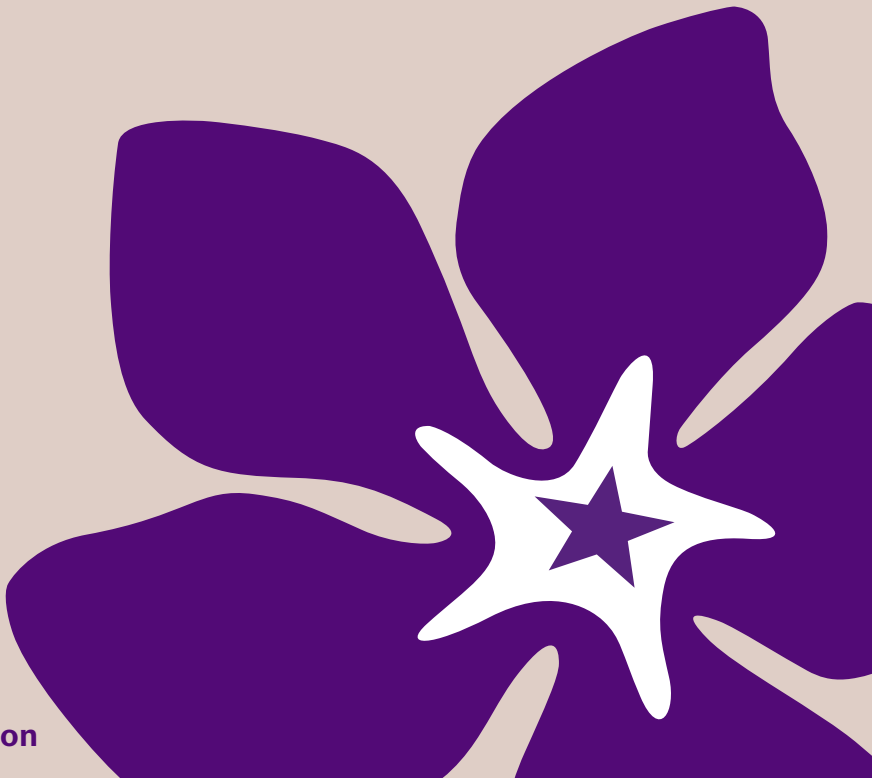




# Clinical trials





**'I was enormously grateful for the opportunity to take part in clinical trials, but before I agreed to do so, I wanted to know as much as possible about those trials. I would recommend to people that they read about trials in general, ask about the specifics – the facts and figures – even ask for a second opinion if they want to.'**


Carol, diagnosed with lymphoma in 2004

Photo credit: Magi Haroun

## How you can help us

We continually strive to improve our resources for people affected by lymphoma and we would be interested in any feedback you might have about this information. Please visit our website at [www.lymphomas.org.uk/feedback](http://www.lymphomas.org.uk/feedback) or email us at [publications@lymphomas.org.uk](mailto:publications@lymphomas.org.uk) if you have any comments. Alternatively please phone our helpline on 0808 808 5555.

We hope you will find the information in this publication useful. If you would like to help make it available to other people coping with lymphoma, then please consider making a donation to support our work at [www.lymphomas.org.uk/donate-book](http://www.lymphomas.org.uk/donate-book). We fully rely on voluntary donations. Thank you.

-  We produce other booklets that give information about lymphoma and what to expect from treatment. Please call us on 0808 808 5555 if you would like a copy of one of the following:

*Lymphoma*

*Low-grade non-Hodgkin lymphoma*

*High-grade non-Hodgkin lymphoma*

*Hodgkin lymphoma*

*Living with lymphoma*

*Young person's guide to lymphoma*

*Tom has lymphoma* (storybook for children with lymphoma)

*Questions to ask about lymphoma*

*All about lymphoma* (EasyRead version)

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### **British Library Cataloguing-in-Publication Data**

A catalogue record for this book is available from the British Library. ISBN 978-0-9929362-7-3



# Introduction

You may be someone who has been diagnosed with lymphoma. Perhaps someone close to you has been diagnosed. You are not alone. Each year in the UK more than 17,000 people are diagnosed with lymphoma (including chronic lymphocytic leukaemia – CLL), making it the 5th most common cancer.

