IMPROVE patient information sheet

Patient information

You are invited to take part in this research trial. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take your time to read through the following information carefully. Ask any questions you may have. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

This study is about preventing TB disease.

This study aims to investigate the best strategy for providing tuberculosis preventative therapy for the **prevention** of TB disease for people living with HIV and cryptococcal meningitis. One quarter of the world's population are estimated to have tuberculosis (TB) **infection** which without tuberculosis preventative therapy may progress to cause TB **disease**. TB infection may cause you no symptoms, however amongst people living with HIV, there is an increased risk that TB infection can progress to cause TB disease. TB remains the most common cause of death in people living with HIV, and is particularly common in Uganda.

There is strong evidence that TB preventative therapy– as recommended for all people living with HIV by the World Health Organisation (WHO) - **prevents** TB infection progressing to TB disease. We wish to understand the best strategy for providing tuberculosis preventative therapy to **prevent** TB disease in patients with cryptococcal meningitis, and to prevent deaths due to TB.

Why have I been chosen?

You have been chosen because you have been diagnosed with cryptococcal meningitis and HIV, and we have found no evidence of TB disease, but we think you have TB infection.

Do I have to take part?

You decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are free to withdraw at any time and without giving a reason. This will not affect the standard of the care you receive.

What will happen to me if I decide to take part?

You will receive treatment for your cryptococcal meningitis and be cared for by our specialist meningitis research team. In addition to the treatment you will receive for cryptococcal meningitis, you will receive additional tuberculosis preventative therapy for the **prevention** of TB disease with 2 drugs (rifapentine and isoniazid). You will be required to take the tuberculosis preventative therapy everyday, for one month.

We wish to understand the best strategy for providing tuberculosis preventative therapy to **prevent** TB disease for patients with cryptococcal meningitis, therefore depending on which trial arm to are allocated to, we will ask you to commence the tuberculosis preventative therapy either **early** as an inpatient (week 2) OR **late** as an outpatient (week 6). This will be decided at random and we do not know which allocation you shall receive at this stage. We anticipate that inpatient commencement of tuberculosis preventative therapy, will make it easier for patients to access tuberculosis preventative therapy.

If you are allocated to the **early** tuberculosis preventative therapy (commencement as an inpatient) study arm, you will need to take at least one dose of the rifapentine and isoniazid as an inpatient, but thereafter – if the doctors looking after you think that you are well enough – you will be able to go home. You do not need to stay in hospital for the whole tuberculosis preventative therapy course, and inclusion in this trial will not delay your discharge from hospital. If you are allocated to the **late** tuberculosis preventative therapy study arm, you will take all of the tuberculosis preventative therapy as an outpatient.

If you take part in the study you will be followed-up for 18-weeks. Once you have been discharged from hospital, you will have to return to our outpatient clinic every two weeks for review with our doctors and nurses; this will be a total of eight outpatient visits. During the time you are taking the study medication (one month total) you will also need to have blood tests on alternate weeks for safety monitoring. After you have completed the course of tuberculosis preventative therapy, these follow-up appointments may be done over the phone where possible.

You will be reimbursed 30,000 Ugandan shillings for your involvement in the study for your time, and transport to outpatient clinic appointments. This payment is specifically for involvement in the IMPROVE TB preventative therapy study, and is in addition to any payment received for inclusion in the parent study.

What are the possible disadvantages and risks of taking part?

There is the possibility of side effects from the drugs used in the study.

Tuberculosis preventative therapy for the **prevention** of TB disease will consist of taking 2 drugs (rifapentine and isoniazid) for one month.

Rifapentine is an antibiotic tablet.. Rifapentine is generally safe and well tolerated but side effects have been reported. Most patients taking rifapentine will notice that their urine, tears, sweat and sputum turns red. This is temporary side effect whilst you are taking the drug, and the colour will return to normal once you stop taking the rifapentine. Some patients report feeling generally unwell when taking rifapentine with flu-like symptoms or nausea, loss of appetite and low blood sugar but these symptoms are again temporary and not generally harmful.

