SUMMARY PATIENT INFORMATION SHEET

Purine-Alkylator Combination In Follicular lymphoma Immuno-Chemotherapy for Older patients: A phase III comparison of first-line R-CVP versus R-FC lite

You have been invited to take part in a research study. Please take time to read the following information and discuss it with others if you wish. This page summarises the treatments and investigations that will happen to you if you choose to take part.

Why have I been chosen?
You have a condition called follicular lymphoma, and are either over the age of 60, or you are thought to be at good candidate for the treatments in this trial.

At present the best treatment of follicular lymphoma is not known. Some treatments may be more effective than others at treating the disease, but they can also have more side effects.

Preliminary studies suggest that a new drug combination called “R-FC lite” might be a particularly good treatment for older patients with follicular lymphoma. The aim of the PACIFICO trial is to compare “R-FC lite” to the drug combination currently regarded as the standard of care (“R-CVP”) to see which is better.

Do I have to take part?
No. It is up to you decide whether or not to take part. If you do you will be asked to sign a consent form. You are 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?
If you agree to take part in the trial, you will have initial tests to check your suitability. If you meet the entry criteria, you will be randomly allocated to receive either R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone) or R-FC lite (rituximab, fludarabine, cyclophosphamide).

We will perform additional blood tests before treatment starts. You will then receive 6-8 months of treatment called the “induction phase”, where you will receive either R-CVP or R-FC lite. The drugs are different, but the treatment schedule is similar.
Once the induction phase is complete, if your disease is in remission you will move onto the next stage of treatment, called the “maintenance phase”. This consists of one drug (rituximab) every 2 months for 12 doses, given over a period of 2 years. It is hoped maintenance treatment will prolong remissions.

You will undergo CT scans and bone marrow biopsies at key stages during the treatment in order to know how well you have responded to the treatment.

All information which is collected about you during the course of this research will be kept strictly confidential.

If you are interested in finding out more information about the study, please read the full Patient Information Sheet.
PATIENT INFORMATION SHEET

Purine-Alkylator Combination In Follicular lymphoma Immuno-Chemotherapy for Older patients:
A phase III comparison of first-line R-CVP versus R-FC lite

We are inviting you to take part in a research study. Before you decide whether to take part, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and talk to others if you wish.

- Part one explains the purpose of the study and what will happen to you if you take part.
- Part two provides more detailed information about the conduct of the study.

Please 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.

Part 1
What is the purpose of the trial?

Doctors and researchers have designed this study to find out whether one combination of drugs (chemotherapy) is more beneficial than another combination of drugs when given to older patients (aged 60 or over) with follicular lymphoma (FL).

Patients who are under the age of 60, but who are thought to be at risk from the potential side-effects of stronger types of chemotherapy, may also enter this trial.

At present we do not know the ideal treatment of follicular lymphoma (FL). Although some of the newer treatments may be more effective than older ones at treating the disease, they can also have more side effects.

It is the balance between these two things that determines how good a particular treatment is. Because older patients are generally less tolerant of side effects, gentler treatments are usually more appropriate in this age group.

The drug combination currently regarded as the standard of care (“R-CVP”) strikes a reasonable balance between effectiveness and side effects but there might be scope for improvement. Preliminary studies suggest that a new drug combination called “R-FC lite” might be a particularly good treatment for older patients with follicular lymphoma.
The aim of the PACIFICO trial is to compare these two treatments directly to see which is better.

If you agree to take part, you will be randomly allocated to one of two groups:

1) R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone)
2) R-FC lite (rituximab, fludarabine, cyclophosphamide)

This means that half of all patients in the trial will be given R-CVP and half will be given R-FC lite, and whether you are treated with one or other type of chemotherapy drug will be decided by chance. Whichever group you are in, we will monitor you closely.

Why have I been chosen?

You have a condition called follicular lymphoma and are either over the age of 60, or you are thought to be at risk from side-effects of alternative drug treatments. There will be 680 patients taking part in the trial throughout the United Kingdom.

Do I have to take part?

No. It is up to you decide whether or not to take part. If you do you will be asked to sign a consent form. A decision not to take part will not affect the standard of care you receive.

What will happen to me during the trial?

