

# ACCEPT

## A phase Ib/II combination trial of acalabrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) for patients with diffuse large B-cell lymphoma (DLBCL).

### We invite you to take part in a research trial

Your doctor or nurse has given you this information sheet because they would like you to think about taking part in the ACCEPT trial.

You are being invited to take part in Phase I of the ACCEPT trial because you have a particular type of lymphoma and your doctors are considering chemotherapy treatment for you.

Before you decide whether or not to take part, it is important for you to understand as much as possible about what is being done and what is involved, so:

- Please take the time to read this information carefully. You may also wish to discuss it with your family and friends before making up your mind
- Please feel free to ask your doctor any questions you may still have after reading this information sheet

**Do I have to take part?** No. It is entirely up to you if you take part in the trial or not. If you choose not to take part, the care you get from your own doctors will not be affected in any way.

**If I start the trial, can I stop if I want to?** Yes. If you choose to take part in the trial, you are free to stop at any point without giving a reason – the standard of your care will not be affected.

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### How to contact us

If you have any questions about this trial or would like to discuss it further, please contact:

**[local investigator name]**  
**[contact details]**

## Important things you need to know about ACCEPT

- The ACCEPT trial is being done so that we can find out more about a new drug (medicine) that might improve the treatment of certain types of cancer. In particular, we wish to see if adding the new drug to one of the normal types of chemotherapy used for your cancer can improve the outcome of treatment.
- All patients in Phase I of the ACCEPT trial will have the chemotherapy drugs rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone given in the normal way. This is a standard treatment for your type of cancer. In addition, all patients will receive a new drug called acalabrutinib. The doses of acalabrutinib will vary in different groups of patients.
- A continuation phase of acalabrutinib only will be given after the completion of all other chemotherapy for a further 56 days.
- All of the drugs used in this trial can cause side-effects; however, you will be closely monitored and any side-effects will be properly treated.
- You will need to sign a consent form before taking part in the trial to confirm that you understand it and agree to take part.
- We would like your permission to collect, store and analyse samples of your blood and tissue.
- Women who might still be able to become pregnant will need to take a pregnancy test before being accepted on the trial. Pregnant women will not be able to take part in the trial.
- All participants **must** be willing to use adequate contraception while taking part in the trial.
- Depending on where your diagnostic tissue sample is held, you may have already been asked to read the Tissue Block Screening Patient Information Sheet and asked to sign a consent form to allow your original diagnostic tumour sample to be sent to Haematological Malignancy Diagnostic Service in Leeds (HMDS). If this is the case, confirmation from HMDS that there is enough tissue in the sample to conduct future testing will be required before you are invited to take part in the study. If you have not been asked to read the Tissue Block Screening Patient Information Sheet then your sample is likely to be easily accessible for transfer to HMDS following consent to this study.

### 1. Why we are doing the ACCEPT trial

Doctors often treat patients with your type of lymphoma, which is a type of non-Hodgkin's lymphoma called diffuse large B-cell lymphoma (DLBCL), with a particular combination of chemotherapy drugs and an antibody: known as R-CHOP. Although this is a successful treatment in most people with lymphoma, for others the lymphoma will not respond to the treatment or the lymphoma will come back after a brief period of remission. Sometimes, these chemotherapy drugs do not work as well as expected because the cancer cells 'block' or 'resist' what the drugs are trying to do. In the ACCEPT trial we are testing a new drug – called acalabrutinib - that may reverse this resistance and make the R-CHOP chemotherapy work better. Scientific tests in the laboratory tell us that acalabrutinib should work on cancer cells in this way. Additionally, in studies where acalabrutinib has been given to people, the results have shown that acalabrutinib seems to have some benefit. However, we need to find out more about acalabrutinib because it has not been tested with the standard R-CHOP chemotherapy that we would normally treat you with.

The ACCEPT trial is being done in two parts (phases):

**Phase I:** First, we need to understand more about how safe acalabrutinib is, how it is processed by the body and how much we can safely give (the dose) when it is used with R-CHOP: this is Phase I of the ACCEPT trial. **You are being invited to take part in Phase I of ACCEPT.**

**Phase II:** If Phase I of the trial is successful, we will continue to treat **future patients** in Phase II, the second part of the trial. In Phase II, we will look at the effect of acalabrutinib combined with R-CHOP on lymphoma and investigate the side effects of acalabrutinib. The amount (dose) of acalabrutinib will have been worked out in Phase I of the trial with patients, such as you. Phase II will include around 15 people with diffuse large B-cell lymphoma because we think this type of lymphoma might benefit from this approach. Therefore, we hope that people with the same cancer as you, might benefit in the future if this trial is successful.

