PATIENT INFORMATION SHEET – PART 1

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

Short title: **UKALL14**

Version: **10.0**

Date **28.06.2018**

Introduction

You are being invited to take part in a 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 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.

What is the purpose of the trial?

The purpose of this trial is to find out more about how best to treat patients with Acute Lymphoblastic Leukaemia (ALL). The more people who take part in these studies, the better the information that we are able to obtain and the more quickly we are able to improve treatment for future patients. For many years the Medical Research Council (MRC) have run trials in Leukaemia with the National Cancer Research Institute (NCRI). Over the years this approach has led to a steady improvement in the treatment of leukaemia. This trial will be run by the NCRI and the Cancer Research UK & UCL Cancer Trials Centre (UCL CTC).

Your doctor will, by now, have explained what Acute Lymphoblastic Leukaemia 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. This information sheet provides details about the trial that we are inviting you to take part in. There is some background information given about the treatment of ALL in general, so that you can see where the treatment you might receive as part of this trial will be different from standard treatment that you would receive anyway.

At this stage your doctor will have asked for a test to be performed on a sample of your bone marrow to look for the presence of a specific genetic variation in the leukaemia cells which is called the 'Philadelphia chromosome'. They may not have the result of this test yet. If the variation is present, your disease is termed 'Philadelphia positive', and in addition to the treatment outlined below, you will be given a drug called Imatinib which has been shown to be beneficial to patients with this genetic variation, and is routinely used when treating patients with Philadelphia positive leukaemia.

The trial asks questions about 3 specific issues in ALL treatment which will be explained below. The rest of the treatment you will receive will be standard treatments that you would receive anyway, whether or not you participate in the trial. There is a flowchart attached to Part 1 of this patient information sheet that clearly sets out the standard and trial treatments for reference.

Standard ALL treatment

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.

(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 2 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.**

Trial question 1: Assessing a new form of a standard drug; L-asparaginase

During the intial (induction) phase of treatment, all trial patients who are found to be Philadelphia negative will be given a drug called Pegylated-asparaginase. This is a new form of a standard drug (L-asparaginase) that is always used in the treatment of ALL.

Patients who receive intensification & consolidation will also be given Pegylated-asparaginase as part of this treatment, in addition to during induction.

The new pegylated form of asparaginase is hoped to be better for the patient and more effective than the standard L-asparaginase treatment, and may be more convenient. Many hospitals in the UK are already using the new form of this drug but information on its risks and benefits have not been collected before in a systematic way in such a large group of patients. We want to make sure we don't just adopt this new form of the drug without taking the opportunity to study its use carefully.

Trial question 2: does the addition of new drugs in the initial (induction) phase of treatment lead to a better outcome?

The main purpose of the UKALL14 trial is to investigate whether new drugs, given with the standard initial induction therapy for ALL can improve the long-term outcome for patients. The drug treatments we are studying have already been used before, either in patients with other diseases or in small numbers of patients with ALL, but we are not certain whether adding one or more of these drugs to best available standard treatments will improve the outcome. Therefore, we are asking if you would be prepared to have one of these drugs added to the best available standard induction treatment by a process of 'randomisation'. By this we mean that neither you

nor your doctor chooses whether you get one of the new drugs but that choice is made by a computer, similar to tossing a coin.

In this trial, there are 2 new drugs to be tested in the induction stage of treatment. One of them applies only to B-cell ALL and one only to T-cell ALL.

B-cell ALL: 1 new drug called Rituximab is to be tested, the "toss of the coin" or randomisation will determine if you get the new drug with standard treatment or best standard treatment without the new drug.

T-cell ALL: 1 new drug called Nelarabine is to be tested. The "toss of the coin" will determine if you get the new drug with standard treatment or best standard treatment without the new drug.

Depending on the time at which you enter the trial, some of the new drugs may not be available. Your doctor will explain if the new drug is available to you or not. If the drug is not available, you may still enter the trial, but you will proceed with standard treatment only.