Serious complications associated with rifapentine use can occur and include liver problems, kidney problems, or abnormalities with your blood cells. This is rare, and the risk is small. You will be

reviewed regularly by our specialist team to monitor you, and you will have alternate week blood tests. Another rare complication which has been reported with rifapentine is an allergic type reaction called a hypersensitivity reaction. We will observe you when you take the first dose of rifapentine to make sure you do not have a reaction.

Isoniazid is the second drug. Isoniazid is generally very well tolerated but can also rarely be associated with liver problems, again we will monitor you closely for this. Abnormalities with your blood cells can also occur with isoniazid which we will monitor for. Skin and nerve reactions have also been reported. We will provide you with a vitamin (pyridxone) to minimise the risk of nerve reactions.

As part of the study, you will need to have blood tests on alternate weeks. On occasion a blood test can be associated with some discomfort but only a small volume of blood is taken which will cause no harm to the body.

What are the possible benefits of taking part?

The aim of this study is to improve uptake of tuberculosis preventative therapy for the **prevention** of TB disease and therefore improve survival for people living with HIV and cryptococcal meningitis. By taking the tuberculosis preventative therapy we anticipate you will have reduced chances of developing TB disease or dying from TB. If you decide to take part, you will be cared for by our specialist meningitis research team and be reviewed daily by our doctors and nurses on the ward. You will be able to regularly ask questions about your health and care as you wish.

What happens when I leave hospital?

When you are well enough, you are able to leave hospital. As an outpatient you will need to continue to take treatment for your cryptococcal meningitis and the tuberculosis preventative therapy. You will subsequently be seen in our outpatient department to review your progress with our doctors and nurses. At the follow up visits we will continue to collect information about your progress for 18 weeks to compare the safety and feasibility of the two tuberculosis preventative therapy strategies under investigation. Counsellors will also talk to you about treatment for HIV.

What if something goes wrong?

If you are harmed by taking part in this research project you will be cared for until your condition improves or becomes stable. London School of Hygiene and Tropical Medicine has Clinical Research Insurance to cover the legal liability of the University to research participants. If you experience harm or injury as a result of taking part in this study, you may be eligible to claim compensation. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain or have any concerns about any aspect of the way you've been approached or treated during the course of this study, please contact the IMPROVE Study Principal Investigator – Dr Jayne Ellis + 256 752 612 236.

What will happen to any samples I give?

If you consent, some of your blood and urine samples will be stored for current and future research studies related to infection and the body's immune response. Samples will have only an identification number and the results will be anonymous. The aim is to better understand co-infections amongst patients with cryptococcal meningitis, and to improve survival. Samples may be analysed outside of this country.

Confidentiality

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised from it. No patient identifiable data will be shared with others, but the anonymised dataset may be shared with third parties. Upon request, participant records will be made available to applicable regulatory entities for study monitoring purposes.

What will happen to the results of the research study?

The results from this study will be used to better understand how best to provide tuberculosis preventative therapy for the **prevention** of TB disease in patients with HIV and cryptococcal meningitis, and will be used in the future to inform improved management strategies for patients.

Who has reviewed the study?

This study has been reviewed and approved by the following regulatory and ethics boards: Uganda National Council for Science and Technology, Mulago Research and Ethics Committee and The London School of Hygiene and Tropical Medicine.

Contact for further Information

If you have any questions relating to this study, if you should have a research related injury or suffer additional medical problems while you are in the study, please talk to your study nurse or doctor.

The 24-hour telephone number, through which you can reach your study doctor or study nurse is + 256 752 612 236**.**

In case of any questions regarding:

- Your welfare and rights as a research participant,
- Any questions or complaints not being answered by your study doctors
- You want to talk to someone besides the research team.

you should contact:

- Dr. Nakwagala Frederick Nelson, the Chairman of the **Mulago Research and Ethics Committee (MREC)** on mobile: 0772325869).
- **Uganda National Council for Science and Technology (UNCST)**, Plot 3 Kimera Road; Ntinda,

Kampala on telephone 0414-705-513.

If you have any questions about this research study, you can ask them now or contact the above doctors later. The study doctors will see you while in hospital.

For More Information

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by United States Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.