## 2. Who is the trial for?

There are different things that your doctor will take into account to make sure that the ACCEPT trial is suitable for you. They will check things like your blood count and how well your kidneys and liver work.

**Phase I** of the ACCEPT trial is for people who have DLBCL and are healthy enough to receive the combination chemotherapy of R-CHOP.

## 3. More about the trial medicine

If you decide to take part in the ACCEPT trial, you will be treated with standard chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone, R-CHOP). This part of the treatment is the same as your doctor is proposing to treat you with if you were not taking part in this trial. We are trying to find out more about the effect of adding the new drug, acalabrutinib, to this standard chemotherapy. In Phase I of the trial, you will receive acalabrutinib as well as the standard R-CHOP chemotherapy.

After starting your treatment, if you are prescribed any new medication it is important that the doctor prescribing it knows that you are on this study. A full list of the medications which are prohibited are on page 17 of this patient information sheet.

***What exactly is the medicine that is being tested?*** Doctors have identified that the genes in your lymphoma may affect how successful your treatment is. Abnormal or unusual behaviour of genes can mean that cancer cells do not die. The purpose of this trial is to test a new drug called acalabrutinib which is known as a 'Bcr tyrosine kinase (BTK) inhibitor', this blocks a protein that is activated in the lymphoma cells. These drugs have been known to improve the chances of chemoimmunotherapy to kill off the cancer cells.

***Has acalabrutinib been given to people before?*** Yes. As of 3<sup>rd</sup> September 2017, more than 2300 participants have been treated in clinical trials involving acalabrutinib, which have been sponsored by Acerta Pharma (the company supplying the acalabrutinib for this trial). The ACCEPT trial is the

next step towards developing this drug for use in patients with other blood cancers, including lymphoma.

***How do the doctors decide how much acalabrutinib I will get?*** In Phase I of the trial, doctors will give the first group of 6-12 patients a fairly low dose of acalabrutinib. If this dose of acalabrutinib is safe and does not cause too many side effects, then a second group of 6-12 patients will be given a higher dose of acalabrutinib. This process of testing acalabrutinib in 6-12 patients and then increasing to the next dose level in the next group of patients is to ensure that the dose level is safe before any increase in the dose. The Phase I part of the trial will be completed at two dose levels for acalabrutinib if it is safe and does not cause excessive side effects.

Once the trial team have confirmed the appropriate dose of acalabrutinib, a further group of patients with DLBCL (Phase II) will be given acalabrutinib at this dose plus R-CHOP chemotherapy. A total of 15 patients with DLBCL will be tested at this acalabrutinib dose. Doctors need to do this so that they can make further checks on safety and side effects. This will be Phase II part of the trial.

If you decide to enter Phase I of the trial, you will be given the current dose of acalabrutinib (i.e. the dose that is being tested at the time you enter the trial).

#### **4. What will I have to do if I decided to take part?**

If you decide that you would like to take part in the ACCEPT trial, your doctor will ask you to sign the informed consent form. After you have signed informed consent, the trial team will need to do some tests to make sure that you are fully suitable to take part - this is called screening. You will be asked to provide two blood samples (2 tablespoons (tbsp) of blood) as part of the screening process, which will be sent to the trial laboratory for analysis. The original biopsy which was taken to diagnose your cancer will also be sent to the Haematological Malignancy Diagnostic Service in Leeds (HMDS) as part of the screening process. The tumour biopsy will be sent along with a copy of your consent form and NHS number, to allow HMDS to confirm you have consented to the trial.

During screening you will be strongly advised against eating or drinking grapefruit, grapefruit juice, Seville orange juice, using herbal remedies or dietary supplements (especially St John's Wort) for the duration of the study.