The chemotherapy treatments are with drugs called R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone), or alternatively R-FC lite (rituximab, fludarabine, cyclophosphamide). All treatments are given in the outpatient clinic, so you do not necessarily need to be admitted to hospital.

Screening

Once you have agreed to take part in the trial, you will have initial tests to check that you are suitable. You will have a physical examination and blood tests including HIV and Hepatitis B and C (treatments for lymphoma can be unsafe if any of these infections are present). You will also have a body scan and a bone marrow biopsy. These tests are routine for all patients with follicular lymphoma.

If you meet all the criteria for entering the trial, you will be randomly allocated to receive either R-CVP or R-FC lite, which must be started within 42 days. We will give you some additional blood tests before treatment is started.

Overview of treatment

This section paints an overall picture of the trial treatment, which is the same for R-CVP and R-FC lite.
The initial 6-8 months of treatment is called the “induction phase” and its purpose is to put the disease into a remission. This is the part of the trial where you will receive either R-CVP or R-FC lite. Although the drugs are different, the treatment schedule is similar.

We will perform CT scans and bone marrow biopsies mid-way through the induction treatment to make sure it is working and again at the end to know how well you have responded. These tests form part of the routine care of all patients with follicular lymphoma who are undergoing treatment.

At the end of the induction phase, most patients will have achieved a remission. A remission may be complete, which means that the disease can no longer be detected. The remission may be partial, which means that the disease has responded to treatment but is still visible on the scans or in the bone marrow.

During the induction phase, we will give you treatment every 3 or 4 weeks, aiming for 8 doses in total, provided that your disease responds to the first 4 doses. You will need to attend twice for each treatment. The first visit is to make sure it is safe to go ahead with the treatment, and the second visit is to actually have it. In some hospitals and treatment units these visits can be rolled into one.

Once you have completed the induction phase you will move onto the next stage of treatment, which is called the “maintenance phase”. This consists of just one drug (rituximab) every 2 months for 12 doses, given over a period of 2 years.

The idea behind maintenance treatment is that it makes remissions last longer. There is good evidence for this effect in patients with relapsed follicular lymphoma and, more recently, the PRIMA trial has demonstrated that maintenance treatment can also be effective for those patients who have responded well to initial treatment for the disease.

You will need to attend twice for each maintenance treatment. The first visit is to make sure it is safe to go ahead with the treatment, and the second visit is to actually have it. In some hospitals and treatment units these visits can be rolled into one.

Once the maintenance phase has been completed, we will stop treatment. You will attend for formal follow-up visits every 4 months for as long as you remain in remission. This called the “follow-up phase”. Since it is important to understand what effect the initial treatment has on subsequent treatments, information about your progress will continue to be collected if you relapse or receive further treatment.

*Will I have to have any extra tests?*

Irrespective of whether you receive R-CVP or R-FC lite, we will perform an additional CT scan and bone marrow biopsy 2 months after the last dose of maintenance rituximab.

These are the only trial tests (other than blood tests) that are above and beyond those performed routinely as part of anti-lymphoma treatment.

*If you are allocated to R-CVP*
R-CVP consists of 4 different drugs: rituximab, cyclophosphamide, vincristine and prednisolone.

The first rituximab dose will be given to you by intravenous infusion (through a thin plastic tube placed in a vein in your hand or arm) over several hours. This intravenous infusion may take most of the day. While you are receiving the intravenous infusion, a doctor or a nurse will watch you closely. At the end of your intravenous infusion, you will need to stay at the hospital or the ward for observation. This is to check that you do not have any side effects from the intravenous infusion. If you do not have any side effects from the infusion, your next 7 cycles of rituximab will be given to you as subcutaneous injections (through a needle inserted under your skin) into your abdomen. The injection will take approximately 6 minutes to complete. However, if your first rituximab dose (cycle 1), which was given as an intravenous infusion, has to be stopped because of severe side effects and you did not complete your first full rituximab dose, you will receive your second rituximab dose also by intravenous infusion. If you do not have severe side effects from the second dose of rituximab given by intravenous infusion, you will then receive your third rituximab dose as subcutaneous injection. If you have severe side effects after your second dose of rituximab given by intravenous infusion, you will stop receiving rituximab on the study. Your study Doctor will then discuss other anti-cancer treatment options with you.

