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ENOS–2
Efficacy of Nitric Oxide in Stroke-2

ENOS-2: Efficacy of Nitric Oxide in Stroke trial-2

Patient Information Sheet Final version 1.3

Date: 12th April 2022

You have been invited to take part in our research study

- We would like you to consider continuing to take part in our research study.
- It is important you understand why the research is being done, and what it would involve if you continued to take part.
- Please take time to read this information. Please ask if you would like more information.
- It is up to you to decide if you wish to continue to take part. If you agree, you are free to withdraw at any time without giving a reason. If you choose not to continue to take part, your medical care will continue in the normal way.
- Thank you for reading this information.

Important things that you need to know

- High blood pressure is common in the first hours and days following a stroke (blockage or bleed in the brain) and increases the risk of patients not making a full recovery
- We are testing a blood pressure lowering patch (GTN) put on your skin for 2 days starting as soon as possible today to see if it helps your recovery from your stroke.
- You will either receive the blood pressure lowering patch or a patch that doesn't have any medicine in it.
  - You will receive all the care you would normally receive whether you are in the study or not.
  - During the study you will have/have had an extra head scan and may have some extra blood pressure measurements and blood tests.

How to contact us

If you have any questions about this study, at any time, please contact the research team at:-

☎ Local details to be inserted

1. Why we are doing this study?

When someone has a stroke (either a blockage or bleed in the brain) there are a few hours after the symptoms begin where the brain cells are at risk of dying but may still be saved. It is possible to give treatments for stroke to help save these 'at risk' brain cells during the few hours and therefore prevent further injury. New treatments are being developed to treat stroke more effectively, but it can be very hard to test whether they work in the first few hours because often patients take longer than this to get to hospital.

High blood pressure is common in the first hours and days following a stroke and increases the risk of patients not recovering fully and being left with some disability. Lowering blood pressure in the first hours and days after stroke with medications might help patients to recover. Although at present we routinely treat high blood pressure for months or years after a stroke, we do not do so immediately after the stroke.

So, in this trial, we are testing a treatment that lowers blood pressure when given immediately on arrival at hospital and soon after patients have had a stroke.

The treatment is called glyceryl trinitrate (commonly known as GTN) and it is a tried and tested drug in other medical conditions such as angina (severe pain in the chest). It acts quickly to relax blood vessels and lowers blood pressure which is very important after stroke. The blood pressure lowering patch has also been tested in more than 4000 patients with recent stroke and was safe and lowered blood pressure. Of these, a few hundred patients received treatment between 3 and 5 hours after stroke and appeared to benefit with less disability. We now need to test more patients in this narrow time window. We do not want to treat earlier than 3 hours, or after 5 hours, because lowering blood pressure with GTN appears not to be beneficial then.

The results of the trial will help doctors decide whether blood pressure lowering treatments like GTN should be given to patients soon after they have a stroke to give them a better chance of getting back to normal.

2. Why have I been invited to take part?

You have been asked to take part because we treated you immediately on admission to hospital with a skin patch containing either the medicine which lowers blood pressure or a patch which looks similar but which doesn't contain any medicine. We used either verbal consent (you or your relative said you would like to take part) or did not take consent to accelerate giving you this treatment and to prevent delays to routine care including brain scanning, and dissolving a blood clot if you had a stroke of blood clot type. We would like around 120 patients who have had a stroke to take part in the study.

3. What will I have to do if I take part?

We will explain the study to you and if you agree to continue to take part, you will be asked to sign a consent form. The consent is so we can contact you in the future to see how the treatment worked. If you have some problems signing then either a relative can sign for you or we can record that you have said that you have would like to continue to take part.

You will have had all the normal medical tests and treatments for your stroke. The hospital staff will/have then put a new patch on your back the day after your

stroke. If you leave hospital before then, you won't need any more patches.

Both patches will be the same – that is all will have blood pressure lowering medicine or won't have any medicine in them. The decision about what patches you get will be decided by chance (rather like tossing a coin) and neither you nor the doctor or nurse are able to choose. This is called randomisation and is done by a special computer programme. This is important as it makes sure equal numbers of patients receive each treatment. This means it is a fair test between treatments.

The patch is covered in gauze to try to make sure that you, your relatives and friends and the medical staff do not know what treatment you have had. This makes the design of the trial better.

If you continue to take part in the study, you will still receive all the care that you would normally receive after a stroke.

A researcher will discuss the trial with you when you are in hospital and answer any questions you or your relatives/friends may have.

In around 3 months from now a researcher will telephone you. They will ask a number of questions to see how well you have recovered from your stroke. The researcher will not know what treatment you have had so if you have guessed please don't tell them.

You are free to stop taking part in the study at any time, without giving a reason. This will not affect the standard of care you receive now or in the future.

4. Possible disadvantages or risks

All drugs have the possibility of side effects. The side effects from the blood pressure lowering patch are generally mild. They can include nausea, vomiting, and headache and we can treat this.

You must inform your doctor or member of the research team if you feel you have had any reaction to the medication, however small.

There is a risk that you could be allergic to the patches and have a skin reaction. If this happens the patch will be removed and the reaction will be treated. You wouldn't need to have any more patches.

If you take part in this study you will have had a head scan as part of routine care. This procedure uses radiation particles to form pictures of the head and provide the doctor with clinical information. This type of radiation can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Taking part in this study will increase the chances of this happening to you from 50.00% to 50.02%. We will/have also take/taken some extra blood pressure measurements, and take an egg-cupful of blood for biomarker and genetic analysis.

5. Possible benefits

Your participation in this study may reduce the symptoms of your stroke or improve your long-term recovery. However, we cannot promise the study will help you, and your participation is voluntary. The information we get from your involvement may benefit other people who may have a stroke in the future.

6. What happens after the study?

Your second patch will be removed on the third day after your stroke. You will continue to receive all the normal care for your stroke but have no more patches as part of the study.

The research team will also collect some data from your medical notes and from a central database.

7. Will my taking part be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, we will use information collected from you [and your medical records] during the course of the research. This information will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database by the University of Nottingham. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at:

https://www.nottingham.ac.uk/utilities/privacy.aspx.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

8. Results of the study

The research findings from this study will be published in medical journals, presented at medical conferences and made available to patient groups/relevant charities. You will not be identified in any way in any publications or reports arising from this study. If you would like a summary of the study findings, we will ask you to provide an address we can send these to.

9. What if there is a problem?

We hope that we have reassured you of all aspects of this research. However, if you have any concerns or questions about any aspect of this study please speak to the study team who will do their best to answer them for you.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure, Patient Advisory and Liaison Service (PALS). Details are available below.

In the event that something does go wrong and you are harmed during the study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation but you may have to pay your legal costs. The normal National Health Service complaints process will still be available to you.

10. Who has reviewed the study?

This study has been reviewed and given a favourable opinion by the Greater Manchester South Research Ethics Committee (REC). The REC looks after the rights, wellbeing and dignity of people invited to take part in research studies. The study has also been reviewed by the University of Nottingham (who is sponsoring this research for the Chief Investigator Professor Philip Bath – a leading stroke researcher), and the Nottingham University Hospitals Charity (which has funded the study).

Thank you for your time

Local PALS details to be inserted