After screening you will need to attend various clinic visits in order to receive your medicines, have examinations and provide samples. As part of your standard treatment, your doctor will assess the extent of your cancer (e.g. by CT scan) and we will collect this information. The trial team will also need to know the details of other medicines that you take during the trial. On the study you will have three extra PET/CT or CT scans, beyond your standard care, to assess your disease.

Routine blood samples will be taken when you attend the hospital in order to monitor your progress. In Phase I of the trial, extra blood samples will need to be taken throughout your cycles so that the levels of acalabrutinib in your blood can be checked (this is called pharmacokinetics).

In order to collect more information about how the drug works (pharmacodynamic and translational studies), we would like your permission to collect, store and test some further samples of:

- **blood** (collected at screening, at various points throughout treatment and at the end of the trial amounting to between 2 tbsp to 6 tbsp depending on the visit), AND,
- **tissue** (optional biopsy)

You can find more about the trial samples in Section 8, 'More about the trial samples'.

If you decide to take part in Phase I of the ACCEPT trial, you will need to attend more clinic visits than if you were receiving standard treatment alone: this is to enable the trial team to check that you are okay and to take further blood samples for analysis. Your standard R-CHOP chemotherapy treatment will be given on day 1 of each cycle.

## 5. What is the treatment schedule?

Each treatment cycle is 21 days and you will have up to 6 cycles of treatment. You will start acalabrutinib at your second cycle. Once the first six cycles are complete you will have two further cycles of the acalabrutinib alone on a 28 day cycle.

### Cycle 1:

| Drug             | Day |   |   |   |   |
|------------------|-----|---|---|---|---|
|                  | 1   | 2 | 3 | 4 | 5 |
| Rituximab        | ✓   |   |   |   |   |
| Cyclophosphamide | ✓   |   |   |   |   |
| Vincristine      | ✓   |   |   |   |   |
| Doxorubicin      | ✓   |   |   |   |   |
| Prednisolone     | ✓   | ✓ | ✓ | ✓ | ✓ |

### Cycle 2 – 6:

| Drug             | Day      |   |   |   |   |
|------------------|----------|---|---|---|---|
|                  | 1        | 2 | 3 | 4 | 5 |
| Rituximab        | ✓        |   |   |   |   |
| Cyclophosphamide | ✓        |   |   |   |   |
| Vincristine      | ✓        |   |   |   |   |
| Doxorubicin      | ✓        |   |   |   |   |
| Prednisolone     | ✓        | ✓ | ✓ | ✓ | ✓ |
| Acalabrutinib    | Day 1-21 |   |   |   |   |

### Continuation Phase:

| Drug          | Day       |          |
|---------------|-----------|----------|
|               | 1         | 29       |
| Acalabrutinib | Day 1- 28 | Day 1-28 |

**R-CHOP** - This will be given on Day 1 of each cycle by infusion (a 'drip') into your vein or injected directly. You will receive the standard dose for this treatment.

**Prednisolone** – Day 1-5 (inclusive) of each cycle. Prednisolone is to be taken orally each day as part of your R-CHOP treatment. You will receive the standard dose of this drug and be asked to take it on the days you are not in clinic.

**Acalabrutinib** – Given on Days 1-21 (inclusive) from cycle 2 through to cycle 6, then given on Days 1-28 for two further cycles. Acalabrutinib is to be taken orally. The capsule will be provided to you in bottles containing 30 capsules. The capsules that are not taken should be returned to the trial team.

**Other medicines** – You will be given other medicines to help stop nausea and vomiting. The exact drugs used will be those normally used at your Cancer Centre.

Chemotherapy often causes a lowering of the immune cells in the body (medical name, neutropenia). During the trial, doctors may decide that it is appropriate to treat this by giving another medicine called G-CSF. If this is needed your doctor will explain this to you.

***Will this treatment schedule change?*** It could change. Some of the most common reasons the schedule may change are:

- At each stage, your doctor must be satisfied that you are well enough to continue receiving treatment. If you are not well enough, your schedule of treatment may change a little or stop, depending on the exact situation. Your doctor will discuss these with you on an ongoing basis throughout the trial.
- Sometimes during the course of a clinical trial, new information becomes available about the trial medicine. If this happens, it may or may not affect your treatment schedule. If anything changes that might affect your treatment, your doctor will discuss this with you and you can decide if you want to continue with the trial. You may be asked to sign an updated consent form.