Every day hundreds of people with lymphoma take part in clinical trials. You might have heard about clinical trials. You might have been asked whether you would be willing to take part in one. This booklet aims to:

- explain what clinical trials are, why they are done, what they involve and how they are organised
- tell you where to learn more about trials that might be suitable for you
- help you to make a decision about whether to take part in a clinical trial.

This booklet uses some scientific words. Words that are in **light brown text** are explained in the glossary on pages 79-84.

Whatever your situation, we hope the information in this booklet helps you to cope with the decisions and challenges ahead.

# Acknowledgements

This is the 4th edition of a booklet that was first written in 2008. We would like to acknowledge the continued support of our Medical Advisory Panel, our Nurse Forum and other advisers, whose ongoing contributions help us in the development of our publications. In particular, we would like to thank the following experts for their assistance in the 2015 revision of this booklet:

Paul Smith, Tumour Group Lead for Haematology and Brain Trials, Cancer Research UK and UCL Cancer Trials Centre, London

Nicola Crosbie, Haematology Research Nurse Specialist, Derriford Hospital, Plymouth

Special thanks to Michael, Diana, Carol and Sue for sharing their experiences of clinical trials. Quotations from Sue's story are featured throughout the book.

We would also like to thank the members of our Reader Panel who gave their time to review this booklet.

## **About our information**

The Lymphoma Association is committed to providing high-quality information for people with lymphoma, their families and friends. We produce our information using nationally recognised guidelines, including the DISCERN tool for information about treatments, the NHS Toolkit for producing patient information, and the Campaign for Plain English guidelines. The Lymphoma Association is an accredited member of The Information Standard

demonstrating our commitment to trustworthy health and care information as well as providing assurances of the quality of our internal processes.

Our publications are written by experienced medical writers in close collaboration with medical advisers with expertise in the appropriate field. Some publications are written by professionals themselves, acting on guidance provided by the Lymphoma Association.

In some instances our publications are funded by grants from pharmaceutical companies. These sponsors don't have any involvement in the content of a publication and have no editorial input.

This booklet has been part-funded by donations from Roche Products Ltd and Janssen-Cilag Ltd.

The information in this booklet can be made available in large print.

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# What are clinical trials?

**Why are clinical trials done?**

**What impact have clinical trials had on the treatment of lymphoma?**

1

A clinical trial is a medical research study involving human participants – usually people affected by disease but sometimes healthy volunteers. Learning about cancer treatment is a constantly evolving process. Every new idea and every new treatment needs to be tested in a scientifically valid way. This is done in clinical trials. Clinical trials of new treatments are only done after extensive testing in the lab, on cells and in animal studies. Clinical trials are planned based on the results of lab and animal studies to ensure that the study is as safe as possible for the people taking part.

## Why are clinical trials done?

Clinical trials for lymphoma are carried out for many reasons, but mainly to test new treatments and to look at new ways of using existing treatments, for example different combinations or doses. If clinical trials weren't done, many treatments would have never been developed or become available. All new treatments for lymphoma have to undergo clinical trials in order to be used by your doctor.

'It was satisfying to think that even if the drug did not work for me, knowledge would be gained from me taking part that might help others in the future (and also maybe me!)

## Treatment trials

Testing how well treatments work

Treatment trials look at new and existing treatments for lymphoma. The most common type of trial is designed to

look at **new treatments** such as new drugs or types of radiotherapy. This type of trial is done to test at least one of the following:

- if a new treatment works (**efficacy** trials)
- how a new treatment works (**mechanism of action**)
- if the new treatment is safe (see below) and how your body processes the drug
- whether the new treatment works better than the current standard treatment
- if the new treatment can work with existing treatments.