The cyclophosphamide and vincristine are given intravenously in all treatment cycles.

The prednisolone is given by mouth as a tablet for 5 consecutive days, starting on the same day as the intravenous drugs. You need to take prednisolone tablets at home regularly and will be asked to complete a diary sheet to record each time you take the tablet. Each treatment visit will typically last most of the working day, although this may vary depending on how well your body tolerates the treatment. The R-CVP treatment will be repeated every 3 weeks.

In addition to the main drugs, you will also receive paracetamol and an antihistamine drug prior to each dose of rituximab to reduce the risk of flu-like symptoms and infusion reactions. You will also receive a drug called allopurinol to reduce the risk of kidney damage by chemicals released from the lymphoma cells as they break down. This is standard practice.

*If you are allocated to R-FC lite*

R-FC lite consists of 3 drugs: rituximab, fludarabine and cyclophosphamide. It is called “lite” because the dose of fludarabine and cyclophosphamide are reduced.

The first rituximab dose will be given to you by intravenous infusion (through a thin plastic tube placed in a vein in your hand or arm) over several hours. This intravenous infusion may take most of the day. While you are receiving the intravenous infusion, a doctor or a nurse will watch you closely. At the end of your intravenous infusion, you will need to stay at the hospital or the ward for observation. This is to check that you do not have any side effects from the intravenous infusion.

If you do not have any side effects from the infusion, your next 7 cycles of rituximab will be given to you as subcutaneous injections (through a needle inserted under your skin) into
your abdomen. The injection will take approximately 6 minutes to complete. However, if your first rituximab dose (cycle 1), which was given as an intravenous infusion, has to be stopped because of severe side effects and you did not complete your first full rituximab dose, you will receive your second rituximab dose also by intravenous infusion. If you do not have severe side effects from the second dose of rituximab given by intravenous infusion, you will then receive your third rituximab dose as subcutaneous injection. If you have severe side effects after your second dose of rituximab given by intravenous infusion, you will stop receiving rituximab on the study. Your study Doctor will then discuss other anti-cancer treatment options with you.

The other 2 drugs (fludarabine and cyclophosphamide) are given by mouth for 4 consecutive days, starting on the same day as the rituximab. The first day of the first treatment visit will typically last most of the working day, although this may vary depending on how well your body tolerates the treatment. Subsequent treatments should take much less time as the rituximab is given subcutaneously. The full combination of drugs will be given every 4 weeks for the first 4 treatments only. Treatments 5 to 8 will consist of rituximab alone and will be repeated every 4 weeks.

In addition to the main drugs, you will also receive paracetamol and an antihistamine drug prior to each dose of rituximab to reduce the risk of flu-like symptoms and infusion reactions. You will also receive a drug called allopurinol to reduce the risk of kidney damage by chemicals released from the lymphoma cells as they break down, and an antibiotic called co-trimoxazole to reduce the risk of infection. This is standard practice.

If your disease does not respond to R-CVP or R-FC lite

In a minority of patients, the lymphoma will not respond to the trial treatment or will progress through it. If you fall into this category, you will not receive any further study treatment and your doctor will decide how best to treat you. However, your doctor and nurses will continue to collect information about your progress.

Quality of life and health economic surveys

A very important aspect of this study involves assessing how your disease or any treatment you receive affects the quality of your life, so our research nurses will ask you to fill in a questionnaire that asks about how you are feeling and what activities you are able to undertake. This will be done before treatment starts, after the 4th and 8th dose of induction treatment and every 4 months thereafter. We will also ask you to fill in another questionnaire that will help us to calculate the costs of the trial treatment to the NHS.

It is very important for you to answer all the questions in the questionnaires for us to assess accurately the impact of both the disease and of the treatment upon you.

Research samples

Throughout the study you will be asked to provide blood samples so your doctor can assess your health and how effective the treatment has been. We are also requesting some extra blood samples for scientific research. These samples should not involve any extra needles
or visits. However, they are voluntary and you should indicate on your consent form if you are happy for them to be taken.

We would also like to use part of your original lymph node biopsy sample for scientific studies that will help us understand more about follicular lymphoma. This sample will have already been taken from you when you were first diagnosed with lymphoma. You should indicate on your consent form if are happy for us to use this sample for research.