Trial question 3: Who will benefit most from a stem cell transplant (also known as bone marrow transplant)?

Stem cell transplant is a widely used treatment for ALL. Presently, there are no firm rules about who should have a stem cell transplant. Different hospitals within the UK often make different decisions about who should and should not have a transplant. Within this trial we have developed some firm guidelines about who should have a transplant based on assessing the 'risk' level of your leukaemia.

If you participate in the UKALL14 trial, your trial doctors will make a decision about whether or not you have a stem cell transplant and which of the 2 types of transplant you receive ("myeloablative", i.e. high dose, or "non-myeloablative") depending on 3 things: donor type, risk of relapse and age as detailed below.

A. If you have a sister or brother who is a tissue type matched donor, it will be recommended that you go ahead for a transplant regardless of your risk of relapse. If you are aged 40 years or less at trial entry, this will be myeloablative (a high dose transplant which includes total body irradiation). If you are 41 or older at trial entry this will be non-myeloablative.
B. If you do not have a matched sibling donor your risk of relapse will determine whether or not you are recommended for a transplant. Your relapse risk following induction therapy will be assessed using a number of special tests done in the weeks following your diagnosis and by your leukaemia cell count at diganosis.
    i. If you are considered to be at low risk of relapse you will continue with intensification, consolidation and maintenance chemotherapy and will not be recommended for a transplant.
    ii. If you are considered to be at high risk of relapse your trial doctor will recommend you for a transplant (if we can find a matched unrelated donor for you). If you are aged 40 years or less at trial entry, this will be myeloablative (high dose including total body irradiation) transplant. If you are 41 or older at trial entry this will be non-myelablative.

Why have I been invited?

You have been chosen to take part because you have ALL. Patients from hospitals all across the UK will also be invited to take part in this trial. In all, we expect approximately 826 patients to take part.

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 by mouth or be about to start.

Initial treatment: induction

For all patients, the first four weeks of induction treatment (phase 1) will be a combination of chemotherapy drugs, which has been used for over 15 years. In total this first period of treatment (phase 1 and phase 2 induction) lasts for about 8 weeks. You will be in hospital some, or possibly, all of this period. Your induction treatment may be accompanied by one of the new trial drugs or not, depending on the outcome of the randomisation as described above. Induction treatment is usually highly successful in initially treating leukaemia so that 'remission' is obtained and more than 9 out of 10 people will go into remission after initial treatment. A bone marrow test at the end of each of the 2 phases of your induction therapy will allow your doctor to give you information on how well the treatment has worked.

The additional drug being tested for B-cell ALL patients is not a chemotherapy drug, but an antibody against markers expressed on the surface of your leukaemia cells. This drug will be given as an injection directly into the vein once a week for 4 weeks during the first part of induction. The injections will be given by your regular nurses taking care of you on the wards.

For those people with T-cell ALL who are going to receive the extra drug, this will be given as an extra course of treatment after both phases of induction. It will be given intravenously as 3 doses on alternate days by your regular nurses. It may be given as either an in- or an out-patient treatment, depending on how well you are feeling.

Assessment of the outcome of initial treatment and determination of your "risk status"

At the end of your initial treatment, regardless of whether you receive the new drugs or not, we will give you an assessment of whether you are "high risk".

We know that Induction treatment needs to be 'consolidated', to prevent your leukaemia from coming back. There are two ways of doing this – either by further chemotherapy or by stem cell transplantation (also known as bone marrow transplantation). Patients who are "high-risk" will be assigned to stem cell transplant wherever possible. This might not always be possible – a donor might not be available or you may not be fit enough to have a transplant. Also, you are free to decide not to have a transplant, even if it is recommended by the trial.

How is my risk status determined?

A blood and bone marrow sample will be taken at the beginning of your treatment and used to find out whether you have a marker which we can use to follow the outcome 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). 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". This will be analysed at your local hospital and they will send the report to the trial laboratory at Newcastle University (Leukaemia Research Cytogenetics Group, LRCG). Leftover cells from your diagnostic samples may also be sent to the LRCG for further analysis. You will then have bone marrow and blood tests after each treatment course to look at your response to treatment and sensitive tests for evidence of leukaemia using genetic methods.