Many clinical trials test **existing treatments**. They compare one kind of standard treatment (sometimes known as the 'gold standard') with another, or compare different ways of using treatments we already know about. Sometimes treatments that are already used for people with other diseases are tested in clinical trials to see if they can help people with lymphoma. Treatment trials are essential for new drugs and procedures to reach the people who need them.

### Assessing treatment safety


Clinical trials don't just test how well a treatment works. They also look at side effects of new therapies to assess their safety and how your body processes a drug (also known as **pharmacokinetic** [PK] or **pharmacodynamic** [PD] studies). It is important to know how people tolerate treatment. Early clinical trials measure how much treatment people can have before side effects become troublesome and help identify the correct dose that can be used.

Some drugs never get past early testing stages. This can be because they cause more side effects than existing

# 1

treatments, or they do not work well enough, or because they cause more side effects than is acceptable when balanced against how well they work (also called the **risk/benefit ratio**).

In some clinical trials, people are monitored for many years to see if they have long-term side effects or develop **late effects**, which are health problems that only develop a long time after treatment. For example, some drugs can affect the strength of your heart and can increase your risk of heart disease. It is important that people who have had treatment for lymphoma enjoy good health after their treatment has finished. Research into late effects is becoming increasingly important as more people are cured from lymphoma or live longer with it.

 Please call our helpline on 0808 808 5555 if you would like to talk to someone about potential side effects of lymphoma treatments.

## Other kinds of trials

There are many other kinds of trials that do not involve treatment. These might still involve tests, such as scans, or you might be asked to give extra samples of blood or tissue (eg from a **biopsy**) for scientists to study. Sometimes, these types of studies are done as part of a treatment trial and you can choose whether you want to enter these additional parts of the trial. Examples of other kinds of trials include:

- **Diagnostic trials**, which look at different diagnostic tests, eg scans, to see which one detects lymphoma most reliably. A growing area of research in diagnostics and treatment optimisation is looking at the tiny changes in the genes of your cells that cause

lymphoma. This can be done as part of a treatment trial or as a separate trial. Your doctor will send samples, eg a blood sample or tissue from your **biopsy**, to a study centre so that they can look at the lymphoma cells in detail. You might hear this called a 'biobank'. These trials aim to find out more about lymphoma so that new, targeted treatments can be designed. They might also help specialists to work out whether you are likely to respond to standard treatment or if you might need different treatment.

- **Follow-up trials**, which look at different schedules or types of follow-up to see which is the most effective and least disruptive.
- **Treatment optimisation trials**, which look at how diagnostic technologies can be used to adapt ongoing treatment. For example, a PET scan part-way through chemotherapy could be used to decide whether you should continue on the same treatment or change treatment.
- **Prevention trials**, which test whether a particular lifestyle choice, diet or drug can prevent cancer from starting. They also test drugs to see if they can stop cancer from coming back.
- **Quality of life trials**, which might measure your recovery rate from treatment, your psychological response to having a cancer like lymphoma or the effects of treatment on your quality of life. This might be measured with questionnaires that you fill in at different stages in the trial. They look at all aspects of how your lymphoma and treatment affect your day-to-day life and wellbeing.

→ Read Michael's personal experience of a treatment optimisation trial on pages 14-15.

# 1

## **Michael's experience of a treatment optimisation trial**

Some clinical trials test how diagnostic technologies, such as scans, can be used to adapt ongoing treatment depending on your response.

Michael was diagnosed with Hodgkin lymphoma in 2010 at the age of 28 and entered the RATHL trial that same year.

RATHL was a phase 3 trial looking at whether PET scans could be used to help make treatment decisions for people with Hodgkin lymphoma. A PET scan was given after 2 cycles of ABVD chemotherapy. Patients with a good response (PET negative) were randomised to continue ABVD or receive AVD, with bleomycin (B) being omitted. This was to reduce the long-term side effects of treatment as bleomycin can cause lung damage. People who didn't respond well (PET positive) were given more intensive chemotherapy.