## **6. What are the possible side effects?**

As with most medicines, all of the chemotherapy medicines used in this trial can cause unwanted side effects. This information sheet does not list all of the known side effects, only the most common.

*Please be aware that you may experience a side effect(s) that we do not yet know about: if you suffer from something that you think may be caused by the trial medicines, please contact your trial doctor/nurse.*

R-CHOP chemotherapy is known to cause the following side effects, though not in all patients:

- Suppression of the bone marrow. This can mean that you do not produce normal quantities of healthy blood cells which could put you more at risk of infection. You may be at risk of anaemia, which can make you pale, tired and short of breath. You may be more at risk of bleeding and it may be harder for your body to stop bleeding.
- Hair loss. Hair loss is usually temporary. Hair will start to grow back a few weeks after treatment is finished.
- Nausea and vomiting.
- Sore mouth, sore throat and mouth ulcers. This is also called mucositis.
- Loss of appetite and change in taste.

- Constipation or alternatively diarrhoea.
- Fatigue.
- Numbness or tingling in hands or feet.

Some other side effects are particular to individual drugs; please see a summarised list below:

| Drug                    | Side effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Rituximab</b>        | <ul style="list-style-type: none"> <li>• Fevers, chills, flu-like symptoms. This is the most common experience. It is usually associated with the first dose. It can be managed with paracetamol and anti-histamines.</li> </ul> <p>Other symptoms, which are less common, include:</p> <ul style="list-style-type: none"> <li>• skin rash or itching</li> <li>• a feeling of swelling in the mouth or throat</li> <li>• a temporary drop in blood pressure</li> <li>• hot flushes or night sweats</li> <li>• headache</li> <li>• throat irritation</li> <li>• runny nose</li> <li>• cough, wheeze or shortness of breath</li> <li>• pain in your enlarged lymph nodes</li> </ul> <p>Rituximab can also cause a flare-up of past viral infections. Please tell your team if you have been infected with serious viruses in the past, such as shingles or hepatitis.</p> <p>Rituximab can worsen heart problems if you already have them, for example angina or heart failure. Talk to your team about this.</p> <p><i>Very rarely the use of rituximab may result in the development of serious skin reactions. If you have concerns about this please discuss this with your trial team.</i></p> |
| <b>Cyclophosphamide</b> | <ul style="list-style-type: none"> <li>• Hot flushes</li> <li>• Dizziness</li> <li>• Strange taste in the mouth</li> <li>• Cystitis (inflammation of the bladder, with some bleeding)</li> <li>• Heart problems</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Doxorubicin</b>      | <ul style="list-style-type: none"> <li>• Red flush and aching along the vein (at the time of treatment)</li> <li>• Red discolouration of urine</li> <li>• Heart problems. Your team will check your heart before and during treatment.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

|                     |                                                                                                                                                                                                                                                                                                                                                                  |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Vincristine</b>  | <ul style="list-style-type: none"> <li>• Nerve damage, also known as peripheral neuropathy. This often causes loss of sensation, tingling or pain in hands and feet. It may cause constipation and bladder problems. It is usually short term, but can persist after treatment finishes.</li> <li>• Cold sensation along the vein</li> <li>• Jaw pain</li> </ul> |
| <b>Prednisolone</b> | <ul style="list-style-type: none"> <li>• Indigestion</li> <li>• Difficulty sleeping</li> <li>• Muscle aches</li> <li>• Change in mood, irritability</li> <li>• Change in blood sugar levels</li> <li>• Increased appetite</li> <li>• Fluid retention</li> </ul>                                                                                                  |

**Acalabrutinib** is an approved drug for the treatment of adult patients with mantle cell lymphoma who have received at least one prior therapy. It is also under investigation for other diseases hence, the side effects are not yet fully known. Side effects can vary from mild to very serious and may vary from person to person. You may have some or no side effects. Everyone taking part in the study will be watched carefully for any side effects. You should talk to your study doctor about any side effects that you have while taking part in the study.

As of 03 September 2017, over 2300 patients have received acalabrutinib in clinical studies, which includes patients with blood cell cancers, solid tumours, or rheumatoid arthritis, and participants who are healthy volunteers or who have mild or moderate liver problems.

