CHOLINESTERASE INHIBITORS TO PREVENT FALLS IN PARKINSON'S DISEASE

CHIEF-PD TRIAL

PARTICIPANT INFORMATION BOOKLET

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Introduction

This leaflet tells you why you are being asked to help us with a research trial and what is involved. The second part of the booklet gives more detailed information.

Part one

Invitation

You are being invited to take part in a research trial organised by the University of Bristol. Please take time to read the following information carefully and talk to other people about it if you wish.

The first part of this booklet gives an overview of the trial. The second section provides more detailed information about the trial and how it will be conducted.

What is the purpose of the trial?

Falls are a common complication of Parkinson's and can lead to injuries and reduced confidence when walking. Previous trials have shown that drugs, called cholinesterase inhibitors, used to treat dementia and memory problems, make walking steadier and may therefore reduce the number of falls that people with Parkinson's experience.

This trial aims to determine whether the drug, rivastigmine, can prevent falls in people with Parkinson's.

To test whether the drug will work, people in the trial will be allocated into two groups. One group will be given the actual drug (the 'Active' group) and the other group a 'dummy' medication (the 'Placebo' group). The placebo looks identical to the active medicine but contains no active drug.

The trial is 'double blind' which means that neither the trial team, your doctor nor you will know which group you are in until the trial is over. In an emergency, a doctor could find out whether you are receiving the active or placebo (dummy) medication. You have a 1 in 2 (or 50%) chance of being in the group that receives the active drug.

If you take part, you will be asked to apply a patch to your skin to your arm, chest or back each day. This patch contains either the active or placebo medication. There are different medication strengths. Starting with the lowest dose, the strength will be increased so long as no troublesome side effects occur. You will take the medication for 12 months during which time you record the number of falls you experience, complete questionnaires and receive telephone calls.

Why have I been chosen?

You may have contacted the trial team or one of your healthcare specialists considered that you may wish to participate.

We are looking for people with Parkinson's **who have fallen in the past year** to take part. We aim to enrol 600 people with Parkinson's to the trial and would like you to consider whether you might be one of them. Once you have read the information, **please return the reply slip** in the envelope provided. If we do not hear from you, a member of the research team will telephone you to discuss taking part and answer any questions you may have.

Do I have to take part?

Taking part in this trial is entirely voluntary. We will describe the trial, go through this information and ask you to sign a consent form. You are free to withdraw from the study at any time without giving a reason. If you withdraw or if you decide not take part, then you will continue to receive normal care from your usual Parkinson's team.

Part two

What happens if I take part?

1. A few days after you receive the information sheet you will be phoned by one of the team

They will ask for some details about your Parkinson's disease and whether you have fallen in the past year and answer any questions you may have after reading the information. If **you would like to take part** and **are suitable** we will organise an appointment for you to attend your local site – which is often your nearest hospital.

2. You receive your appointment letter and questionnaires

You will receive a letter confirming your appointment and some questionnaires that ask about symptoms of Parkinson's. If you are able and willing, please complete these before your appointment. This saves some time but is not essential.

3. First trial visit

During your visit, the research team will ask you about having Parkinson's, your health and what medications you take. They will perform some short physical tests. The team will explain what taking part involves and answer any questions you have. If you agree to participate you will sign a consent form and your involvement in the trial will last for one year. If you decline to take part, you will not be asked to do anything else.

Once you are enrolled in the trial you will be allocated either the 'Active' (real) or 'Placebo' (dummy) medication. This process is done automatically by a computer system that randomly allocates you to one of the two groups. Some further tests of your memory, walking and physical function will be performed, and you will be asked questions about your quality of life, health and wellbeing.

At the end of the visit, you will be given the first pack of medication to take home with you as well as a diary where you will record any falls you have and the dose of medication you are taking. You may be given details of how this information can also be recorded online or using an app.

4. At home, apply the medication patches and record any falls

A booklet will tell you all about how to take the medication each day. In the diary you are asked to record what strength (low, medium or high) of patch you apply that day and any falls that occur. We ask that you post us this diary each month in the pre-paid envelopes that you will be given.

We will telephone you each month routinely to see how you are getting on with the medication, remind you which strength of patch to apply, check details of any falls you have had and answer any questions you have.

5. Collect more medication

The first pack of medication contains enough to last for 2 months. You will need to collect new medication packs after 2 months and after a further 5 months (i.e. 7 months after starting the trial).

6. Second trial visit

After 12 months, you will undergo similar assessments to those used in the initial visit. This will include the physical examination, blood pressure recording, questionnaires, walking tests and tests of Parkinson's.

What is the medication being tested?

The medication is called rivastigmine. It is currently used to treat people with different forms of memory impairment, including that associated with Parkinson's disease. We therefore already know a lot about its safety, effectiveness and side effects.

