

PATIENT INFORMATION SHEET**'Registration only' sub-study**

Trial title: A randomized trial for adults with newly diagnosed acute lymphoblastic leukaemia

Short title: UKALL14

Version: 2.0

Date 11.09.2017

Introduction

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. Take time to decide whether or not you wish to take part.

The UKALL14 trial

For many years, the National Cancer Research Institute (NCRI) have run several trials in Acute Lymphoblastic Leukaemia (ALL), which have led to a steady improvement in the treatment of ALL. The UKALL14 trial is one such study and has been running since late 2010. The main aim of the trial was to test four drugs: pegylated asparaginase, rituximab, nelarabine and palifermin, to see if they could improve patients' response to treatment when given in addition to standard chemotherapy.

The trial also investigated a number of scientific questions about ALL, in which samples from patients' bone marrow biopsies were sent to a laboratory to learn more about ALL, how well it responds to treatment, and what it can tell us about how likely patients are to suffer a relapse later on.

There were two main "randomised" study questions, one investigating whether rituximab improved treatment for patients with B-cell ALL, and one investigating whether nelarabine improved treatment for patients with T-cell ALL. Several hundred patients from hospitals across the UK are already participating in the randomised part of this study.

Recruitment to the randomised question for the type of ALL that you have is now closed, but it will take some time for the results of the question to be known. In the meantime, we are asking patients with newly-diagnosed ALL to take part in a 'registration only' sub-study to help us continue to learn more about ALL. This information sheet explains more about the UKALL14 'registration only' sub-study, and what is involved.

Why have I been invited?

You have been chosen to take part in this sub-study because you have recently been diagnosed with ALL. Your doctor will have by now explained what ALL is, how it will affect you, and what treatment is needed. You will know whether your leukaemia is of the "B-cell" or "T-cell" type.

The randomised part of the trial for the type of ALL that you have is now closed, so you are being invited to take part in the 'registration only' sub-study to help us learn more about leukaemia.

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 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?

Consent

If you agree to take part, you will be asked to sign a consent form. You may have already started your initial treatment by this time with a dose of steroid.

Treatment

As a 'registration only' patient, you will receive the standard ALL treatment as chosen by your local hospital. We will collect information about what treatment you receive for ALL and how your disease responds to treatment. After your treatment is finished, we will collect information on the progress of your leukaemia once a year. It is normal practice for patients with ALL to continue to see their doctors regularly once they complete treatment, so you will not need to have extra visits for the study.

A bone marrow sample (1 teaspoon), or blood sample (2-3 tablespoons) if bone marrow is unavailable, will be taken at the beginning of your treatment to find out whether you have a marker which we can use to follow the outcome of your leukaemia treatment using a very sensitive special test called "minimal residual disease testing" (MRD). In most cases, this test would be done as part of standard treatment outside of the trial too. MRD testing will be performed at University College London Cancer Institute. We will also look to see if your leukaemia has genetic alterations known as "cytogenetic abnormalities". You will then have bone marrow and blood tests after each treatment course to look at your response to treatment. It is normal practice for patients with ALL to have bone marrow and blood tests before starting treatment and at the end of each block of treatment, so you will not need to have any extra tests for the study, but slightly more bone marrow (1 teaspoon per sample) will be taken when you have your routine tests.

The standard treatment for ALL consists of chemotherapy drugs to destroy the leukaemia cells. The treatment is divided into stages, which are the same for both B-cell and T-cell types. Each stage has been given a name to help doctors and patients keep track of where they are in the treatment. You will be given the treatment that your doctor thinks is most appropriate for you given your age, fitness and the nature of your disease. You are likely to have some of the following courses of treatment.

- (i) Initial chemotherapy treatment, called Induction, is given to achieve disease remission, which means that your bone marrow function and blood counts return to normal and when doctors look under the microscope they can't see any leukaemia cells. Induction therapy is given in two parts, called 1 and 2.
- (ii) Immediately after induction therapy, patients are given further chemotherapy called Intensification, aimed at preventing leukaemia cells from getting into the fluid around the brain and spinal cord. Not all patients will receive this treatment.

- (iii) Consolidation treatment is more chemotherapy treatment. Patients who are already in remission must be given more therapy in order to prevent the disease relapsing (coming back). Not all patients will receive this treatment.
- (iv) Maintenance treatment is a lower dose chemotherapy, which is given as an out-patient treatment – mostly as tablets but sometimes as 3 monthly injections. This is also used to prevent the leukaemia coming back. Not all patients will receive this treatment.
- (v) Stem Cell Transplant (also known as bone marrow transplant) for patients who have a suitable donor and are at the highest risk of relapsing. Patients who receive stem cell transplantation don't always have intensification, consolidation and maintenance as well.

