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PREVENTT

Preoperative intravenous iron to treat anaemia in major surgery

Patient Information Sheet

PATIENT INFORMATION SHEET (Part 1)

Study Title: **PREVENTT** (Preoperative intravenous iron to treat anaemia in major surgery)

A randomised controlled clinical trial.

Protocol reference number: 12/0246

Invitation paragraph

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. A member of our team will go through the information sheet with you and answer any questions you have. Please take time to read the following information carefully. Talk to others if you wish.

Part 1 tells you the purpose of this study and what will happen if you take part.
Part 2 gives you more detailed information about the conduct of the study.

Please ask 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?

We are interested in looking into new ways of managing anaemia and blood transfusion use in patients undergoing surgery. Anaemia, which means you have a low blood count (also called Red Blood Cell count or haemoglobin), is a common problem in patients undergoing surgery. The normal practise for patients with anaemia is for them to receive a blood transfusion during or after surgery. We know that those patients who are anaemic before their operation are two to three times more likely to receive a blood transfusion. Although very safe, blood transfusions come from a limited supply of volunteer donors and are a resource that is quite costly to the NHS.

In this study we wish to find out whether giving iron therapy helps increase people's blood count before their operation and reduces the need for blood transfusion. Iron can be given in tablets but these are poorly absorbed from the stomach and can take many weeks to correct anaemia. We propose to use iron as an injection through the vein (intravenous). This means we can give the equivalent of 2-3 months of oral iron in one quick infusion. This has been used in many smaller groups of patients and has been shown to be safe and effective. The infusion takes a minimum of 15 minutes and will be given at least 10 days before the planned surgery. To see if this reduces the need for blood transfusions during or after the surgery, we will compare patients who have received the iron therapy injection against those given a normal saline injection.

Why have I been chosen?

You have been chosen to take part because you are soon to undergo surgery and have been identified as having anaemia by your doctor. The anaemia was detected by a measurement of your blood. The study is looking to select 500 patients in hospitals throughout the UK to help with this research.

Do I have to take part?

No. It is up to you to decide whether or not to take part. We will describe the study and go through this information sheet. 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 still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

You will be part of the study for approximately 8 months (no longer than your normal clinical care). We may decide at a later stage to collect some further information on you using MRIS (Medical Research Information Service).

Participation in this trial will not affect your planned surgery and your consultant is happy for you to be involved.

If you agree to take part you will be asked to sign a consent form and will be given a copy of this form. Before you can enter the study, a number of standard tests and screening tests specific for this study will be performed to ensure that it is safe and suitable for you to receive the study treatment. The study will run as part of your normal care in the preparation for surgery. Therefore, we will time the tests and infusion wherever possible to coincide with your normal hospital appointments.

As part of normal routine assessments for surgery your doctor will ask questions about your medical history. Your vital signs (height, weight, heartbeat, blood pressure, and temperature) will be measured, an Electrocardiogram (ECG) will be performed (to measure your heart rhythm) and blood samples will be drawn for routine tests (3-4 teaspoons). Also, if you are a woman of child-bearing age, your doctor will ask you to do a pregnancy test at the start of the study. We do not require to repeat these tests, but ask permission to have access to your medical notes to obtain the results.

Once the tests have shown that it is safe for you to receive the study treatment, you will be enrolled into the study. Sometimes we do not know which is the best way of treating patients. To find out we need to compare different treatment groups. We will put people into two groups and give each group a different treatment. The results are compared to see if one is better.

To try to make sure the groups are the same to start with, each patient is put into a group by chance. This is called randomisation.

For the study we will take some extra blood to measure more in depth levels of iron within the blood. The amount of extra blood to be taken is about 10 mls (2 small teaspoons worth). You will also be asked to fill out three questionnaires which ask about your quality of life, which will take about 10 minutes to complete. The nurse will help you with this if required.

Following randomisation you will receive an infusion (drip) into a vein over 15 minutes. This infusion will be either normal saline (placebo) or normal saline with iron. Neither you nor your doctor will know which treatment infusion you will be receiving, although, if your doctor needs to find out (in an emergency) he/she can do so. The only person who will know is the nurse/doctor administering the drip into your arm.

To deliver the treatment infusion we will need to place a drip into a vein. We can also use this for the blood tests, so every effort will be made to limit the number of needle punctures you may need. Very occasionally the nurse or doctor may not be able to place the drip or needle into a vein, and you will be asked if you would be willing to allow another attempt to access a different vein.