**Blood samples**

You will have blood samples taken for standard blood tests every time you attend for treatment. These blood tests are essential for your doctor to be able to tell if you are well enough for your treatment.

In addition, if you have given consent we would like to take other blood samples from you before the start of treatment and at other times in the study for use in scientific studies that will add to the trial results. If, at any point through the trial, you do not want us to collect these further blood samples you can tell your doctor and it will not affect your taking part in the trial.

**What are the alternatives for treatment?**

If you decide not to participate in the study, then your doctor will discuss other options with you, for example, standard treatment with R-CVP.

**Are there any side-effects associated with these treatments?**

Although generally well tolerated, like all anti-lymphoma treatments, both R-FC and R-CVP can cause side effects. There are mild side effects which are common, and some more severe side effects that affect only a minority of patients. You will receive additional medication alongside your anti-lymphoma treatment to minimise the risk of troublesome side effects. However, these drugs may also have side effects.

The section below deals in more detail with the possible side effects of the study treatment. Particular emphasis is given to those drugs which are not routinely used in follicular lymphoma or which are used in a non-standard way.

**Side Effects of rituximab**

Rituximab forms part of the routine treatment of follicular lymphoma. It is normally given intravenously (i.e. into a vein) over several hours. However, in the PACIFICO trial the rituximab is given subcutaneously (i.e. as an injection under the skin). Giving rituximab subcutaneously has the advantage of taking less than 10 minutes. Available evidence suggests that rituximab should be no less effective when given subcutaneously and have no more side effects compared with intravenous administration. However, since subcutaneous administration of rituximab does not form part of the standard treatment of follicular lymphoma, it is important to consider the possible side effects in some detail.

Several side effects are associated with rituximab, some of which have the potential to be severe and occasionally life-threatening. All of the side effects detailed here relate to those
observed with intravenous rituximab administration. With the exception of infusion-related side effects the side effects of subcutaneous rituximab are expected to be similar.

**Infusion/ Injection-related side effects.** Many of the side effects reported with rituximab relate to its intravenous administration (by vein). These may include: fever and chills, nausea (feeling like you are going to throw up), vomiting (throwing up), fatigue (feeling tired or weak), headache, skin rash, redness of the skin, itchiness, wheezing or tightness in the chest, shortness of breath, difficulty breathing, sensation of the tongue or throat swelling, throat irritation, rhinitis (runny nose), temporary low blood pressure, flushing, dizziness on standing up, fast heartbeat, chest pain, or pain where your cancer is located.

These side effects are most likely to occur within 30 minutes to 2 hours after starting to receive rituximab intravenous infusion, but may also occur after drug has been given. The symptoms are usually mild to moderate, and can be easily treated. Rarely, these reactions can be severe. These unwanted effects are less common after the first treatment and may be less common during subcutaneous injections (under the skin) of rituximab (). You may be given paracetamol, an antihistamine, and a corticosteroid within 1 hour before the rituximab is administered by vein or under the skin to prevent these side effects from occurring. If you notice any difficulty breathing, feel hot or shivery, have hives or an itchy rash, tell your study Doctor or study staff who is administering rituximab immediately; and delivery of the drug will be slowed down or stopped for a while. When these symptoms go away, or improve, the drug can be continued.

If you are a patient with a high tumour burden (have a lot of cancer cells) you may be at increased risk of severe cytokine release syndrome. Symptoms included dyspnoea (difficult or laboured breathing; shortness of breath), asthma, hypoxia in addition to fever, chills, shivering, hives (a raised, itchy area of skin) and angioedema (like hives but affects a deeper skin layer). The syndrome may also be associated with features of tumour lysis syndrome such as high levels of uric acid, potassium and phosphates in the blood, low levels of calcium in the blood, acute kidney failure and can be associated with respiratory failure and death. These reactions typically occur within one to two hours of commencing treatment and if you are at risk you will be very closely monitored during your first treatment with rituximab. This may include preventative measures such as splitting the dose of rituximab; having over two days as opposed to one) or reducing the infusion rate. Should you show any signs of such a reaction the study Doctor or study staff will stop delivery of the drug and provide supportive treatment.

