Part 1 Patient Information Sheet

TARDIS

Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke

Sponsored by the University of Nottingham

Local Investigators: ……

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.
Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Unfortunately you have suffered a stroke. Your stroke has been caused by a blood clot blocking a blood vessel that carries blood to one part of the brain.

The current guidelines recommend using a drug called clopidogrel or a combination of 2 drugs called aspirin and dipyridamole for stroke or transient ischaemic attack (mini stroke). They are antiplatelet (blood thinning) medications and work by acting on cells in your blood called platelets and reduce your risk of another stroke by making the platelets less 'sticky'. In this study we want to find out if intensive antiplatelet treatment using all three antiplatelet drugs is better than the current guideline treatment in preventing further strokes.

Why have I been chosen and do I have to take part?

You have been chosen because you have had a recent stroke or mini-stroke and we feel that you fit the requirements for this research project. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw from the study at any time and without giving a reason. The standard of care you receive will not be affected.

You cannot take part in the trial if any of the following apply to you:

- Age less than 50

- The symptoms caused by your stroke (or mini-stroke) lasted less than 10 minutes
- Intolerance of aspirin, dipyridamole or clopidogrel
- If your stroke is caused by a bleed
- If you potentially need other blood thinning drugs such as warfarin
- Extremely high blood pressure
- A history of significant bleeding within the past year
- Planned surgery in the next 3 months
- Dementia
- Recent heart attack (therefore needing to take clopidogrel)
- Participation in another drug trial
- Female of child bearing potential

What will happen to me if I take part?

The flow diagram below helps to summarise what will happen if you take part.

Day 0 (the day you enrol):

You will start your trial medications and we will ask you questions about your stroke, medical history and perform a medical examination. We will also take a small sample of blood (see below).

Day 7±1

We will ask how you are managing with the trial medications and that you have not had any other problems. If you have already been discharged from hospital then we can arrange to see you at home, or pay for transport for you to come and see us. A second blood test is also performed.

Day 35±3

We will test how you have recovered from your stroke by doing a neurological examination, ask if you have managed with the trial medications and also do a blood test to check that you are not anaemic. If you have been discharged from hospital then we can arrange to see you at home, or pay for transport for you to come and see us. We will see you on the ward if you are still recovering in hospital.

Day 90±7

This is the last assessment and done over the telephone. We complete a questionnaire about how you have recovered from your stroke, what you can do for yourself, a short memory test and questions about your quality of life and mood. If we cannot get in touch with you then we will send this questionnaire to you in the post.

End of the trial

The extra blood tests (about 8 teaspoons in total) will look at blood counts and other substances related to how platelets work. We would also like to see if variations in your genetic code are related to your stroke and if these genes affect how you respond to treatment (there is a separate consent form to sign if you are happy with this).

What do I have to do?

You will be allocated to receive either current guideline treatment (clopidogrel alone or combined aspirin and dipyridamole) or to have all three medications

(aspirin, dipyridamole and clopidogrel) for 1 month. All other medications will be continued as normal. We will need to see you at the times shown in the flow diagram.

What is the drug being tested?
The study is not testing individual drugs, but the safety and efficacy of intensive antiplatelet treatment versus current guideline treatment. The drugs being used in the trial are prescribed regularly for people who have had stroke or heart attack. They work by making the blood less sticky to help prevent further blood clots.

You have an equal chance that you will be asked to take aspirin, dipyridamole and clopidogrel or guideline treatment for one month. The guideline treatment may be clopidogrel alone or a combination of aspirin and dipyridamole depending on your local hospital guidelines and your doctor. After 1 month you will go back to recieving standard treatment.

What are the side effects of these drugs?
All the antiplatelets drugs used in TARDIS are commonly prescribed in stroke patients and so the side effects are well described. Clopidogrel may cause acid indigestion, diarrhoea or abdominal pains. Dipyridamole may cause headache, dizziness and indigestion. Aspirin may cause indigestion, buzzing or ringing in the ears, stomach ulcers or anaemia. Like all drugs, antiplatelet medications may occasionally cause allergic reactions such as skin rash.

However the most important side effect of antiplatelet medications is bleeding. It is usually minor such as bruising in the skin but can occasionally be major. In the first part of TARDIS, 2.1 patients out of every 100 patients had a major bleeding episode. We expect that the risk will be slightly lower in those patients on guideline treatment and slightly higher in those on intensive antiplatelet treatment.