The drip will be given through black tubing so you will not see the colour of the infusion. This is because the iron is brown in colour and the saline is clear coloured. There will also be a cover over your arm and drip so you will not see the infusion going through. However you will be carefully monitored by the nurse/doctor throughout. The drip will take a minimum of 15 minutes to go through.

Once your infusion has been completed, the nurse will give you a diary and a card containing contact details. The diary is to record any admissions that you have to hospital or visits to the GP (health resource use). The nurse may call you at home to remind you to complete this diary. The card that the nurse gives you must be carried with you at all times. If you are admitted to hospital for any reason then please let the nurse/doctor know you are taking part in the PREVENTT study. There will be a contact number on the card for them to use if required.

The nurse will also give you three short questionnaires about your quality of life to take away with you. You should complete these at home about 10 days after you received your infusion. When you come back to hospital for your operation you should bring these three completed questionnaires with you and give them to the nurse. The nurse may call you at home to remind you to complete these questionnaires.

When you attend the hospital for your planned operation we will repeat the blood tests to

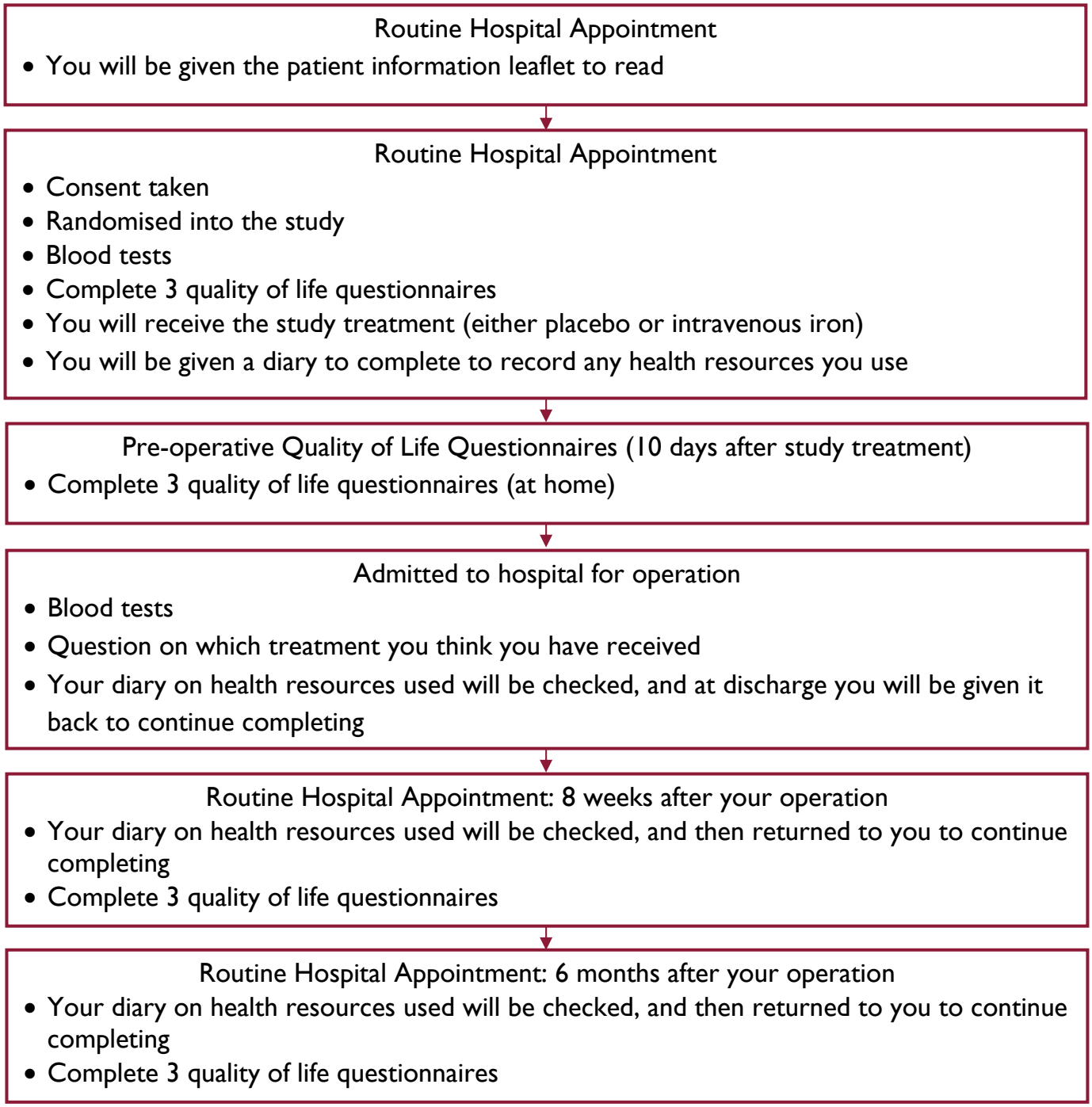
measure more in depth levels of iron within the blood. The amount of extra blood to be taken is the same, about 10 mls (2 small teaspoons). We will also ask you which treatment you think you were given. Please tell your doctor or study staff if you experience any unusual symptoms.

