the problems that it caused, any treatment given, and the results of other tests), and your progress over the 90 days post treatment. In order to do this we will need to collect personal information including your NHS or CHI number, name and contact details.

All relevant CT and MRI scan pictures will be saved on computer files for analysis. Your personal details will be removed from all records and computer files. Scans and documents will include a study number. Scan files will be transferred for analysis to the University of Glasgow, and will be stored longer term at the University of Glasgow.

Will my taking part in this study be kept confidential?

All information about your participation in the study will be kept confidential. The information will be held securely and anonymously in electronic format under the provisions of the Data Protection Act 2018 and the General Data Protection Regulation. Your data will be stored in a secure database held in the University of Glasgow. Your contact details will be stored in a separate secure database at the University of Glasgow to allow the research team at University of Glasgow/NHS Greater Glasgow and Clyde to contact you to undertake follow-up assessments by telephone, email or post. Your completed consent form for this study will be securely sent to the University of Glasgow where it will be stored with restricted access. Where identifiable data are collected access will be limited to the study monitors and research team wherever possible, but it may become necessary for other members of the trial team from NHS Greater Glasgow and Clyde and the University of Glasgow to access this data under certain exceptional circumstances. All members of the trial team are appropriately trained in the use of data collected from participants and will not access this data without reason. Your participation will be noted in your medical records and, if you consent to the study, your GP will also be informed.

If you agree to take part in this study, approved members of the study team will be able to access your medical records where it is relevant to you taking part in this study. It is a requirement that relevant sections of your medical notes and research data may be looked at by responsible individuals from the research team, research regulatory authorities, the NHS or monitors appointed by the study sponsors to check that the research is properly conducted and the interests of those taking part are adequately protected. Some of your

information collected as part of this study may be shared with NuvOx Pharma. Information may also be shared with a company called Ariello. Ariello will monitor safety data of $NanO_2$ on behalf of NuvOx Pharma. No identifiable information will be shared with Ariello or NuvOx Pharma.

No participants will be named or identified in any way in any public report and it will not be possible to identify any individual from the study results. You will be given an option to receive a summary of the study results.

Since it is important that we make the most of medical research data, we may in future undertake further analysis of the data from the study. We may also share de-identified data from the study, including brain scans, with other researchers, both in the UK and in other countries, with the aim of improving understanding and treatment of stroke. No personal data will be shared.

Do I have to take part?

No, it is up to you to decide whether or not to take part in this study. Taking part in medical research in the UK is entirely voluntary and you should feel under no pressure to take part if you do not think it is right for you.

A member of the study team will discuss the study with you and what it involves. You can then make an informed decision on whether or not you wish to take part.

You are free to withdraw from the study at any time without giving a reason. If you decide not to take part or change your mind at any time, this will not affect your current or future care in the NHS. If you decide not to take part then you will receive the usual care treatment(s) for a patient with your condition.

Your participation in this study may also be stopped at any time without your consent if it is in your best interests, or if you do not consent to continue in the study after being told of changes in the research that may affect you. The study organisers (Sponsors) may also decide to stop the study.

What if new information becomes available?

We will let you know during the period of your involvement in the study if there is new information about the risks and benefits of $NanO_2$ that could affect your willingness to continue to take part in the study.

Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. This is done to protect your safety, rights, wellbeing and dignity. The study, this Participant Information Sheet, Informed Consent Form and other study documents have been reviewed and given a favourable opinion by <REC NAME> (reference number XXXXX).

The study has also been reviewed by the Medicines and Healthcare products Regulatory Agency (MHRA), the UK competent authority.

The study is registered on XXXXX

Can I get further information about the study?

You are encouraged to ask any questions that you may have before, during or after treatment. If you have any specific queries about any aspect of this study, please speak to the researchers who will do their best to address any questions or concerns. Your local research contact is:

<Name of local contact> <Telephone number and email address>

Can I get independent advice about taking part in the study?

Independent advice on this specific study is available from *<insert details>*

Thank you for reading this Information Sheet.

Disclaimer

The University of Glasgow and NHS Greater Glasgow and Clyde are the co-sponsors for this study based in the United Kingdom. We will be using information from you and/or your 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 information and using it properly. The University of Glasgow and NHS Greater Glasgow and Clyde will keep identifiable information about you for the duration of the trial.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information by contacting the Data Protection Team at https://www.nhsggc.org.uk/patients-and-visitors/faqs/data-protection-privacy