In some cases the symptoms above can be signs of hypersensitivity to rituximab and further can develop into an anaphylactic reaction at which point medical intervention will be required. These reactions typically occur within a few minutes of administration and the study Doctor and study staff will monitor you closely for any signs of these reactions. Should you show any signs of such a reaction the study Doctor or study staff will stop delivery of the drug and provide supportive treatment.

**Infections.** Patients with NHL are at a higher risk of infection because of their cancer and its effect on their blood. Treatment with chemotherapy drugs that affect the blood can also result in a higher risk of infection. Because of the way rituximab works to kill blood and tumour cells, it may further increase the risk of infection. Decreases in certain blood cells important to fighting infection have been seen along with mild and serious infections in other
research studies with rituximab. Your study Doctor will check your blood regularly in this study for signs of these risks in you. You should also be aware of the signs of infection and tell your study Doctor if they occur. The signs of infection can include: fever (temperature at 38°C or higher), sore throat, cough, any redness or swelling, and pain when passing urine.

A serious infection of the brain and spinal cord called Progressive Multifocal Leukoencephalopathy or PML has been reported in patients receiving rituximab. Cases of PML with fatal outcome have been reported after disease progression and retreatment. You must tell your study doctor immediately if you have memory loss, trouble thinking, difficulty with walking, loss of vision or blurred vision.

Recurrence of Hepatitis B infection (signs and symptoms include yellowing of the skin or eyes (jaundice), feeling of sickness, tiredness, loss of appetite, joint pain and abdominal pain) leading to liver failure has been reported in patients receiving rituximab. You must tell your study doctor immediately if you have the signs indicated.

Cardiovascular reactions. Most frequently reported cardiac reactions are temporary changes in blood pressure associated with the infusion/ injection. Further events such as angina, cardiac arrhythmias such as atrial flutter and fibrillation (heart rhythm problems), heart failure and/ or heart attacks have occurred in patients treated with rituximab in some cases with a fatal outcome. You will be monitored carefully by your study Doctor for any indications of these events particular if you have any history of cardiac problems.

Gastrointestinal disorders. Gastrointestinal (bowel) perforation has been reported in patients receiving rituximab in some cases with a fatal outcome. In the majority of these cases rituximab was administered with chemotherapy.

Most common side effects, reported in more than 1 in 10 people are: infections both bacterial and viral (such as pneumonia, herpes and bronchitis); reduction in number of white blood cells (which may or may not cause fever); infusion/ injection related reactions (as detailed above); nausea (feeling sick); skin rashes/ itching; bald spots on the scalp; fever (>38°C); chills; physical weakness; headache; decreased ability to fight infection.

Common side effects, reported in more than 1 in 100 but less than 1 in 10 people are: Infections such as sepsis (infection of the blood); fungal infections; return of hepatitis B or worsening of a new infection of hepatitis B; reduction in the number of red bloods and platelets; over-sensitivity to rituximab (more severe forms of infusion/ injection related reactions detailed above); increased blood sugar levels; weight loss; excessive fluid in the face and body; aching muscles and joints; abnormal sensations of the skin (numbness, tingling, prickling, burning); redness of the skin; bruising of the skin; increased sweating; feeling restless, insomnia; dizziness; anxiety; increased production of tears and inflammation of the eye; ringing sound in the ear; ear pain; heart disorders (heart attack, irregular or increased heart rate); changes in blood pressure; inflammation/ irritation and or tightness of the lungs, throat or sinuses; increased cough; rhinitis (runny nose); vomiting; diarrhoea; abdominal pain; ulcers in the mouth of throat; constipation; indigestion; loss of appetite; muscle pain and generalised pain; tumour pain; flu-like symptoms; multi-organ failure.
Uncommon side effects, reported in more than 1 in 1,000 but less than 1 in 100 people are: blood clotting disorders; aplastic anaemia; haemolytic anaemia; depression; nervousness; change in taste; asthma; bronchiolitis obliterans (a rare lung disease); hypoxia (low levels of oxygen in the blood); abdominal enlargement; pain at infusion/ injection site.