During your hospital stay we will obtain information from your medical notes regarding your recovery and whether you have experienced any complications or have needed to have a blood transfusion. This information will be collected on the third, fifth, seventh and fourteenth day after your surgery. Once you are ready to be discharged from your planned operation, you will be asked to carry on completing your PREVENTT diary until you are seen in outpatients. The nurse may call you at home to remind you to complete the health diary. Participation in the study will not delay your discharge from hospital.

Following your discharge from hospital you will be seen in the outpatients clinic as normal at 8 weeks and 6 months after your operation. At both these appointments you will be asked again to complete the three short questionnaires. The nurse will review your health diary. As part of normal routine care after surgery your doctor will ask questions about your medical history and do a physical examination. Your vital signs (weight, heartbeat, blood pressure, and temperature) measured, and blood samples may be drawn for routine tests (3-4 teaspoons). We can obtain these results from the medical notes

After this your involvement in the study will finish.

Below is a flowchart which summarises what will happen to you:



Expenses and payments

You will not be paid for participating in this study, however, travel expenses will be covered for any extra appointments that are required as part of the PREVENTT study, and which are not part of your routine visits for surgery.

What will I have to do?

The drug that we are investigating is intravenous iron and its effect on blood transfusion during

surgery.

You should continue to take all your current tablets, and they will be recorded as part of the research study. You must tell your study doctor about any other medication you are taking or using. The study medication and certain other medicines can interact with each other. Remember to mention anything you bought over the counter in a pharmacy without a prescription – including vitamin pills or other supplements, herbal and homeopathic remedies. In particular tell your study doctor if you are planning to take part in a research study involving another medicine.

Oral iron tablets (if prescribed) should not be started for at least 5 days after you have received the trial treatment (infusion).

It is important that you agree to attend any extra appointments if they are required, complete your patient diary and health questionnaires during the duration of the study. If you feel that this is not possible please let the nurse/doctor know.

Carry with you at all times a card (the same size as a credit card) which the study doctor will give you at your first visit. Cards like this are given to everyone who takes part in this kind of study; they include phone numbers to contact in any emergency.

Certain medical conditions require care when giving the study drug. It is important to tell your doctor if you have an infection, asthma, eczemas, and allergies, are pregnant or have any liver disorders.

Other than any dietary advice you have already been given by clinicians, there are no restrictions to your diet or lifestyle whilst you are involved in the study.

What is the Drug being tested?

Ferinject is an iron preparation, a medicine that is used to treat anaemia. It contains iron in the form of an iron carbohydrate. Iron is an essential element required for the oxygen-carrying capacity of haemoglobin in red blood cells and of myoglobin in muscle tissue. Moreover, iron is involved in many other functions necessary for maintenance of life in the human body.

Ferinject is used for the treatment of patients with iron deficiency, when oral iron preparations are ineffective or cannot be used. The aim of the therapy is to replenish body iron stores and to remedy anaemia, a lack of red blood cells due to iron deficiency.

Ferinject will be given as a one dose drip infusion via injection through the vein (intravenous). You will receive up to 20 ml of Ferinject, corresponding to 1000 mg of iron. As Ferinject is diluted

with a saline solution for infusion, it will be given over a 15 minute period.

You must not receive Ferinject if you are known to be hypersensitive (allergic) to ferric carboxymaltose or any of the other ingredients of Ferinject, have iron overload (too much iron in your body) or disturbances in utilisation of iron (where iron present in the body cannot be used properly).

What are the alternatives for diagnosis or treatment?

As far as we are aware there are no other alternative treatments to correct anaemia prior to surgery, apart from a blood transfusion. As mentioned iron tablets could be used but this is not routine practice as they only deliver a low dose of iron and can take many months to restore the body's iron levels. Many patients find iron tablets difficult as they can cause stomach ache and constipation.