Initial treatment: intensification

Immediately after induction, patients will receive drugs to treat any leukaemia cells which may be in their nervous system (intensification). These are given through small injections into the spine called lumbar punctures and are part of standard treatment and not part of the trial. This treatment may not be given to some patients, depending on the type and timing of a stem cell transplant.

Looking for a stem cell /bone marrow donor

With your and their permission, all full siblings (sisters and brothers) will be tested to see if they have a matched tissue type to you. If your siblings are not a match, we may seek an unrelated donor depending on your risk status. By the time you come to the end of induction, most patients will know whether a donor is available or not.

What happens if my leukaemia is "high risk"?

If you are high risk, knowing that your leukaemia is at considerable risk of returning, even if you are in remission now, we will recommend you have a stem cell transplant even if you do not have a matched sibling. This transplant will be part of the trial and we will assess the benefits of using an unrelated donor, from a register, for your transplant. Depending on your age (older or younger than 40 at trial entry) we have 2 ways of doing the transplant. We know that the transplant can be a very hard treatment to tolerate in older people and we plan to find out if using a more gentle form of transplant preparation (conditioning regimen) for the transplant can be as effective as the high dose treatments we usually use.

We will use two tests to see how well these more gentle transplants are working. The first is called 'chimerism', and looks at how much of the donor's DNA is present in the blood. Patients who have these less intensive transplants will need to have an extra blood test every 3 months for the first 2 years after transplant for this test to be done. This is a standard test after transplants, and will be done at your hospital's laboratory. An anonymised copy of your chimerism test results will be sent to UCL CTC. The second test looks for very low levels of leukaemia in the bone marrow. Patients having less intensive transplants will have an extra bone marrow sample taken every 3 months for the first 2 years after transplant for this test to be done. If either of the tests show the transplant is not working fully any more, patients may be given 3-monthly infusions of lymphocytes from their stem cell donor to 'boost' the transplant and help control their leukaemia.

What happens if my leukaemia is "standard risk"?

If your leukaemia is standard-risk, i.e. nothing about your disease makes us worried that you are at high risk of relapsing, you will be recommended to stay on standard treatment unless you have a brother or a sister who can be a stem cell (or bone marrow) donor. You will have two more 'phases' of treatment: consolidation and maintenance.

Consolidation treatment lasts about 9 weeks. You will have a number of chemotherapy drugs, some of which are given as an injection directly into the vein, some taken by mouth, and some given through lumbar punctures.

Maintenance lasts for 2 years. You will need to take some drugs by mouth each day, and attend clinic for injections into your veins and lumbar punctures. You will need to have regular blood tests to monitor your blood counts, as the dose of your drugs may need to be changed to keep your blood counts at a safe level.

What if there is a problem?

Any complaint about the way you have been dealt with during the clinical 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 trial. The doctors and nurses working on this trial at your hospital will not get any payment for putting you in to the trial.

What will I have to do?

You will be in hospital for much of your treatment. You will also have side effects which can make you feel unwell and unable to carry on work for a while. These side effects occur in all standard chemotherapy for ALL. Almost all of the drugs you will be treated with will be the standard treatment for ALL unless you are 'randomised' to get one of the new drugs to be tested during induction therapy.

You will be prescribed a number of different drugs throughout your treatment which will be explained to you. It is very important that you take these drugs as they are prescribed to you.

Some of the drugs given as part of the trial can affect your ability to drive or operate machinery – there is more information about this in "what are the side effects of any treatments given when taking part" below. It is important that you follow the advice given.

What are the alternatives for diagnosis or treatment?

ALL is a rapidly advancing type of leukaemia which, without treatment, is usually fatal within a few weeks. If you were not on this trial, you would receive one of the standard treatments that are included in this trial. Additionally, you may also be recommended to have a stem cell transplant, depending on your doctor's assessment of your risk of relapsing. You also have the option of not receiving any treatment at all although this is not recommended.

