Patient Information sheet for Clinical Trial

(PRINTED ON LOCAL HEADED PAPER)

Study title:
A randomised Phase II trial of Imatinib versus Hydroxychloroquine and Imatinib for patients with Chronic Myeloid Leukaemia in Major Cytogenetic Response with residual disease detectable by quantitative polymerase chain reaction (PCR)

Short title:
CHlorOquine and Imatinib Combination to Eliminate Stem cells (CHOICES)

1. 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. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take your time to decide whether or not you wish to take part.

2. What is the purpose of the study?

The purpose of the study is to work out whether the combination of Imatinib and the investigational drug hydroxychloroquine is more effective than Imatinib alone in reducing or eliminating residual leukaemic cells in patients with chronic myeloid leukaemia and to find an acceptable dose of hydroxychloroquine that can be given without causing unmanageable side effects.

3. Why have I been chosen?

You have been chosen because you have been diagnosed with chronic myeloid leukaemia and your disease has responded to treatment with Imatinib. Despite your response to Imatinib you have residual (a small amount) leukaemia cells left in your blood and bone marrow that are detectable by a sensitive laboratory test called polymerase chain reaction or PCR.

4. Do I have to take part?

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. If you decide to take part, you are still free to withdraw at any time 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.

5. What is involved in the study?

You will undergo some standard tests before you begin your participation in the study. Most of these tests would be the same if you were not taking part in the study. These include standard blood tests, ECG, blood testing for PCR and possibly a single bone marrow test. However some additional tests are a pregnancy test for all women of child bearing age and a simple eye test at screening for all patients randomised to the study.

If you consent to go into the study you will be randomised to either continue your Imatinib treatment as before, or to continue Imatinib as before with the addition of hydroxychloroquine. Randomisation means that patients taking part will be put into one of these two treatment groups and compared. Patients are put into the groups by computer and neither you nor your study doctor will be able to choose which group you go into. This helps ensure that the type of patients in each group is similar and the treatments can be compared fairly. You have the same chance of receiving either Imatinib alone or Imatinib and hydroxychloroquine in this trial. Regardless of which treatment you receive as part of the study you may require to have more frequent follow-up visits with your doctor. At the most these will be 6 weekly for the first 3 months and then once every 3 months until 48 weeks. Please see the attached study visit schedule detailing the number and duration of your visits as part of the study.

If you receive hydroxychloroquine you will take this for up to 12 months (48 weeks) depending on how well you tolerate it and how effective it is.

Some patients on study will be requested to have additional tests, which will require that you spend longer at the hospital for some visits, to assess how hydroxychloroquine is working which include:

- additional blood tests to measure the levels of Imatinib in your blood (pharmacokinetics – see below: 10 patients from each arm of the study)
- additional blood tests to measure the levels of hydroxychloroquine in your blood (pharmacokinetics – see below: 10 patients from the hydroxychloroquine arm of the study)
- additional blood tests to assess the effect of the addition of hydroxychloroquine against leukaemia cells in your blood (10 patients from each arm of the study)
- 2 additional bone marrow tests to assess the effect of the addition of hydroxychloroquine against leukaemia cells in bone marrow (10 patients from each arm of the study). For these additional bone marrow tests 20ml (4 teaspoons) of bone marrow rather than 5ml (1 teaspoon) will be taken in a single sample

The information that will be collected will be to do with the effectiveness of the drugs against your leukaemia and side effects that you may have whilst on study. As stated above, we are asking permission for some additional blood tests to measure the amount of drug in the blood over time.

After the first 48 weeks, we will ask all patients to come to hospital for follow up on a three monthly basis, when your study doctor will offer you a check-up and blood tests.

6. What is the drug or procedure that is being tested?

The basic or standard treatment for CML is called Imatinib which you will already be taking as a once a day oral dose taken at the same time each day. You will continue to take this as prescribed. You may upon entry into the study be allocated to take another drug, hydroxychloroquine, which is the drug being tested in this study.

7. What are the known risks of the study or the side effects of any treatment received?

The known side effects of Imatinib treatment include weight gain, nausea, diarrhoea, dyspepsia, abdominal pain, rash or itching, fatigue, sore throat, cough, dizziness, fever/chills, insomnia, depression, flu, constipation, headache, low blood counts, night sweats, weakness, shortness of breath, decreased appetite, fluid retention and oedema. These side effects are usually temporary and may be treated with medications. As you will have been taking Imatinib now for at least 1 year you should have a knowledge of these known side effects.

