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Patient Information Sheet

Maraviroc Add-on therapy for Steatohepatitis in HIV

Short title: MASH

PART 1:

Invitation to take part:
We would like to invite you to take part in our clinical research study. Before you decide, it is important for you to understand why the research is being done and what it will involve for you. **One of our team will go through this Patient Information Sheet with you and answer any questions you have.** 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. Talk to others about the study if you wish.

Thank you for reading this.

What is the purpose of the study?
Non-alcoholic fatty liver disease (NAFLD) has become a common liver disease in HIV patients. It is defined by the accumulation of fat in the liver. This is mainly due to the complications of obesity, including diabetes, hypertension and high serum lipids, but there may be additional complex factors due to HIV infection. Accumulation of fat in the liver puts patients at risk of developing inflammation and scarring in the liver (non-alcoholic steatohepatitis 'NASH') which can progress to cirrhosis and liver cancer. Unfortunately, there is no approved medication for NASH.

We wish to test whether treatment with Maraviroc, a medication already licensed for the treatment of HIV infection and with additional anti-inflammatory effects, can reduce inflammation in the liver in patients with HIV and NASH.

Why have I been chosen?
All patients in our clinics with a diagnosis of HIV and NASH are being considered for this trial. The MASH trial will involve about 30 patients from six sites in the UK and Germany. We are hoping that the information we gather from this trial will help to improve the future care for patients like you.

Do I have to take part?
No. It is up to you to decide to take part. If you do decide to take part having read this information sheet and discussed it with a member of the study team, you will be asked to sign a consent form. You will also be given a copy of the signed consent form to keep. It is important that you know that you are still free to withdraw at any time and without giving us a reason. If you decide not to take part or if you withdraw later, this will not affect the care that you receive from the doctors and nurses.

If you decide to withdraw from the study, data and samples you have given up until that point will still be used and analysed as part of our research unless you state otherwise, in which case your samples will be destroyed.

What will happen to me if I take part?
When you come to the hospital, we will discuss the study in detail with you. If you wish to proceed with taking part in the trial, we will ask you to sign a consent form. You will then be asked some basic background information about your health, have a brief physical examination by a doctor and some blood tests. If you have not had a liver biopsy within the last 12 months, you will have a liver biopsy to confirm your eligibility for the study and to help us assess the impact of Maraviroc on the liver. **If this liver biopsy does not meet the eligibility criteria, you will not proceed with the study and you will proceed with standard clinical care.**

If you have already had a liver biopsy within 12 months that meets eligibility criteria, you will not require a repeat screening biopsy. However, we will ask your permission to use this liver tissue for the research project.

Eligible patients will be invited back for the baseline visit, where you will have some more blood tests and bedside liver scans. We will then ask you to take the study medicine Maraviroc twice daily for 48 weeks in addition to your standard treatment. The dose will vary depending on your other medications but your current antiretroviral medication will not change. It is very important you understand how the study drug fits into your existing medication schedule- this will be discussed in depth with you by a member of the study team.

After starting the trial, you will be asked to come to the hospital for reviews 2, 12, 24, 36, 48 and 52 weeks after starting the study (a total of 7 visits). At week 48 the maraviroc treatment will be stopped and you will have further liver scans and a liver biopsy (see below).

At the week 52 visit we will perform a final clinical review and blood test, and discuss the results of the tests (including liver biopsy) conducted during the study.

We will ask your permission to access your medical notes to obtain clinical information relevant to the study.

Liver Biopsy
The study is investigating whether Maraviroc has a beneficial effect in the liver of patients with NASH. Therefore, we need to review liver biopsy tissue before and after treatment. This is important because the severity of NASH can only be done using liver biopsy. We will use these samples to investigate whether maraviroc has reduced the inflammation in the liver, which is the main objective of the study.

A liver biopsy is a procedure to obtain liver tissue for microscopic examination. You will be asked to stop any medications you may usually be prescribed to reduce blood clots (e.g. aspirin) up to a week before the biopsy. You will be asked to lie flat and place your right arm behind your head. The doctor will clean the area on the right lower side of your chest over the liver. He will then numb the area with a local anaesthetic. He will ask you to hold your breath and not move while he places the needle into the liver and withdraws a small core of tissue which remains trapped inside the needle. The actual biopsy lasts a few seconds. Afterwards, bedrest and blood pressure measurements are ordered. You will usually go home four hours after the procedure following review by a doctor.

About 20-30% of patients feel some discomfort for a few hours after the procedure. Some patients have a persistent ache for a couple of days afterwards, which can be controlled with simple painkillers. Only 3-5% experience severe pain, but this can also be treated.

All liver biopsies will be conducted using ultrasound guidance which reduces the risk of complications. Therefore, the risk of a more serious complication such as bleeding or local tissue damage is exceptionally rare (1/1000- 1/10000) and most of the time there are therapeutic procedures to treat them.

Although no procedure is absolutely safe, liver biopsy is a valuable diagnostic test which is routinely used in the clinical care of patients with liver disease.