What are the possible disadvantages and risks of taking part?

Everyone who agrees to take part will receive standard treatment. Some people will receive additional drug treatments to standard ones. We hope that the additional treatments might mean your chance of having a long term future without leukaemia is higher. However, we are not

certain of that and this is the reason why we are doing a trial. Outside of a trial, these new drugs are not licensed for the treatment of ALL and would not be prescribed to you, so by entering the trial, there is a chance you might receive a new drug which might be of benefit to you. It is also possible that the new drug would neither benefit nor harm you and the outcome would be the same as if you had standard treatment only. Finally, although we don't think this will be the case, we can't be absolutely sure that the new drugs won't cause additional side effects and complications and make your outcome worse. The side effects and leukaemia responses of all patients on trial will be closely followed both by the trial doctors and coordinators and by an independent data and safety monitoring committee. If there is any evidence that the trial drugs are much better or much worse than the standard treatment, the trial will be stopped.

What if I am breastfeeding, pregnant or planning to become pregnant?

Breastfeeding or pregnant women will not be eligible to take part in the trial. If you are breastfeeding or pregnant, you need to disuss this with your doctor straight away before starting any treatment for your leukaemia.

For women:

Please share this information with your partner if it's appropriate.

It is not known if the chemotherapy drugs used in this study are harmful to unborn babies and it is also possible that these drugs may be present in breast milk. Therefore if you are breast-feeding or pregnant you will not be able to take part in the study.

If you are potentially able to get pregnant you will be asked to take a pregnancy test (urine or blood) before entering the study to ensure you are not pregnant.

You must agree to use at least 1 reliable form of contraception during your treatment. This must continue throughout treatment and for 12 months after you finish your treatment. Oral contraception is not an effective method of contraception while on treatment with Oncaspar. Ask your doctor for advice on the best contraceptive method that you can use.

If you do become unexpectedly pregnant during the study, you must immediately inform your study doctor so we can help you decide appropriate action. We would discuss referral for specialist counselling on the possible risks to yourself and your unborn baby.

For men:

Please share this information with your partner if it's appropriate.

It is possible that the study medicine will affect sperm or semen and therefore you should not father a child during this study, or for a safety period of 12 months after treatment. If your partner might become pregnant you must use at least 1 reliable form of contraception during treatment and for 12 months afterwards. If your partner becomes pregnant during the study, or within 12 months of your stopping treatment, you must tell your study doctor immediately.

Fertility Advice
Due to the possibility of treatment-related infertility the doctor or nurse will provide you with information on egg cryo-preservation **OR** sperm banking if you wish.

What are the side effects of any treatment received when taking part?
Unfortunately, all of the available treatment options for acute lymphoblastic leukaemia have side effects, as do the new drugs we are testing. As with any drug, there is always a chance that you will experience unwanted effects. You will be carefully monitored for any problems and you are encouraged to report anything that is bothering you to your doctor. If you have any questions, you should contact your study doctor.
The side effects experienced may vary from person to person and can range in how serious they are from mild to severe; they can resolve promptly or can be long-lasting. Some side effects may never go away, and some side effects can result in death. Below, we have listed some of the common side-effects of the drugs being used in this trial. This is not a complete list, but your study doctor will be able to answer any questions that you may have and will be able to provide you with more information. You should not hesitate to report anything that upsets you or may be troubling you to your Doctor, even if you do not think it is connected to the trial drugs.

Most patients will experience the following at some stage during treatment and would do if they were receiving standard chemotherapy for ALL outside the trial.