Very rare side effects, reported in less than 1 in 10,000 people are: Severe viral infection Progressive Multifocal Leukoencephalopathy (PML) (a fatal brain disease); tumour lysis syndrome (release of toxins from broken down tumour cells); cytokine release syndrome (release of cytokines from broken down tumour cells); anaphylaxis (allergic reaction); cranial neuropathy (nerve problems); heart failure/ sever cardiac events; vasculitis (blood vessel inflammation); respiratory failure; interstitial lung disease; gastro-intestinal (bowel) perforation; severe skin reactions; toxic epidermal necrolysis (damage to the skin surface); kidney failure.

You will be closely monitored during treatment for any signs of these side effects and treated accordingly if any problems are seen.

Additional precautions:

• Because some of the medications given with rituximab may cause dizziness or sleepiness, you should arrange for someone else to drive you home after each treatment.
• Some vaccines should not be given with rituximab. You should tell your study Doctor if you are planning to have any vaccines.
• Your doctor may instruct you not to take your blood pressure medication 12 hours before and delay taking until after your infusion of rituximab is complete.

Please note that there may be additional risks associated with the long-term use of rituximab, or the combination of rituximab with chemotherapy, that are currently unforeseen.

Side effects of fludarabine

There is a 50% chance that you will be allocated to receive treatment with R-FC (rituximab, fludarabine, cyclophosphamide). Rituximab and cyclophosphamide form part of the standard treatment for follicular lymphoma but fludarabine is not routinely used in previously untreated patients. It is therefore important to consider in some detail the possible side effects of fludarabine. These are summarised below, although it should be noted that the current PACIFICO protocol employs a reduced dose of chemotherapy (fludarabine and cyclophosphamide) in the R-FC treatment group. This is because results from other trials have suggested that a lower dose can be just as effective but have fewer side effects than the standard dose.

Most common side effects, reported in more than 1 in 10 people are: Infections caused by various bacteria and viruses, some of them unusual; anaemia (low red cells), low platelets (leading to bruising and bleeding) and low white cells (leading to an increased risk of infection); cough, nausea, vomiting and diarrhoea; fever, fatigue and weakness.

Common side effects, reported in more than 1 in 100 but less than 1 in 10 people are: serious blood disorders (acute leukaemia and myelodysplasia) – this side effect is mainly
seen in patients who have received high doses of fludarabine plus other chemotherapy
drugs or radiation treatment; loss of appetite; numbness and tingling in the hands and feet,
visual disturbance, sore mouth, rash, fluid retention, chills, feeling generally unwell.

Uncommon side effects, reported in more than 1 in 1,000 but less than 1 in 100 people are:
autoimmune disorders (disease caused by the immune system attacking normal cells)
targeting red cells (autoimmune haemolytic anaemia), platelets (immune thrombocytopenic
purpura or ITP) or both (Evans’ syndrome); blistering skin rash (pemphigus); rapid tumour
breakdown resulting in metabolic changes and kidney failure; confusion; inflammation and
scarring of the lungs; bleeding into the gut, inflammation of the pancreas or liver.

Very rare side effects, reported in less than 1 in 10,000 people are: lymphoma-like illness
driven by the glandular fever virus; agitation, fits and coma; inflammation of the nerve
supplying the eye resulting in blindness; heart failure and heart rhythm abnormalities, skin
cancer and severe skin rashes.

Very occasional reports: bleeding into the brain, lungs or bladder.

Side effects of drugs other than rituximab and fludarabine

All of the other drugs used in the PACIFICO trial can produce side effects. The most
important side effects are summarised in the Table below.

<table>
<thead>
<tr>
<th>Drug</th>
<th>R-CVP</th>
<th>R-FC lite</th>
<th>Common Side Effects</th>
<th>Less Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>✓</td>
<td>✓</td>
<td>General tiredness, Infection, Nausea, Loss of appetite, Thinning of hair</td>
<td>Bruising &amp; bleeding, Anaemia</td>
</tr>
<tr>
<td>Vincristine</td>
<td>✓</td>
<td></td>
<td>Constipation, Numbness or tingling in the fingers and toes</td>
<td>Stomach ulcers which can bleed, Temporary change in eyesight, Muscle weakness</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>✓</td>
<td></td>
<td>Fluid retention, Stomach irritation, Easy bruising, Mood swings, High blood sugar levels (diabetes)</td>
<td>Stomach ulcers which can bleed, Temporary change in eyesight, Muscle weakness</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>✓</td>
<td>✓</td>
<td>Skin rash</td>
<td>Allergic reactions, Low blood counts</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>✓</td>
<td></td>
<td>Skin rash, Headache, Nausea, Diarrhoea</td>
<td>Allergic reactions, Low blood counts</td>
</tr>
</tbody>
</table>
G-CSF