What are the possible disadvantages and risks of taking part?

The only disadvantage, for agreeing to the study, may be the need for one extra hospital attendance.

Before participating you should consider if this will affect any insurance you have and seek advice if necessary.

What are the side effects of any treatment received when taking part?

When taking part in a clinical study, like this one, there may be some risks associated with the drug being researched which is iron. Iron infusions have been on the market since 1954. Ferinject is a modern preparation (since 2007) and over 6,600 patients have already received this medication in studies. Generally intravenous iron is very safe and well tolerated. However, there are known side effects that have been seen in patients receiving iron.

People react differently to drugs and we cannot always anticipate what the reaction might be. If you do experience any side effects, you will be required to notify the study team immediately. The contact details are given at the end of part 1 of the information sheet.

The most commonly reported side effect is nausea, which occurs in about 1 in 32 patients.

Other known side effects, which may occur, are headaches, dizziness, high blood pressure, injection site reactions (e.g. pain, irritation, discolouration), increased liver enzyme (alanine aminotransferase increased) and/or low phosphate (hypophosphataemia).

Other uncommon side effects (occur in less than 1 in 100 and more than 1 in 1,000 patients receiving iron) are allergic reaction (hypersensitivity), sensation of pain (paraesthesia), a change in

your taste sensation (dysgeusia), high heart rate (tachycardia), low blood pressure (hypotension), redness in the face (flushing), difficulty breathing (dyspnoea), vomiting, upset stomach (dyspepsia), abdominal pain, constipation, diarrhoea, itching (pruritus), hives (urticaria), redness of the skin (erythema), rash, muscle, joint and/or back pain (myalgia and arthralgia), muscle spasm, fever (pyrexia), tiredness (fatigue), chest pain, swelling of the hands and/or the feet (oedema peripheral), pain and/or chills.

In all the clinical trials reported to date (including over 6000 patients) there has been no report of increased side effects in patients receiving the intravenous iron compared to those patients who received the placebo.

It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Women who could become pregnant must use an effective contraceptive during the course of this study (i.e. intrauterine device or oral contraceptive and condom). Abstinence, i.e. not having sex, is not considered a contraceptive method. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her research doctor and you and your baby will be monitored with your consent.

If you are a man whose partner could become pregnant, you should use a reliable, medically approved effective double barrier method of contraception during the study (i.e. intrauterine device and condom or spermicide and condom). The study doctor will discuss this with you. Abstinence, i.e. not having sex, is not considered a contraceptive method. If you think your partner may have become pregnant during the study, tell the doctor immediately.

What are the possible benefits of taking part?

We cannot promise that this study will help you directly but the information we get from this study might help improve the treatment of people undergoing surgery and lower the need for blood transfusions.

What happens when the research study stops?

You will only receive the study drug as a one dose infusion, and will not as part of this research receive any further treatment with this drug. The hospital will continue to follow you up in outpatients and treat any conditions or complications if required. The results of the study will be available once all 500 patients have been recruited and completed their follow up.

The results will be published in a medical journal. Once this has happened, if you would like to know which treatment you received or to know the results then please contact the nurse/doctor listed at the bottom of this information sheet.

What if there is a problem?

Any complaint about the way you have been dealt with during the clinical study or any possible harm you might suffer will be addressed. The detailed information concerning this is given in Part 2 of this information sheet. If you have any concerns or complaints you should contact your study doctor in the first instance.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

Contact Details:

Your Doctor

Name *add name* Tel. Number: *add Tel. number*

Your Research/Specialist Nurse/Research Fellow *delete as appropriate*

Name *add name* Tel. Number: *add Tel. number*

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes we get relevant new information about the treatment being studied. If this happens, we will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, we will make arrangements for your care to continue. If you decide to continue in the study we will ask you to sign an updated consent form. Or on receiving new information, we might consider it to be in your best interests to withdraw you from the study. If so, we will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, we will tell you why and arrange your continuing care.

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

You can withdraw from treatment but keep in contact with us to let us know your progress. Information collected may still be used. Any stored blood or tissue samples that can still be identified as yours will be destroyed if you wish.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Their contact details are on the last page of this leaflet.

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available.

If you suspect that the injury is the result of the Sponsor's (University College London) or the hospital's negligence then you may be able to claim compensation. After discussing with your study doctor, please make the claim in writing to Mr Toby Richards who is the Chief Investigator for the clinical study and is based at the PREVENTT Trial Office, Division of Surgery and Interventional Science at University College London (UCL). The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Participants may also be able to claim compensation for injury caused by participation in this study without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your study doctor in the same way as above.