- Hair loss – most patients lose some or all of their hair. It will grow back once the therapy is finished.
- Low red blood cell counts resulting in tiredness and dizziness and shortness of breath. You will receive regular blood transfusions to overcome these symptoms.
- Low platelets (the cells that make your blood clot) resulting in an increased risk of bleeding and bruising. You will receive platelet transfusions to counteract this and you should be careful not to cut or bang yourself while your platelets are low.
- Low white blood cell counts resulting in a high risk of infection. If you have a temperature or feel unwell, you should tell your trial doctor or nurse immediately so they can start you on antibiotics. Infections can occasionally be life threatening.
- Nausea and vomiting – medications are given with your treatment to prevent or alleviate this.
- Sore mouth – medications are given with your treatment to prevent or alleviate this.
- Diarrhoea.
- Temporary or permanent infertility. Your medical team will discuss treatment options with you before starting treatment.

There is also a small risk that you might die as a result of your treatment for leukaemia.

Your medical team will monitor you closely for side effects and you should report any side effects to them. Blood transfusions and/or other medications will be prescribed to prevent or reduce these.

Rituximab
The side effects of Rituximab which is given for patients with B-cell type ALL are generally mild and some of these can be reduced with medicines. Side effects can begin during the first dose of the drug and may continue for a few hours afterwards, but are usually milder with following doses. Specifically the side effects of Rituximab might include the following:

- Flu-like symptoms: These can include a high temperature, chills, weakness, muscle aches, tiredness, dizziness and headaches. They can occur while the rituximab is being given, but do not usually last long.
- Low blood pressure: This may happen during the infusion, so your blood pressure will usually be regularly checked. People who normally take medicines to lower their blood pressure may be advised by the doctor to take these at least 12 hours before rituximab is given.
- Feeling sick (nausea) and occasional vomiting: Your doctor can now prescribe very effective anti-sickness drugs to prevent or greatly reduce nausea and vomiting. If the sickness is not controlled, or if it continues, tell your doctor. They can prescribe other anti-sickness drugs that may be more effective.
- Allergic reactions: You may have an allergic reaction to rituximab. Signs of this include skin rashes and itching, a feeling of swelling in the tongue or throat, irritation of the nasal passages, wheezing, a cough and breathlessness. You will be monitored closely during your treatment, but let your nurse or doctor know if you have any of these symptoms. To help reduce the chance of developing an allergic reaction, antihistamines can be given before the infusion. The infusion can also be slowed down or stopped until the reaction is over.
- The company that make Rituximab have warned that a very small number of people (<1/10,000) taking Rituximab for lymphoma and leukaemia have developed severe skin reactions known as Stevens-Johnson syndrome. This syndrome is not specific to Rituximab, a number of other drugs are known to cause it. However, although it is usually treatable it can be severe and some of these people died. The skin reaction can happen during treatment with Rituximab, or in the first few months after finishing treatment. The main symptoms are a rash and blistering of the skin. If you develop a rash during or after your Rituximab treatment, please contact your study doctor immediately.
- The company that make Rituximab had advised that it should not be given to patients who have, or have had, hepatitis B or hepatitis C infection. If you agree to take part in the trial, you will be tested for hepatitis B and C. Please inform your clinician if you are aware that you have been exposed to either of these viruses.

Nelarabine

Some patients who are treated with Nelarabine, which is given to patients with the T-cell type of ALL, experience neurological side-effects. Sometimes these can be severe, and they may not go away completely. In rare cases they may result in permanent disability. Symptoms may include:

- confusion or clumsiness
- lack of balance or coordination
- weakness or trouble walking
- numbness and tingling in the hands, fingers, feet, or toes
- problems with buttoning clothes or picking up small items with your fingers
- blurred vision
- seizures (convulsions)
- dizziness
- extreme sleepiness.

You must not drive or operate machinery if you experience confusion or drowsiness which can impair your ability to react whilst taking nelarabine.

Pegylated Asparaginase

The side effects of Pegylated Asparaginase are very similar to L-asparaginase, the standard drug given to patients with ALL in the UK. Specifically, changes to liver function are very common, so your doctor will monitor your liver function closely during treatment.