- Bone pain (especially the back)
- Enlarged spleen
- Injection site reaction
- Headache
- Tiredness

- Allergic reactions
- Skin rash

Antihistamines, e.g. Chlorpheniramine

- Drowsiness
- Nausea

- Nausea
- Abdominal pain
- Palpitations
- Dizziness
- Allergic reactions

Paracetamol

- Skin rash
- Liver damage with overdose

You should talk with your study Doctor or research staff if you have any questions or concerns regarding the potential side effects of the study drug.

What are the possible benefits of taking part?

We hope that the treatments will help you. However, we cannot guarantee this. Even if being part of this study does not benefit you as an individual, the information obtained may help us to improve the future treatment of patients with follicular lymphoma.

What are the possible disadvantages and risks of taking part?

We expect the R-FC lite combination to be at least as good as R-CVP (the current standard treatment). However, it is possible that R-FC lite might not be as good as expected, either because it is not as effective as anticipated or because it has more side effects.

In addition, taking part in this trial will also involve having one more CT scan than you would normally have as part of the routine treatment of follicular lymphoma. For an average sized person, it is estimated that the radiation associated with this extra scan will increase the risk of developing cancer by about 1 in 1,000. This figure could be up to 50% higher in larger people owing to the higher radiation dose required.

As chemotherapy treatment might harm unborn children you should not take part in this trial if you are pregnant, breast-feeding or you intend to become pregnant during the study. If you are a woman who might become pregnant, or a man who has a partner of child bearing age, you must agree to use a reliable form of contraception during the trial i.e. two forms of contraception, one of which must be a condom. This should be continued for one year following treatment. If you or your partner should become pregnant during the course of the study, you must tell your study doctor immediately.

What if there is a problem?

---

### LCTU
Liverpool Cancer Trials Unit

### CANCER RESEARCH UK
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be appropriately addressed. See Part 2 for more detail.

**Will my taking part in this study be kept confidential?**

Yes. All information which is collected about you during the course of this research will be kept strictly confidential. With your permission we will inform your GP and the Liverpool Cancer Trials Unit (co-ordinating centre) of your participation in the study. Other than this, any information about you that leaves the hospital will have your name and address removed so you cannot be identified from it.

**Contact for Further Information**

If you have any further queries regarding this study or about any of the treatments described above, please feel free to ask your doctors any questions about the study or about any of the treatments described above.

Please contact Research Nurses Alice Ngumo or Tracey Stammers

On tel. no. 01296 315908

Or contact Haematology Consultants via Haematology Secretaries on

On tel. no. 01296 316053

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participating in the trial, please read the additional information in Part 2 before making any decision.

---

**Part 2**

**What if new information becomes available?**

Sometimes during the course of a research project, new information becomes available about the treatment/drug that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your research doctor will make arrangements for your care to continue. If you decide to continue in the study we will ask you to sign an updated consent form.

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

If the study is stopped for any other reason your doctor will tell you why and will arrange your continuing care.
**What will happen if I don’t want to carry on with the study?**

You are free to withdraw from the study at any time and without giving a reason. This would not affect the standard of care you receive.

If you didn’t want to continue with the study treatment, we would still like you to attend follow-up visits every 4 months. If you did not wish to continue attending hospital, we would be grateful if you would allow us to keep in touch with your General Practitioner to let us know your progress. If you withdraw, information collected may still be used with your permission.

If you wanted to remain on the study treatment but didn’t want information about you to be collected, this would be allowed if your haematologist or oncologist considered it to be in your best interests.

Any stored blood or tissue samples that can still be identified as yours will be destroyed if you wish.

**What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Your hospital will give you details.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed and this is the result of someone’s negligence, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated but you may have to pay for your legal costs. The normal National Health Service complaints mechanisms should be available to you (if appropriate).

In the event of defective products then you may have grounds for a legal action for compensation against the manufacturer, but you may have to pay for your legal costs.