What if there is a problem?

Any complaint about the way you have been dealt with during the trial or any possible harm you might suffer will be addressed. Detailed information concerning this is given in Part 2 of this information sheet.

Expenses & payments

You will not receive any payment or reimbursement of expenses for taking part in this sub-study. The doctors and nurses working on this trial at your hospital will not get any payment for putting you in to the sub-study.

What will I have to do?

Your doctor will describe the planned standard treatment you will receive. For this sub-study, you will also be asked to provide additional blood and bone marrow samples for processing at UCL.

What are the possible disadvantages and risks of taking part?

It is not anticipated that you will experience any side effects as a direct result of taking part in this 'registration only' sub-study.

Your doctor will have explained the possible side effects of the treatment that they plan to give you as standard. Common side effects of chemotherapy include hair loss, low blood counts, increased risk of infection, nausea and vomiting, sore mouth, diarrhoea and temporary or permanent infertility.

If you consent to take part in this sub-study, you will have blood and bone marrow samples taken at the same time points as in standard care, but an extra amount of blood or bone marrow will be taken. You may experience pain and bruising after samples are taken, and you will need to keep your bone marrow biopsy site clean to stop it from getting infected. Your doctor or nurse will give you more information about this.

What are the possible benefits of taking part?

You will receive the standard ALL treatment used at your hospital, which has been developed by doctors to effectively treat ALL. It is hoped that the information and samples you provide as part of this sub-study will help us to understand ALL better and help us develop better treatments for patients in the future.

Contact for further information

If you have any concerns or questions about this trial, please contact [Local investigator name and contact number] who will be pleased to give you further information.

In the event of medical emergencies out of hours, you should contact [local contact].

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision. Thank you for reading this information.

PATIENT INFORMATION SHEET – PART 2

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

You can withdraw from the sub-study at any time without giving a reason and this will not affect the standard of care you receive. If you withdraw from the sub-study, we will still need to use the data collected up to your withdrawal.

What if there is a problem?

Every care will be taken in the course of this clinical trial. 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 Professor Adele Fielding who is the Chief Investigator for the clinical trial and is based at University College London Hospital. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may 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 clinical trial 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 wish to complain or have any concerns about the way you have been approached or treated by members of staff or about any side effects you may have experienced due to your participation in the clinical trial, the normal NHS complaints mechanisms are available to you. 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>.

Will my taking part in this trial be kept confidential?

If you consent to take part in a clinical study such as this one, relevant aspects of your medical records will be sent in confidence to Cancer Research UK and University College London Cancer Trials Centre (UCL CTC), who are managing the study. UCL CTC, like the NHS, is registered under the data protection act to hold patient information in secure storage to be accessed only by appropriate staff involved with this trial. Occasionally, trained staff from UCL CTC or regulatory authorities will need to visit the hospital to review your notes to check that the information being provided is correct. Information from your medical notes will also be passed to the local Registry, the Regional Cancer Registry, the Leukaemia Research Cytogenetics Group and UCL Cancer Trials Centre. Information collected for the study may also be used by investigators working on the trial outside the EU, possibly in the United States. Your initials, date of birth and NHS/CHI number will be shared with UCL CTC, the MRD laboratory at UCL Cancer Institute and the Leukaemia Research Cytogenetics Group. At all times, your details will be handled by fully trained staff and will remain confidential and secure. No individual patients will be identified when the results of the study are published. Your General Practitioner (GP) will however be informed of your participation in the study.

What will happen to any samples I give?

Blood and bone marrow samples will be collected and processed at your hospital as normal. Small samples of your blood and bone marrow will also be sent to named personnel at UCL Cancer Institute for further analysis. We will request that any surplus samples left over may be donated to a cell bank and we will ask for you to agree to this on the consent form. However, you are

within your rights to refuse to donate any leftover samples. In this instance, any leftover samples will be destroyed after analysis.

Will any genetic tests be done?

Yes, as mentioned in part 1, we will test to see if your leukaemia has any 'cytogenetic abnormalities' that may influence the treatment. These genetic tests are only done on your leukaemia cells. The genetic changes we find in your leukaemia cells are not changes taking place in the rest of your body.