The medication comes in <u>patch form</u>. A patch is applied to the skin and replaced with a new one each day.

The medication strength will be increased at 2 and 7 months. If troublesome side effects occur, we may advise you stay on the current dose and not increase the strength.

Will it affect other medications I take?

The medication does not interfere with other Parkinson's medications.

You can continue taking all your other medications as normal throughout the trial. Your doctor can prescribe virtually all other medications normally. However, you would not have other drugs for memory prescribed at the same time.

If you were to need a general anaesthetic to undergo an operation, then it would be important to let the anaesthetist (the doctor who puts you to sleep for the operation) know that you are participating in this trial. The medication could be temporarily stopped for the day of the operation if necessary.

Does the treatment have any side effects?

The side effects are very common, but it is important to remember that not everybody encounters them and only affects around 1 in 10 patients. Common side effects (affecting 1 to 10 patients in 100) are feeling dizzy, loss of appetite, stomach problems such as feeling sick (nausea) or being sick (vomiting), diarrhoea and stomach aches, heartburn, indigestion, urinary tract infections, urinary incontinence, anxiety, depression, headache, feeling agitated or delirious, rash or skin reaction where the patch was applied unusually slow movements or movements you can't control or the signs of Parkinson's disease get worse or getting similar signs – such as stiff muscles.

Some patients are at higher risk of developing side effects from the medication used in this trial. If you have any of the following conditions your doctor and the research team will talk about this before you agree to take part:

- Heart rhythm disturbances (called Sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block)
- Predisposition to, or active stomach ulcers
- Increased risk of urine obstruction or seizures
- History of asthma or obstructive pulmonary disease (COPD).
- Significant liver impairment

If you decide to take part in the trial, we will give you very detailed information about the patches including how to apply them and what to do if side effects occur.

What will happen if I get side effects?

Depending on how severe the side effect was we may suggest:

- Continuing with the patches and seeing if the symptoms resolve
- Seeking treatment for the side effect e.g. from your GP
- Reducing the strength of dose
- Stopping the medication completely

If you have to stop the skin patches because of side effects, it is still very important that you come to the final appointment at 12 months **and** complete the fall diaries and questionnaires.

What about expenses and travel?

It is not anticipated that you will incur any costs by participating in this study. Your local team may be able to help organise transport to and from the hospital and will cover the cost of reasonable travel expenses including parking. We will give you prepaid envelopes to return the diaries.

What will I be expected to do?

You will be asked to (a) attend hospital twice for the assessments and twice to collect study medication, (b) take the study medication as directed (c) complete questionnaires and diary and receive monthly telephone calls from the research team.

What are the alternative treatments?

Physiotherapists often work to improve the strength and balance of people with Parkinson's who fall. You can still have physiotherapy if you take part in this trial and continue your normal Parkinson's medications as well as any drugs you take for other conditions.

What are the risks and discomforts of taking part?

Study Visits

Once enrolled, you will need to attend hospital on two occasions for about two and a half hours. These visits are in addition to your normal visits to your Parkinson's specialist. The assessments are quite detailed and therefore may cause tiredness and fatigue. Every effort will be made to ensure you are comfortable.

Possible Side Effects

Like all medicines, the treatment can cause side effects, although not everybody gets them. You may experience side effects more frequently when you start your medicine or increase the dose. In most cases side effects will gradually disappear as your body gets used to the medicine. Because the medication is already used to treat memory problems we know a lot about the side effects. We have listed some of the commoner ones, but it is important to remember that not everybody encounters them.

What are the possible benefits of taking part?

If you are allocated to the group that receives the active medication your walking unsteadiness and/or balance may improve and therefore you may be less likely to fall, but there is no guarantee. You may be reassured and benefit from the extra visits and phone calls in the trial. We cannot promise the trial will help you but the information we get from this study will improve the treatment of people with Parkinson's disease in the future.

What happens when the research study stops?

You will be asked to take the medication for 12 months. If you noticed benefit, then any further supply of the medication would need to be discussed and arranged through your normal Parkinson's specialist. They may only be able to prescribe the same or similar medication if you develop more significant memory problems. We will not be able to tell you whether you received the active or placebo (dummy) treatment until after all the participants have completed the trial and the data has been analysed.

What if I have a concern or complaint?

If you have a concern about any aspect of this trial, you should ask to speak to the researchers who will do their best to answer and resolve your queries. If you are still unhappy you can contact your site PALS service who will be able to provide further details in taking your concern or complaint forwards.

What if new information becomes available during the trial?

Sometimes we get new information about the treatment being studied. If this happens, your research team will tell you and discuss whether you should continue in the trial. If you decide not to carry on, you will be withdrawn from the trial. If you continue in the trial, you may be asked to sign an updated consent form.