**Will my taking part in this study be kept confidential?**

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the Liverpool Cancer Trials Unit or their collaborators who are also involved in organising this research project. They may also be looked at by representatives of regulatory authorities and by authorised people from the Trust or other NHS bodies to check that the study is being carried out correctly. All these people and organisations will have a duty of confidentiality to you as a research participant, and nothing that could reveal your identity will be disclosed outside the research site or the Liverpool Cancer Trials Unit.

Data collected during the study may be transferred for the purpose of analysis/registration within or outside the European Economic Area. Some countries outside Europe may not have laws which protect your privacy to the same extent as the Data Protection Act in the UK or European Law. We will take all reasonable steps to protect your privacy.

Your NHS number will be used to request information on your hospital visits from the NHS Information Centre. In addition, the trials unit may use these routine electronic NHS health
care data gathered from the NHS Information Centre to follow your progress if this is not available from your hospital or General Practitioner.

Involvement of the general practitioner / family doctor (GP)
With your consent, we will inform your GP of your involvement in the trial. Any other medical practitioners who treat you, for example if you are admitted to hospital for any reason, will also be informed.

What will happen to any samples I give?
Regular blood samples will be taken and analysed at your hospital as a routine part of your treatment.

In addition, and with your permission, we would like to collect additional blood samples (taken at the same time as the routine samples). These research samples will be sent to the University of Liverpool, where they will be stored for a use in a range of research projects in Liverpool and elsewhere. The aim of this research is to understand more about follicular lymphoma and its treatment. In addition, the biopsy specimen that was used to diagnose your lymphoma will be sent to the University of Liverpool for “central pathological review” in order to confirm the diagnosis of follicular lymphoma. With your permission, we would also like to keep part of this tissue sample for research that will add to the results of the trial and improve our understanding of follicular lymphoma.

The samples will be kept in a secure place until we need them; nobody outside of the study will have access to any confidential information that you give to us. Confidential details (such as your name, address and GP details) will be kept locally and will not be made available to collaborators.

Your sample will be coded and the researchers carrying out tests on the samples will not be given any information other than what is needed to carry out the tests and analyse the results. Coded is not the same as anonymous. It will be possible to use the codes to identify that a result is from your sample. However, we do not plan to do this unless there is a good research reason to do so. We will maintain this information so that we can properly manage the samples donated. For instance, sometimes we may need to update our record of your clinical details to help us interpret the results of tests.

With your permission, your samples will be transferred to different research groups around the UK and abroad for a range of scientific studies. These samples will be used only for investigating lymphoma and its treatment and will not be used for any commercial purposes. All research performed on your stored samples will be peer-reviewed and approved by an appropriate ethics committee.

Will any genetic tests be done?
All cancers, including lymphoma, are caused at least in part by genes that you may already carry in your DNA, or that accumulate in the DNA of tumour cells for reasons that we do not fully understand. Our goal is to understand the genetic and molecular basis of follicular lymphoma. This could lead to earlier detection of the disease and to the development of more effective treatments, with the potential of cure or prevention. It is therefore very
important to study genes of potential importance to follicular lymphoma as part of this study. Your DNA will only be used for research projects that advance the understanding of follicular lymphoma and its treatment.

**What will happen to the results of the research study?**

It is intended that once the study is complete a report will be written and the results will be published to make them available to the public. They may also be used to apply to the regulatory authorities to make the treatment widely available. You will not be named or identified in any publication.

**Who is organising and funding this research?**

This research project is funded by Cancer Research UK, whose support provides core funding for staff to co-ordinate this trial. It is being sponsored by the Royal Liverpool and Broadgreen University Hospital NHS Trust and the University of Liverpool. Your doctor will not receive any payment for including you in this study.

**Who has reviewed the study?**

The study has been favourably reviewed by the Cancer Research UK Clinical Trials Awards and Advisory Committee (CTAAC), the National Cancer Research Institute (NCRI) Lymphoma Clinical Studies Group (CSG), and a Multicentre Research Ethics Committee.

Both CTAAC and the NCRI CLG have cancer patient representatives, so that cancer patients have reviewed this trial favourably. Cancer patient representatives have also helped write this information sheet.

Thank you for taking the time to read and consider this information sheet. If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.