The side effects of Pegylated Asparaginase which will be given to patients who are Philadelphia negative can include:

- Low blood counts
- Bleeding
- Thrombosis (blood clots)
- Diarrhoea, nausea and vomiting
- Sore mouth
- High blood sugar and fats
- Feverwith low number of white blood cells
- Pain
- Rash
- Allergic reaction
- Changes to liver, kidney and pancreas function, which can be very severe
- Infections
- Hypoxia (reduced flow of oxygen)
- Decreased appetite and weight loss.
- Nervous system changes such as confusion, loss of consciousness, muscle weakness and seizures

You must not drive or operate machinery if you experience confusion or drowsiness which can impair your ability to react whilst taking pegylated asparaginase.

Stem Cell Transplant: Your transplant doctor will explain the side effects of a stem cell transplant to you in detail if and when it is decided that you should have a transplant. Specifically, the side effects of stem cell transplantation might include the the problems detailed below:

- Immediate problems occur due to side effects of the transplant treatment. These usually resolve within a couple of weeks. A very sore mouth and throat is common, along with a high temperature due to the suppression of your white blood cells.
- Later on problems can continue after you have left hospital:
    - Continued infections due to the suppression of your immune system
    - Graft versus host disease (this is a particular illness that occurs when the transplanted donor cells 'reject' cells in your body after your transplant)

Patients aged 40 years or under at the time of trial entry who are eligible for stem cell transplantation will be treated with a myeloablative conditioning regimen, this includes total body irradiation. These patients will undergo a CT scan or a test dose before the total body irradiation. This will allow the doctors to work out what dose they should give the patient in order to protect the patient's organs, such as lungs, as much as possible. The combination of total body irradiation and CT scan or test doses is standard treatment for ALL and does not represent any additional exposure to radiation above a patient who is not on the trial being treated with the same procedure. One CT scan is equivalent to about 4 years of natural background radiation exposure. This level of exposure is very unlikely to put you at significant health risk. We all have a one in five

chance of getting a fatal cancer even if we never have an x-ray, so this CT scan represents a very small addition to this underlying risk from all causes.

What are the possible benefits of taking part?

We hope that all the treatments given will help you. The aim of the trial is to compare benefits of different treatments, since we genuinely do not know if adding the new treatments will help. The information we get from this trial may help us to treat future patients with ALL better.

Data from the GRAALL-2005 study, presented at a conference in 2015, has suggested there is a benefit to giving rituximab to patients with B-cell type ALL. It is important to note that this study was conducted in a more selected group of patients than UKALL14, and was asking different research questions to the UKALL14 trial. If you choose not to go into the UKALL14 trial there is no guarantee that you will receive rituximab outside of the trial, as it is not currently funded for ALL on the NHS.

What happens when the trial stops?

If the trial finishes while you are still receiving treatment you will continue to be treated on the trial protocol until your allocated treatment is completed.