Side effects that may occur with acalabrutinib include:

#### Hemorrhage (Bleeding)

Events of bleeding have occurred in patients treated with acalabrutinib. These include minor events such as nose bleed, bruising, or ecchymosis (bleeding in skin) and major events which could be fatal such as internal bleeding in the bowel or bleeding in the brain. If you are using any blood thinners (drugs that prevent your blood from clotting e.g. aspirin or warfarin) your risk of bleeding may be increased.

#### Infections

Infections have been reported to occur in patients receiving acalabrutinib. The most commonly reported infections were upper respiratory infection, sinus infection, and pneumonia (lung infection). Infections that are uncommon or rare, but which can result in severe disability or death, have also occurred in patients receiving acalabrutinib. These infections include hepatitis B virus (HBV) reactivation and progressive multifocal leukoencephalopathy (PML). HBV reactivation is where a type



of liver virus infection becomes active again if you had a previous infection with that virus. PML is a rare, serious brain infection caused by a virus, usually in patients with weakened immune systems, and can result in severe disability or death.

Tell your study doctor right away if you experience any symptoms of an infection such as fever, runny nose, sore throat, cough, and feeling tired. If you have previously had HBV or any other viral liver infection, your study doctor may need to monitor you closely.

#### Cytopenias (Low Blood Cell Counts)

Patients receiving acalabrutinib can sometimes experience low blood cell counts. Your study doctor will do blood tests while you receive acalabrutinib to check your blood cell counts, which include:

- White blood cells - cells that fight against infections
- Red blood cells – cells that carry oxygen throughout your body
- Platelets – cells that help your blood to clot

#### Second Primary Malignancies

The development of a second cancer has been reported to occur in some patients who receive acalabrutinib. If you develop a second cancer, you may need to stop the study drug, and your doctor may need to do further tests.

#### Atrial Fibrillation/Atrial Flutter

Atrial fibrillation and atrial flutter are abnormal heart rhythms, which have been reported to occur in some patients who receive acalabrutinib. Atrial fibrillation or flutter may occur more commonly in patients with other risk factors for cardiac (heart) disease, such as hypertension (high blood pressure), diabetes mellitus, acute infections, or a previous history of atrial fibrillation. While atrial fibrillation or flutter often may not cause symptoms, some patients may experience palpitations (feeling like your heart is beating too hard or too fast), fainting, chest pain, or shortness of breath. If you have any of the symptoms described above, tell your doctor. Your doctor may give you other medicines to reduce your symptoms.

Acalabrutinib side effects considered caused by the drug that occurred in safety data for over 600 patients receiving acalabrutinib monotherapy (treatment with only acalabrutinib) in clinical studies for blood cancers are provided in the table below.

| <b>Very Common (at least 10% of patients)</b>                                                                                                                                                                                                                                                    | <b>Common (at least 1% but less than 10% of patients)</b>                               |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Headache</li><li>• Bruising events (<i>including bruises, petechiae (pinpoint red or purple spots on the skin), and increased tendency to bruise</i>)</li><li>• Bleeding</li><li>• Diarrhea (<i>frequent or loose stools</i>)</li><li>• Nausea</li></ul> | <ul style="list-style-type: none"><li>• Nose bleeds</li><li>• Severe bleeding</li></ul> |

|                                                                                                                                                                                             |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| <ul style="list-style-type: none"> <li>• Constipation (<i>bowel movements that are infrequent or hard to pass</i>)</li> <li>• Vomiting</li> <li>• Abdominal pain</li> <li>• Rash</li> </ul> |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|

## 7. What will happen at the end of the trial?

You will have an end of treatment clinic visit approximately 4 weeks after your last dose of chemotherapy. After the end of treatment visit there will be a continuation phase for 56 days, of the acalabrutinib drug. Once the continuation phase is complete you will remain in the trial and be followed-up for two years.

## 8. More about the trial samples

Depending on where your diagnostic sample is held, you may have already been asked to read the Tissue Block Screening Patient Information Sheet and asked to sign a consent form. If this is the case then your original biopsy will have already been sent to Haematological Malignancy Diagnostic Service in Leeds (HMDS). Confirmation from HMDS that there is enough tissue in the sample to conduct future genetic profiling will be required before you are invited to take part in the study. If you have not been asked to read the Tissue Block Screening Patient Information Sheet then your sample is likely to be easily accessible for transfer to HMDS following consent to this study.