Regardless of this, if you remain unhappy and wish to complain formally, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study, the normal National Health Service complaints mechanisms are available to you. Officers from the Patient Advice and Liaison Service (PALS) are available in all hospitals. They offer confidential advice, support and information on health-related matters to patients, their families and their carers. You can find your local PALS office on the PALS website http://www.pals.nhs.uk/officemapsearch.aspx. Please ask your study doctor if you would like more information on this. Details can also be obtained from the Department of Health website: http://www.dh.gov.uk.

Alternatively, the Independent Complaints Advocacy Service (ICAS) is a national service that supports people who wish to make a complaint about their NHS care or treatment. Contact your local ICAS office through PALS, or ask your research nurse for your local contact number. If you wish you can find your local contact number on the following website:- http://www.nhs.uk/choiceintheNHS/Rightsandpledges/complaints/Pages/NHScomplaints.aspx

Will my taking part in this study be kept confidential?

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically at your treating hospital and the main hospital site managing this research under the provisions of the 1998 Data Protection Act. Your name will not be passed to anyone else outside the research team or the Sponsor (UCL), who is not involved in the study. You will be allocated a study number, which will be used as a code to identify you on all relevant forms. Any information about you which leaves the hospital/surgery will have your name and address removed so that you cannot be recognised.

Your records will be available to people authorised to work on the study but may also need to be made available to people authorised by the Sponsor (UCL), and the organisation responsible for ensuring that the study is carried out correctly. This is the Clinical Trials Unit at the London School of Hygiene and Tropical Medicine. By signing the consent form you agree to this access for the current study and any further research that may be conducted in relation to it, even if you withdraw from the current study.

The information collected about you may also be shown to authorised people from the UK Regulatory Authority (the Medicines and Healthcare Products Regulatory Authority); this is to ensure that the study is carried out to the highest possible scientific standards. All will have a duty of confidentiality to you as a research participant.

If you withdraw consent from further study treatment, unless you object, your data and samples will remain on file and will be included in the final study analysis.

In line with the regulations, at the end of the study your data will be securely archived for a minimum of 20 years. Arrangements for confidential destruction will then be made.

Will my GP be informed of my involvement?

With your permission, your GP and other doctors who may be treating you, will be notified that you are taking part in this study. There will be no other information passed onto them.

What will happen to any samples I give?

Most of the blood results that we record are part of your routine care.
Any blood samples that are taken as part of the research study will be taken at your local hospital and transferred to a central laboratory for analysis. The blood will only be identified by using your unique study number. The blood will be frozen at -80°C. The samples will be transported to a laboratory in central London called The Doctors Laboratory (TDL). The bloods will be analysed. Any serum excess (blood product) will be stored for future research. All results will be sent to the statistician who is based at the London School of Hygiene and Tropical Medicine (LSHTM). This is where the staff organising this study are based. You will not be told of the results of these study specific blood tests.

The samples will not be transferred outside of the UK.

Unless you withdraw your consent, we will ask you to gift your blood to the people running the study and in so doing give up all future claims to its use that may include further research.

What will happen to the results of the research study?

The results of the study will be available after it finishes and will be published in a medical journal and be presented at a scientific conference. The data will be anonymous and none of the patients involved in the study will be identified in any report or publication.

Should you wish to see the results, or the publication, please ask your study doctor.

Who is organising and funding the research?

The research is being organised by UCL (University College London). However the organisation and running of the study is being done at LSHTM (London School of Hygiene & Tropical Medicine), where the unit is experienced in running studies like this. The funding for PREVENTT is a grant from the National Institute for Health Research (NIHR). The funding for the NIHR comes directly from the government. Your own doctor does not get paid anything directly for putting you into 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 interests. This study has been reviewed and given favourable opinion by Welwyn (now Hatfield) Research Ethics Committee.

Further information and contact details

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the drug involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor. If you require any further information or have any concerns while taking part in the study please contact one of the following people:

Your Doctor

Name *add name* Tel. Number: *add Tel. number*

Your Research/Specialist Nurse/Research Fellow *delete as appropriate*

Name *add name* Tel. Number: *add Tel. number*

If you decide you would like to take part then please read and sign the consent form. You will be given a copy of this information sheet and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.

Trial website: **preventt.lshtm.ac.uk**