Contact for further information

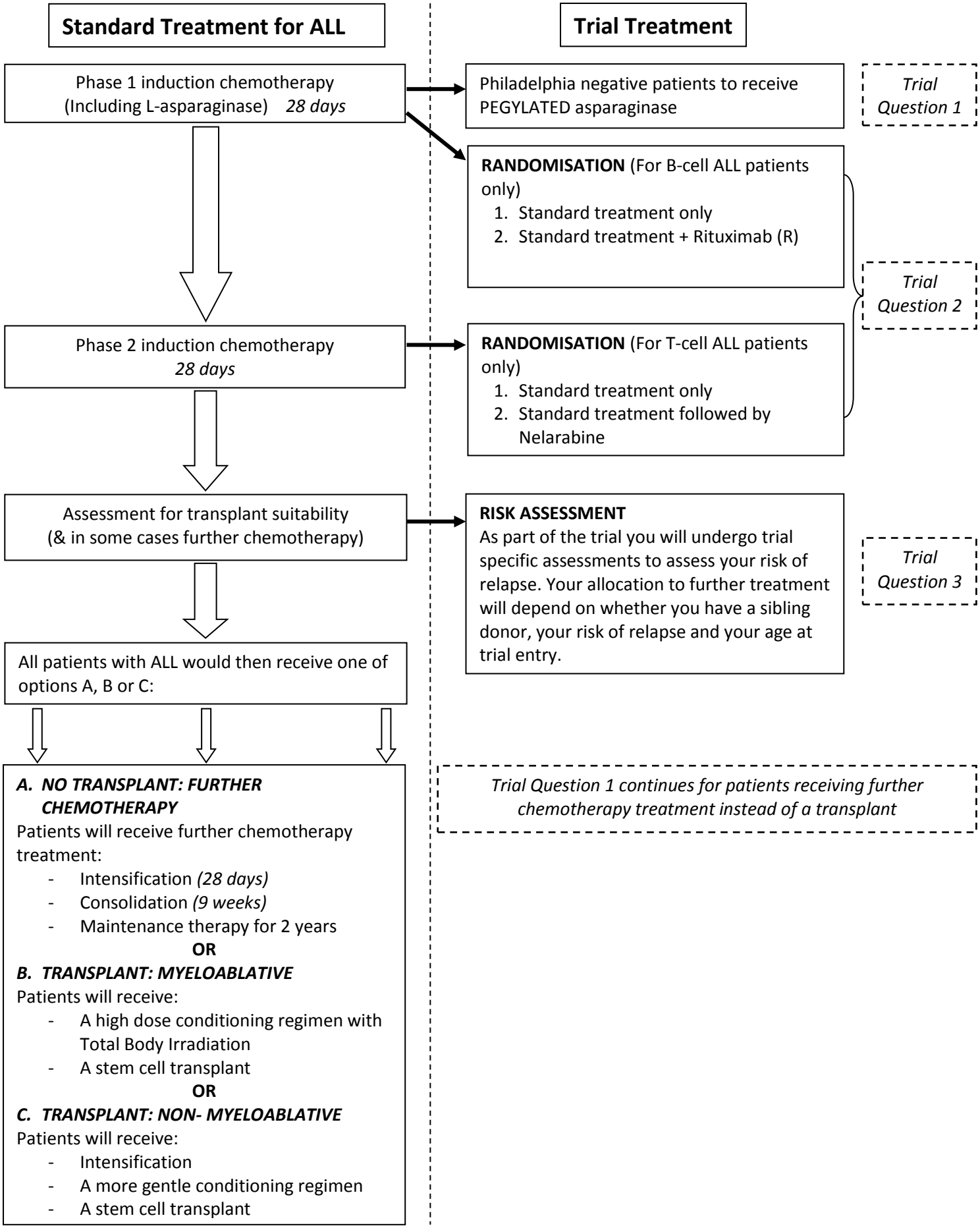
If you have any concerns or questions about this trial, please contact [Local investigator name and contact number] who will be pleased to give you further information.

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.

UKALL14 Flowchart showing standard treatment for ALL patients plus additional trial treatment



PATIENT INFORMATION SHEET – PART 2

What if relevant new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment or drug that is being studied. If this happens, your trial doctor will tell you about it and discuss with you whether you want to continue in the trial. If you decide to withdraw from the trial, the Cancer Trials Centre (UCL CTC) will be informed and your care will continue at your current hospital. If you decide to continue in the trial you will be asked to sign an updated consent form.

Also, on receiving new information your trial doctor might consider it to be in your best interests to withdraw you from the trial. He/she will explain the reasons and arrange for your care to continue at your current hospital.

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

You can withdraw from the trial at any time without giving a reason and this will not affect the standard of care you receive. If you withdraw from the trial we will still need to use the data collected up to your withdrawal. Or, you may also withdraw from treatment but keep in contact with us to let us know your progress, allowing us to continue to collect valuable information about your disease and response to treatment.

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 clinical trial 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 clinical trial doctor in the same way as above.

Regardless of this, if you wish to complain, 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 clinical trial the normal national Health Service complaints mechanisms are available to you. Please ask your clinical trial 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

Please ask your trial doctor if you would like more information about this.