In the trial, your original biopsy and two extra samples of blood will be sent to the Haematological Malignancy Diagnostic Service in Leeds (HMDS), prior to the start of your first cycle of treatment, for analysis. Within the trial we will need to take a number of additional blood samples from you at regular time points through the trial, please ask your trial team for exact details. We need to take these blood samples at specific times throughout the trial after you have taken acalabrutinib so that we can assess the level of the drug in your blood over time: this is called pharmacokinetics. Please be aware that these blood samples will be sent to BASi Sample Management in the USA for the pharmacokinetic testing.

In addition to these Pharmacokinetic blood samples, we would like to collect and store some samples of your blood and tissue so that we can do some further studies in the future. We would like to do this because doctors need to understand exactly how the drug works in the body (these studies are called pharmacodynamic and translational studies). This information, along with the other results collected in this trial, will be used to get a better understanding of how acalabrutinib works and how it interacts with lymphoma.

Collection, storage and testing of your tissue (as listed below) for the pharmacodynamic and translational studies are optional:

- **Optional tissue samples** – if you choose to participate in this optional sample, it will involve two biopsy during the course of the study. One will be taken prior to your acalabrutinib treatment (baseline) and the second during cycle 2 of treatment on day 8.

The majority of your pharmacodynamic samples will be sent to the Acerta Pharma Laboratory in Holland. The remaining pharmacodynamic blood samples will be analysed at the WISH Laboratory, Southampton General Hospital. All of your samples will be coded: this means that your samples will be labelled with a code number, not your name. Neither you nor your relatives will be contacted about them once they have been taken.

With your consent, any remaining samples may be used in future ethically approved studies. You can agree to this or decline on the informed consent form.

Please note that you can still participate in the main part of the trial even if you decide that you do not want the additional tissue samples to be taken, stored and tested for this part of the research, or in any other future ethically approved studies.

## **9. What are the possible benefits, risks and disadvantages of taking part in the trial?**

Clinical trials are designed to reduce the risks and increase the benefits to the people who take part, regardless of which treatment they get. However, we cannot guarantee any specific treatment benefits or that there are no risks involved when taking part in a clinical trial.

### **Possible benefits:**

- You will be helping to further our knowledge of how to treat cancer and this will benefit society and others with the same condition in the future

### **Possible risks/disadvantages**

- The trial treatment may not control your lymphoma
- There may be some unpleasant side effects (please see the side effects section, section 6, for more information)
- There could be risks to your child if you, or your partner, are/or become pregnant, or breastfeeding (please see the pregnancy and contraception section, section 10, for more information)
- You will need to attend more clinic visits and provide more blood samples than if you were not taking part in the trial

### **Radiation Risks**

- During the trial, you will have contrast enhanced CT scans or PET scans with CT component to assess your lymphoma, and blood tests to check your general wellbeing. These tests use radiation, which has a limited increase to your risk of cancer in the future. These tests are part of standard care but you will receive three additional scans by taking part in the trial.
- You will also be required to have an echocardiogram or MUGA, depending on your hospital's practice, to ensure you are well enough to receive the full dose of chemotherapy.

## **Risk Explanations:**

A **contrast enhanced CT scan** involves radiation, using X-Rays to get a detailed image of the body area. The main risk of the radiation is there is a small chance it may cause a cancer many years after exposure. The CT scans also require a contrast injection, which some patients may have an allergic reaction too. In certain patients it could cause kidney damage and it is recommended that if you have previously experienced problems, please let your doctor know.

In comparison a **PET-CT scan** differs from a contrast enhanced CT in that a radioactive isotope is given to you, the patient. The PET-CT scanner detects how much of isotope your body absorbs and uses a computer to create an accurate image of the scanned body area. As with CT scans, this involves radiation which has a small chance of causing cancer many years after exposure, though it is higher than a CT scan due to the extended time within the scanner. It is considered that for a patient with your medical condition this represents a very small risk.