The known side effects of hydroxychloroquine, the drug being investigated within the study, include skin rash, nausea, diarrhoea and headache. In this study hydroxycholoquine will only be taken for 12 months but it will be given at higher doses than is generally recommended; however, it is very unlikely that changes to your vision will occur. In this study hydroxychloroqine will only be taken for 12 months therefore it is extremely unlikely that any eyesight changes will occur. If eyesight changes do occur they are likely to be mild but could be permanent. However, as a precaution your study doctor will arrange for an eye test before starting treatment with hydroxychloroquine and your vision will be checked by very careful eye tests if you report any change in your vision during the treatment period.

There may be unknown side effects due to the combination of Imatinib and hydroxychloroquine and this is why all your side effects will be recorded throughout the duration of the study.

Sometimes during the course of a research project new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you about it and discuss with you, whether you want to continue in the study. If you decide to withdraw your consent, your study doctor will arrange 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 study doctor might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons for this and arrange for your care to continue.

Pregnancy

It is possible that if the treatment is given to a pregnant woman, it might harm the unborn child. Pregnant women must not therefore take part in this study, nor should women who plan to become pregnant during the study take part. Women who are at risk of pregnancy will 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. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her study doctor.

8. What are the possible benefits of taking part?

We hope that all the treatments will help you. You may benefit directly from participation in this research study if the addition of the investigational medication hydroxychloroquine reduces or kills CML stem cells, which would help to extend your disease free period.

9. What information will be held about me?

Information which is collected about you during the course of the study will be kept strictly confidential. Any information about you which leaves the hospital will

have your name and address, date of birth and all identifiable information (including patient/hospital/NHS number) removed so that you cannot be recognised from it.

Occasionally, at any time during or after the study your doctor (Investigator), the Trial Office staff and worldwide government regulatory agencies will be allowed access to your medical records, which identify you by name. This is so that we can check that the study is being carried out correctly. Any information that leaves the hospital will have your name and address removed so that you cannot be recognised from it.

Your GP will be informed that you are participating in this study and will be updated on your progress regularly, just as if you were receiving standard treatment.

All information regarding your medical records will be treated as strictly confidential and will only be used for medical purposes. Your medical records may be inspected by competent authorities and properly authorised persons, but if any information is released this will be done in a coded form so that confidentiality is strictly maintained. Participation in this study will in no way affect your legal rights.

10. Studies on tissue and genes.
We will be investigating your cancer tissue (from the biopsy samples) for changes in the DNA, RNA and proteins to investigate the effectiveness of the two drugs under study, Imatinib and hydroxychloroquine. Further research, as yet undefined, may be carried out but will only be undertaken with appropriate ethical approval providing you indicate this on the consent form.

11. What happens when the research study stops?
The research study stops at the end of 24 months for all patients. Patients who were allocated to take the study drug hydroxychloroquine will stop taking this at 48 weeks and will continue with Imatinib treatment as before. Patients who were allocated to Imatinib only will continue as before. We will continue to monitor your progress.

12. What will happen if the findings may affect you personally?
If during the study, we discover information that could be relevant to your interests or health we will let you know.

13. What if something goes wrong?
If you are harmed by taking part in this research project, 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 regarding this study, the normal National Health Service complaints mechanisms are available to you.

14. What will happen to the results of the research study?
We plan to publish the results of the research study so that the information that we have found will be available to all. This is likely to be one or two years after the study has completed. Please contact your study doctor if you wish to see a copy of this. You will not be mentioned personally in any report or publication.

15. Who is organising and funding the research?
The study is being organised through the Medical Research Council, Cancer Research UK Clinical Trials Unit Glasgow, Professor Holyoake at Greater Glasgow and Clyde NHS Board and the Beatson West of Scotland Cancer Centre in Glasgow with the other participating centres being Professor Richard Clark at the Royal Liverpool University Hospital and Dr David Marin at Imperial College London.

16. Withdrawal from the project
Your participation in the trial is entirely voluntary. You are free to decline to enter or to withdraw from the study any time without having to give a reason. If you choose not to enter the trial, or to withdraw once entered, this will in no way affect your future medical care.

17. Who has reviewed the study?
This study will have been reviewed by West of Scotland (1) Research Ethics Committee and many Research Development Committees throughout the United Kingdom. Please contact your study doctor for any further information about these bodies.

18. Contact for further information *(fields for local information to be added)*

Hospital Name : _____

Dr _____ and the research team, Department of Haematology,

Tel No:

Fax No:

Emergency contact number:

(and ask for on call registrar for Haematology).