Will my taking part in this trial be kept confidential?

Details about you, your treatment, any side effects you have, how your cancer responds, and how you are during and after treatment will be recorded in your medical notes, and information will regularly be sent to the UCL CTC. The study information collected will be used to help improve our knowledge of treating ALL. UCL CTC will be provided with your initials, date of birth and NHS number, but this information will be stored securely and handled according to data protection

guidelines. Samples sent to the MRD laboratory at UCL Cancer Institute and the LRCG at Newcastle University will be marked with your initials and date of birth to prevent samples being mixed up with those for another patient. These details will be stored in a secure location and will not be shared with anyone else.
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 LRCG and UCL Cancer Trials Centre. Information collected for the trial may also be used by investigators working on the trial outside the EU, possibly in the United States.
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 trial are published. Your General Practioner will however be informed of your participation in the trial.

More detailed information about how your data is used can be found in Appendix 1 of this document.

What will happen to any samples I give?
Blood samples taken for the trial will be collected and processed in exactly the same way as other samples taken in your hospital. Small samples of your blood and bone marrow will also be sent to named personnel in other NHS hospitals, UCL Cancer Institute, and the LRCG 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. Some of these tests are done as standard at your local hospital's cytogenetics laboratory, however they may also send leftover cells to the LRCG at Newcastle University who will carry out extra tests as part of the trial.

What will happen to the results of the research trial?
The results of the trial will not be available until all patients taking part have completed the trial, this should be in the next few years, depending on the rate of subject entry to the trial. This will allow time to recruit enough patients and to follow them up for a sufficient period of time. 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 trial 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 acute lymphoblastic Leukaemia in adults, and will be run by the Cancer Research UK & UCL Cancer Trials Centre (UCL CTC). The funding is provided by Cancer Research UK.
The new drugs being tested in this trial (Rituximab & Nelarabine) are being provided free of charge by Roche and Novartis.
Your hospital may receive financial reimbursement if they choose to use a particular brand of granulocyte colony-stimulating factor for supportive care called Lenograstim.

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 http:// http://www.macmillan.org.uk

Thank you for reading this information sheet.

APPENDIX 1 – Information about how your data are processed

Details about you, your treatment, any side effects you have, how your cancer responds to treatment, and how you are during and following study treatment will be recorded in your medical notes. The study information collected will be used to help improve our knowledge of treating ALL. This is in the public interest as it may lead to improvements in future treatments.

University College London (UCL) is the sponsor for this study based in the United Kingdom. UCL will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about you for at least 5 years after the study has finished, as required by law for clinical trials.

Your rights to access, change or move your information are limited, as UCL need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, UCL will keep the information about you that we have already obtained. To safeguard your rights, UCL will use the minimum personally-identifiable information possible.

You can find out more about how UCL use your information at http://www.ctc.ucl.ac.uk/Privacy.aspx. This includes details of how to contact UCL's data protection officer and how to make complaints to the Information Commissioner's Office (ICO).

Your hospital will collect information from you and your medical records for this research study in accordance with our instructions.

Your hospital will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study.

Individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your hospital will pass your NHS number, initials and date of birth to UCL along with the information collected from you and your medical records. The only people in UCL who will have access to information that identifies you will be people who audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

Your date of birth and initials may be marked on samples that are sent to the central laboratories for the trial. This helps to ensure that the samples are not mixed up with samples for another patient by mistake. The laboratories will store your information securely and will not share it with anyone else.

Your hospital will keep identifiable information about you from this study for at least 5 years after the study has finished.

UCL will collect information about you for research from your hospital site. This information will include your NHS number, initials, date of birth and health information, which is regarded as a special category of information. UCL will use this information to conduct our research.

When you join the study, you will be assigned a unique study number. This study number will be used instead of your name and will be linked to all of your study data. This is called pseudonymised data, and you cannot be personally identified from this.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in UCL and other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research**.**

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified, your data will only be used in research that has been independently reviewed by an ethics committee.