An **Echocardiogram**, which will be used depending on your hospital's local practice, uses an ultrasound wave to give your doctor a visual display of how your heart is working. In comparison a **MUGA** (depending on your hospital's local practice) creates video images of the lower chambers of your heart to detect any irregularities. These scans will measure the amount of blood pumped by your heart.

## **10. More about contraception and pregnancy during the trial**

### **Women**

If you are pregnant or breast feeding, you will not be able to enter the ACCEPT trial. Women who can bear children must agree to use highly effective forms of contraception or abstinence during the study and for 12 months after the last dose of trial drug and will need to have a negative pregnancy test at screening (prior to starting treatment). Please be aware that if you become pregnant during the trial, you will not be able to continue taking part in the trial.

You must also agree to use **two** highly effective forms of contraception from the start of your trial treatment, throughout the trial and for 12 months after finishing treatment. Highly effective contraception options will be discussed with you by your study doctor.

### **Men**

If your partner is pregnant or breast-feeding, we advise you to use barrier method contraception to make sure that the baby is not exposed to the trial drug.

If you have a partner of child bearing potential, you must agree to use **two** highly effective forms of contraception from the start of your trial treatment, throughout the trial and for 12 months after finishing treatment. You must refrain from any sperm donation from the start of your trial treatment, throughout the trial and 12 months after finishing treatment. Highly effective contraception options will be discussed with you by your study doctor.

**\*\* If you or your partner becomes pregnant during the trial, you must tell your trial doctor immediately because we will need to follow the pregnancy to check that the trial drug has not caused any problems. \*\***

**Future fertility** – chemotherapy can affect your ability to have children in the future so, you may wish to discuss this, and the possibility of storing eggs/sperm, with your doctor.

## **11. What are the alternative treatments?**

If you prefer not to take part in the ACCEPT trial, your doctor will be able to discuss all treatment options with you. Please be reassured that it is entirely up to you whether or not you decide to take part in the ACCEPT trial. If you decide not to take part, the standard of your care will not be affected in any way.

## **12. Other questions you may have about the trial**

### ***What does informed consent mean?***

No one can enter you in the clinical trial without your permission. To help you decide if taking part in a clinical trial is right for you, the trial doctor/nurse should discuss the trial with you in depth. The most important thing is that you should feel satisfied that you know enough about the trial to make an informed decision. You should feel free to ask as many questions as you need to. In addition, you should be given as much time as you need to make your decision – you should not feel rushed.

If you decide to take part in the trial, you will be asked to sign a consent form which confirms that you agree to take part. The original consent form will be filed securely at the hospital. A copy will be kept in your medical notes, a copy sent to the SCTU via secure e-mail and held securely, a copy sent to HMDS and a copy provided to you. At the end of the trial the original consent form will be archived by the hospital who took the consent for a period of 25 years and will be stored separately from any non-identifiable information provided. The copy sent to the SCTU and HMDS will be destroyed as confidential waste prior to the trial being archived.

### ***Will my details be kept confidential?***

University Hospital Southampton NHS Foundation Trust is the sponsor for this study based in the United Kingdom. The sponsor and the Southampton Clinical Trials Unit (SCTU), who are acting on behalf of the sponsor, 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 the sponsor and SCTU are responsible for looking after your information and using it properly. University Hospital Southampton NHS Foundation Trust will keep identifiable information about you for 25 years after the study has finished.

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

You can find out more about how we use your information at <https://www.southampton.ac.uk/ctu/about/index.page>.

[Insert name of local NHS site] 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 University Hospital Southampton NHS Foundation Trust, the SCTU and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [Insert name of local NHS site] will pass these details to University Hospital Southampton NHS Foundation Trust along with the information collected from you and your medical records. The only people in the University Hospital Southampton NHS Foundation Trust and the SCTU who will have access to information that identifies you will be people who need to 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, NHS number or contact details with the exception of trained and authorised staff who work at the Haematological Malignancy Diagnostic Service Lab (HMDS). Staff at HMDS are employed by The Leeds Teaching Hospital NHS Trust. A small number of staff from this lab will see your NHS number and signed consent form, as these must be sent along with the tissue samples that you give during your time on the trial for analysis. The reason for this is so that the lab can confirm that you have given your consent for them to analyse your samples as part of this trial. Your details would be stored electronically by HMDS along with your tissue sample results on their secure NHS servers, the paper copies of your consent form and NHS number are destroyed as confidential waste.