What will happen if I don't want to carry on with the trial?

If you wish to withdraw from the trial completely you will be withdrawn, and we will not contact you further other than to organise the return of any medication. Any information we have collected up until the point you withdraw will be used in our analysis of the trial results. We will ask you **why** you wish to withdraw but you are under no obligation to give us a reason.

If you wish to **stop taking the trial medication** then it is **very important** you still return for your assessment at 12 months, complete the diaries and receive monthly telephone calls. We need to try and get results from everyone who took part to analyse the results of the study.

There may be instances where your doctor or healthcare professional may withdraw you from the trial on your behalf if there is a clinical need for you to do so (such as if you become pregnant or develop dementia during the trial). Any information we have collected up until the point you withdraw will be used in our analysis of the trial results.

What happens if something goes wrong?

In the event something goes wrong, and you are harmed during the research study there are no special compensation arrangements. There are no special compensation arrangements in place as rivastigmine is not an experimental medicine. The University of Bristol has Clinical Research Liability Insurance to cover the liability of the University to research participants in the event of negligent harm caused as a result of the trial. However, if something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action, but you may have to pay your legal costs.

What personal data will we be collecting?

If you enrol in the trial we will collect personal information from you (e.g. your name, age and similar information) as well as information from your medical records. Both the local site research team and the central research team will be collecting your data. You will be asked for this information by your local research team at your hospital and this will be shared with a central research team based at the University of Bristol who will be coordinating the phone calls and questionnaires on a monthly basis.

The NHS site will pass these details to the research team along with the information collected from you and your medical records. The only people in the research team who will

have access to information that identifies you will be people who need to contact you or who will audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

The NHS site will keep identifiable information about you from this study for 15 years after the study has finished.

How will we use your personal data?

University of Bristol is the sponsor for this UK-based study. We will use information supplied by you and your medical records 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 Bristol will keep identifiable information about you for 15 years after the study has finished.

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

Your data may be accessed for monitoring, audit and inspection purposes by UK regulatory authorities or by the University Hospitals Bristol NHS Foundation Trust who will assist in monitoring the safety and conduct of the study.

You can find out more about how we use your information here: http://www.bristol.ac.uk/infosec/policies/ and the central trial team can put you in touch directly with the information governance manager at the University.

NHS Digital/ISD/PEDW

If you agree to take part in the CHIEF-PD trial, we will also collect some data about you from NHS Digital (England), Information Services Division Scotland (ISD) or Patient Episode Database for Wales (PEDW). These public bodies collect information from all hospitals on behalf of the Government. All this information is routinely collected by the NHS whenever you have hospital treatment. We will use data that includes information about whether you have attended hospital for any reason. NHS Digital/ISD/PEDW will link your NHS number to data which will provide information about any deaths of people taking part in the trial. To obtain this important information we will ask your permission to share your full name, gender, NHS number, postcode and date of birth with NHS Digital/ISD/PEDW. This data will be sent and analysed by the University of Bristol research team working on the trial.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. When you are enrolled you will be issued with a Patient Identification Code. This will protect confidentiality during routine collection of your data. However, if it becomes necessary to identify you (e.g. to find out which allocated group you are in because of an emergency) senior research staff will have access to your personal contact details.

With your permission, your GP and Parkinson's specialist will be informed of your participation in the study.

Your local hospital site will use your name, NHS number and contact details to contact you about the trial. They will make sure that relevant information about the study is recorded for your care and oversee the quality of the study. Individuals from University of Bristol, monitoring and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your local hospital site will pass these details to University of Bristol along with the information collected from you and/or your medical records. The only people in University of Bristol who will have access to information that identifies you will be people who need to contact you to record side effects and collect information about falls or audit the data collection process.

Will my data be used in future research?

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research**.**

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for health and care research and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

What will happen to the results of the study?

When the trial has ended the results of the trial will be presented at scientific meetings and be submitted for publication in medical journals. We will post the results on our website, which includes a summary, and publicise them via our newsletter. At the end of the trial you will receive a letter explaining whether you were allocated the active or the placebo medication.

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, wellbeing and dignity. This study has been reviewed and approved by South West – Central Bristol Research Ethics Committee and given the reference 19/SW/0043.

Contact for further information

Thank you for reading this information booklet. If you have any questions or wish to discuss the study further, please contact: chief-pd@bristol.ac.uk

What next?

Please complete the reply slip, if we do not receive this we will contact you to see if you are still interested in participating.

You **do not** need to complete the consent form yet. The local research team will go through the form with you at the appointment if you wish to take part. It is included for your information.

If you have any questions, please contact us using the information listed on the front of this booklet.