What will happen to the results of the research study?

The results of the study will not be available until all patients taking part in the randomised UKALL14 trial have completed their trial treatment and been followed up for enough time to analyse the results. This is expected to be around the end of 2022. The results will then be published in scientific journals and presented at national and international meetings. It will not be possible to identify you in any publication or presentation of the research findings. If you wish, you may contact your study doctor to obtain a copy of the results.

Who is organising and funding the research?

This trial is being organised by the National Cancer Research Institute (NCRI) subgroup on ALL in adults, and will be run by UCL CTC. The funding is provided by Cancer Research UK.

Who has reviewed the trial?

This trial has been reviewed by Cancer Research UK, and the London - Fulham Research Ethics Committee (formerly known as Charing Cross Hospital Research Ethics Committee & West London REC 2). It has also been reviewed at your hospital by the Research & Development Department.

Further information and contact details

If you have any questions about this trial, you should contact:

Doctor:

Research Nurse:

If you have any questions about research in general, you can contact Macmillan Cancer Support, who are an independent organisation providing support and counselling to help people live with cancer. They can be contacted at Macmillan Cancer Support, 89 Albert Embankment, London, SE1 7UQ; Telephone 020 7840 7840; or visit their website at www.macmillan.org.uk.

Thank you for reading this information sheet.

Consent Form: Part 1

'Registration only' sub-study

Study title: A randomized trial for adults with newly diagnosed acute lymphoblastic leukaemia

Short title: UKALL14

Version: 2.0

Date: 11.09.2017

Centre Name: _____ Trial Number: _____

Name of Researcher:		Please initial to agree
1.	I confirm that I have read and understand the Patient Information Sheet – 'Registration Only' sub-study dated 11.09.2017 (version 2.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	<input type="checkbox"/>
2.	I understand that my participation in the trial is voluntary and that I am free to withdraw at any time, without giving any reason, without affecting my medical care or other legal rights.	<input type="checkbox"/>
3.	I understand that samples of my blood and bone marrow will be taken and sent to named personnel at UCL Cancer Institute for further analysis.	<input type="checkbox"/>
4.	I understand that sections of any of my medical notes may be looked at by responsible individuals involved in the running of the trial (including trial staff based at UCL CTC), or authorised personnel from the NHS Trust R&D for audit or other regulatory authorities where it is relevant to my taking part in research, and that I may be followed up through usual NHS mechanisms (e.g. NHS Information Centre). All access to my data must be compliant with the Data Protection Act 1998. I give permission for these individuals to have access to my records.	<input type="checkbox"/>
5.	I understand that information from my medical notes, including my initials, date of birth and NHS/CHI number will be passed to the local Registry, the Regional Cancer Registry, the Minimal Residual Disease laboratory at UCL Cancer Institute, the Leukaemia Research Cytogenetics Group and appropriate central trials offices. In all cases, personal details will be treated with the strictest security and confidentiality. I give permission for my information to be collected, stored, passed on for national registration and used for research in these central trials offices, laboratories and by investigators outside the EU, possibly in the United States.	<input type="checkbox"/>
6.	I understand that my General Practitioner will be informed of my involvement in this study and may be contacted to supply details of my progress.	<input type="checkbox"/>
7.	I agree to take part in the above study.	<input type="checkbox"/>

Name of patient	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

(3 copies: 1 for patient, 1 for researcher, 1 to be kept with hospital notes)

Consent Form: Part 2

'Registration only' sub-study

Study title: A randomized trial for adults with newly diagnosed acute lymphoblastic leukaemia
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Centre Name: _____ Trial Number: _____

	Name of Researcher:	Please initial to agree
1.	I understand that part of the diagnostic material taken prior to entering this sub-study may be recalled for use in future research. I understand that this will be anonymised and linked to the trial data through my unique trial number, date of birth and initials. No other personal data will be held. I understand separate ethics approval will be sought before the use of this material for future studies, but that I will not be contacted further about this. Future research may involve molecular, genetic and tissue microarray studies, or new techniques.	<input type="checkbox"/>
2.	I give permission for any surplus blood and bone marrow samples left over to be donated to a cell bank.	<input type="checkbox"/>

Name of patient _____ Date _____ Signature _____

Name of person taking consent (if different from researcher) _____ Date _____ Signature _____

Researcher _____ Date _____ Signature _____

(3 copies: 1 for patient, 1 for researcher, 1 to be kept with hospital notes)