[Insert name of local NHS site] will keep identifiable information about you from this study for 25 years after the study has finished.

Non-identifiable data, managed by the Southampton Clinical Trials Unit, will be held on servers located in the EU and USA and access will be strictly controlled and all applicable Data Protection legislation will be abided by. In collaboration with the Southampton Clinical Trials Unit a selection of laboratories across the UK will have strictly controlled access to your anonymised data, with the exception of HMDS who will hold your NHS number and signed consent form. This information will contribute to a better understanding of this disease and will be used by investigators who will not have access to any data that will identify you.

With your permission, we will tell your General Practitioner (GP) that you are taking part in the ACCEPT trial. Your medical records will be available to those involved in your clinical care and authorised individuals from the Sponsor or the Sponsor's delegates from the Southampton Clinical Trials Unit and Regulatory Authorities.

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 this organisation and in 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.

**You can agree or decline to this use of your data for future research by third parties on the informed consent form.**

***What happens if something goes wrong?***

If you decide to take part in the ACCEPT trial and feel concerned about any part of the trial at any point, you should contact your research doctor/nurse as soon as possible. Your clinical research team will do their best to help you and answer your questions.

If you wish to complain, or have any concerns about the way you have been approached or treated during the ACCEPT trial, the normal NHS complaints system will be available to you, this service is called the Patients Advice and Liaison Service (PALS). For the contact details and further information please check [www.nhs.uk](http://www.nhs.uk) or your local trusts website.

Please be aware that if you are harmed as a result of taking part in the ACCEPT trial, there are no special compensation arrangements. If you are harmed because of someone's negligence, you may be able to take legal action but you may have to pay your own legal costs.

If you have private medical insurance you may wish to check with your provider before agreeing to take part in this trial to make sure that your participation will not affect your cover.

***Who is organising and funding the trial?***

The trial is being coordinated by the Southampton Clinical Trials Unit. The trial is being funded by Acerta Pharma (the manufacturer and supplier of acalabrutinib) and has been endorsed by Cancer Research UK, New Agents Committee. The Sponsor is University Hospital Southampton NHS Foundation Trust. The study has been ethically reviewed by the South Central – Berkshire Research Ethics Committee and regulatory reviewed by the Medicines and Healthcare products Regulatory Agency (MHRA).

***What will happen to the results of the trial?***

At the end of the trial, any results will be analysed and presented at national or international meetings, and will also be published in a medical journal. You will not be personally identified in anyway in any reports or publications that come from the ACCEPT trial. A lay version of the trial results will be prepared and made available for patients and members of the public, please ask your doctor.

### **13. Contact information**

If you have any further questions about your illness or available treatments please discuss them with your doctor. If at any stage you have questions about the ACCEPT trial, or would like to discuss your participation in more detail, please contact:

**Doctor's name: (insert)**

**Name of treatment centre: (insert)**

**Telephone number: (insert)**

Further information about cancer, treatments and taking part in trials can be found on the Cancer Research UK website: [www.cancerresearchuk.org](http://www.cancerresearchuk.org)

Macmillan Cancer Support can also provide support and information: <http://www.macmillan.org.uk/>



## LIST OF PROHIBITED DRUGS

| Type of Drug                                                                            | Name of Drug                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| strong cytochrome P450 3A4 (CYP3A4) inhibitor/inducer                                   | <u>Inhibitors of CYP3A</u><br>boceprevir<br>clarithromycin<br>conivaptin<br>grapefruit juice<br>itraconazole<br>ketoconazole<br>indinavir<br>lopinavir/ritonavirb (combination drug)<br>mibefradil<br>nefazodone<br>nelfinavir<br>posaconazole<br>ritonavirb<br>saquinavir<br>telaprevir<br>telithromycin<br>voriconazole<br><br><u>Inducers of CYP3A</u><br>carbamazepine<br>phenytoin<br>rifampin<br>St John's wort |
| Proton pump inhibitors<br>Must be stopped prior to starting cycle 2 of trial treatment. | omeprazole<br>esomeprazole<br>lansoprazole<br>dexlansoprazole<br>rabeprazole<br>pantoprazole                                                                                                                                                                                                                                                                                                                          |