It may be necessary for the doctors to start an 'anti-acid' tablet if you are not already taking one to help protect the stomach from bleeding risk. This 'anti-acid' tablet should not be taken at the same time as *enteric-coated* aspirin (to avoid premature drug release).

What are the possible disadvantages and risks of taking part?
The main disadvantage is that all three drugs together could cause bleeding. This will be monitored very closely by asking regularly about side effects and monitoring your blood counts. The total amount of time on all three medications will only be 1 month.

If you do notice any bleeding, then you must report it immediately as a large bleed can be fatal if it is not treated. If you are is still in hospital, you should tell the research doctor or the doctors and nurses on the ward. If you are out of hospital you should tell the research doctor or the GP. Bleeding can present itself in a number of ways and you should report any of the following symptoms:

- Bruising
- Heartburn, or acid indigestion
- Any new stroke symptoms (caused by
- Bleeding from the skin more excessively than normal if you cut yourself

a bleed in the brain) such as increased arm, leg and face weakness, new numbness, new speech or visual disturbances
- Vomiting or coughing blood
- Bleeding from the rectum or any black stools
- Nose bleeds
- Blood in your urine
- Blackouts

What are the possible benefits of taking part?
We think that the combination of the three drugs will reduce the chance of having another stroke so soon after this one. However, we cannot promise this and there may be no benefit. The information we get from this study will help in deciding the best treatments for stroke.

What happens when the research study stops?
Once you have completed your participation in the study, you will continue to take treatment that is usual for stroke based on current local and national guidelines..

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2.

Contact Details:
If you have any problems, concerns or other questions about this study, you should preferably contact the investigator first via _____ (Research Nurse / Medic), Tel _____. If you have any complaints about the way the investigator has carried out the study you may contact the hospital complaints department, Tel _____

This completes Part 1 of the Information Sheet.
If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2: Patient Information Sheet

What if relevant new information becomes available?
Sometimes during the course of a research project, new information becomes available that may have implications regarding your continuation in the study. If this happens, the research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, the research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form. Also, on receiving new information, your research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

What will happen if I don't want to carry on with the study?
You can withdraw from the trial at any time. We would appreciate if you keep in contact with us to let us know your progress. Information collected may still be used. Any stored blood samples that are identifiable can be destroyed if you wish.

What if there is a problem?
If taking part in this research project harms you (e.g. an allergic reaction) there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism is available to you.

Will my taking part in this study be kept confidential?
Yes. When you enter the trial your local research doctor or nurse will record information on your medical condition, your medical history and the progress of your treatment. Some of this information may be taken from your medical notes. This information will be used for the purpose of determining if the trial has any benefits. The information recorded will include details on the type of stroke, how severe it is and when it occurred, what tablets you take and your contact details. Scan data, which has been made anonymous, may be shared with allied research projects and used for education and research.

Your contact details, and those of a relative or friend that you provide, will be passed to the Trial Coordinating Centre in Nottingham and the National Coordinating Centre in your country. This will enable the three month telephone follow up to take place. All patient information is confidential and your GP will be notified of your participation in the trial.

The coordinating sites may use central databases to obtain additional follow-up information on patients enrolled into the trial. In the UK, this will involve use of the NHS Medical Research Information Service..

What will happen to any samples I give?
The blood samples will be tested or stored (frozen). These samples will be kept securely in a laboratory with access limited to research staff. The samples will be labelled in a confidential way at all times. After the blood has been tested the sample will be destroyed. You will not be told the results of the blood tests.

What will happen to the results of the research study?
The results of the study will be published in medical journals and sent to Health Authorities. However, any personal details will be kept strictly confidential and no information will be given through which you can be identified. At the end of the trial you will be able receive a summary of the trial results by contacting the research team on the numbers below, or you could view the results on the trial website (www.tardistrial.org).

Who is funding the research?
The British Heart Foundation is funding this study and no member of the research team is being directly paid for including you in this study.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people called a Research Ethics Committee to protect your safety, rights, well being and dignity. This study has been reviewed and approved by South East Research Ethics Committee.

Contact for Further Information
If you have any problems, concerns or other questions about this study, you should preferably contact the investigator first, via _____ (Research Nurse/Medic), Tel _____. If you have any complaints about the way the investigator has carried out the study you may contact the Hospital Complaints Department, Tel _____.

You will be given a copy of this Patient Information Sheet and a copy of the signed Consent Form to keep if you decide to take part.

Thank you reading this sheet.