Blood samples

We will take 7 blood samples (up to 100ml, including your usual clinical blood tests) throughout the 52 weeks of the study to help us with the research.

The research samples will be frozen and stored in a licensed Tissue Bank for use in this project. One blood sample will be used for DNA extraction to assess for genetic variants associated with fatty liver disease. We also ask your permission to transfer any leftover liver tissue and blood (including extracted DNA) at the end of our research to a fully regulated Biobank, which can then be used in future ethically- approved research projects within or outside the UK investigating liver disease. If your samples are used for future research projects, this will be part of Imperial College's Hepatology and Gastroenterology Biobank. This is a fully NRES approved tissue biobank and any samples used for future studies will be made anonymous so you cannot be identified. All research studies and the release of samples from the Biobank are reviewed, approved and managed by an independent Governance Committee. If you do not want us to use the samples in this way, please indicate this on the Informed Consent Form.

What are the possible disadvantages and risks of participating in the MASH trial?

Liver biopsy is an invasive procedure with some rare complications as described above.

You will need to remember to take your study medicine twice a day for 48 weeks. The medicine being used in this study is already licenced and is used in clinical care and is well tolerated. Common side effects include postural hypotension (a fall in blood pressure when you stand up), nausea, headaches and depression. The study drug can also less commonly cause more serious side effects such as damage to the kidneys and liver and severe rashes. Finally, you will be advised to avoid pregnancy and sperm donation for the duration of the trial until 10 days after taking the study drug. The study investigator will be happy to discuss other known potential side effects at your request. You will have to come to hospital for 4 extra outpatient appointments and blood collections, but this will mean that your doctors will be seeing you more frequently.

What are the possible benefits of participating in the MASH trial?
We cannot promise that the trial will help you personally, although we do hope that the care you receive as part of this study will reduce harmful inflammation in the liver caused by NASH. The knowledge we gain from the trial and looking at your samples in the laboratory during and after your treatment should help us to improve the treatment offered to patients with HIV and NASH in the future.

PART 2:

Who is organising and funding the research?
The MASH trial is funded by Viiv Healthcare, the manufacturer of maraviroc, but is sponsored by Imperial College. The trial was designed by a group of doctors who are experts in liver diseases. The doctors (investigators) conducting the research are not being paid for including you or anyone else in the trial.

What are the alternatives?
If you choose not to take part in the trial you will receive normal standard of care.

What happens when the trial stops?
Once your participation in the trial is complete, maraviroc treatment will be stopped and you will resume normal clinical care under your consultant team and general practitioner (GP). You will only be in the study

for 52 weeks, but we expect that the trial will run for 18 months (recruiting patients and treating them) and then all the data will be analysed. The results of this research will be published in international medical journals.

What if relevant new information becomes available?
Sometimes during a trial new information becomes available about what is being studied. If this happens, your trial doctor will discuss this with you and whether you wish to continue in the trial. If you decide to leave the trial, your trial doctor will arrange for your care to continue according to the best available information at the time.

What if there is a problem?
If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during this trial, the normal National Health Service complaints mechanisms are available to you. You can talk to PALS (the Patient Advice and Liaison Service) at your hospital.

Will my taking part in this trial be kept confidential?
We would like to inform your GP that you are participating in this study as you will be on drug treatment for 48 weeks. We will ask for your permission to do this on the Consent Form that you will need to sign before you start on the study. Occasionally staff from the regulatory authorities, or the Research Ethics Committee (that approved the study), or staff from the regulatory department of this hospital, may need to visit the hospital to review your hospital records to check that the information being provided is correct and to ensure that the trial is being run properly. These staff will treat your information confidentially.

What will happen to the results of the trial?
The results of the MASH trial may take approximately 1 year to be reported. The results will be published in a medical journal and presented at appropriate clinical conferences. You will not be identified in any report or publication. It is not intended that we shall provide you with a copy of the scientific trial report, but if you would like to receive a copy please let your doctor know. The results are important as they may answer several questions for doctors looking after patients with HIV and fatty liver disease and could improve treatment for patients in the future. The best treatments available to patients now are because of trials such as this.

Who has reviewed the trial?
The protocol has been peer- reviewed by international experts in the field. The East of England Research Ethics Committee has reviewed and approved this trial under their REC reference 17/EE/0387.

Thank you for taking the time to consider participating in the MASH trial. You will be given a copy of this Patient Information Sheet and if you do decide to take part, a copy of your signed Informed Consent Form for you to keep.

If you have any further questions please ask your trial doctor or nurse.

Contact for further information regarding this trial:

Name: Dr Maud Lemoine (Trial Doctor) Telephone: 020 3312 6454

Name: Dr James Maurice (Clinical Research Fellow) Telephone: 020 3312 6454

Where to find more information about liver disease

If you have any further questions about your disease or clinical trials, please discuss them with your trial doctor. You may find it helpful to contact the British Liver Trust or St Stephens AIDS Trust, who provide a helpline, website and publications about liver disease and HIV respectively.