Initial results presented in 2015 suggest omitting bleomycin is safer and just as effective in people who have a good response to the first 2 cycles of ABVD. For people who didn't respond well, giving more intensive treatment early gave a better chance of going into remission.



Michael says: 'When I was diagnosed with Hodgkin lymphoma, I was told that I may be eligible for a clinical trial. I was keen to find out more.

Although I only had 48 hours to make a decision on whether to enter the clinical trial, I was given plenty of information and felt I could ask as many questions as I wanted. I spoke to my family about entering the trial and they were all very encouraging about it, which I found really reassuring.

I had 2 rounds of ABVD and was then randomised. My randomisation was to continue with 4 more sessions of ABVD. My treatment was from September 2010 to March 2011. It should have been 6 months but my treatment was delayed because I got a cold in late December and was in hospital for 8 days getting over it.

While the study did not include extra trips to hospital, I was monitored very closely, including additional blood tests. I also had GCSF injections frequently and CT and PET scans. The research nurses kept me informed on how the treatment was going.

I've been cancer free for more than 4 years. I'm now married and have a baby on the way.

I was happy to be involved and hope that by entering a clinical trial I will be helping to improve treatments for people in the future.'

1

Whatever the aim of a trial, it will be designed to answer a set of questions. The research team will collect information on how well the test or treatment worked, whether it caused any side effects and how the trial participants coped with the test or treatment. The results will be vital in the development of preventative strategies, screening programmes, diagnostic tests and treatments.

## **What impact have clinical trials had on the treatment of lymphoma?**

Safe and effective lymphoma treatments rely on evidence provided by clinical trials. This evidence is important for the continued improvement of lymphoma treatment. If you are having, or have had, treatment for lymphoma, you have benefited from trials done in the past, both in the UK and in other countries. The clinical trials taking place now will help improve lymphoma treatments in the future.

Not only have treatment trials improved and continue to improve treatment for lymphoma, other types of trials have helped our understanding of lymphoma, how it is diagnosed, the best way to follow-up people after treatment and the impact of lymphoma and its treatment on quality of life.

→ There is more information on how researchers measure results using 'response to treatment' and survival figures on pages 66-67.

## Summary

Clinical trials are medical research studies involving human participants. Trials only take place after extensive testing in the lab, on cells and in animal studies.

Clinical trials for cancer are done for many different reasons. They can look at treatments, screening tools or methods, diagnosis, the molecular biology of the disease, the best ways to monitor response or follow-up people after treatment, and prevention strategies. They also look at quality of life during and after treatment.

Clinical trials done in the past underpin the treatments that are now available for people with lymphoma.

1

# How are clinical trials carried out?

**What are the phases of clinical trials?**

**What are randomisation, blinding and placebos?**

2

## Diana's experience of a phase 3 trial testing a new way of using an existing treatment

Some clinical trials test new ways of using existing treatments.

Diana was diagnosed with follicular lymphoma in 2006 at the age of 59. She relapsed in 2010 and again in 2013. Following her last relapse, she entered a trial testing different ways of using rituximab.

**Rituximab** (MabThera®) is currently (2015) given for up to 2 years as **maintenance therapy** after successful treatment of low-grade non-Hodgkin lymphoma with rituximab in combination with chemotherapy. This study was designed to test whether prolonging maintenance beyond 2 years, to be given until the lymphoma progressed, was more effective at preventing relapse than 2 years' maintenance followed by observation. Rituximab was also given in the newer, subcutaneous form (given by injection under the skin over 5 minutes) instead of the usual intravenous form (injected into a vein over several hours).

After their initial 2 years' subcutaneous rituximab maintenance, participants were randomised to receive prolonged maintenance or observation. The trial is ongoing but no longer recruiting participants at time of writing.

Diana says: 'I was very happy being on the trial as I hoped it would help me and also enable me to give something back.

Initially, I had no adverse reactions and would encourage anyone offered a clinical trial to consider it seriously.

I had 9 treatments with rituximab but did not reach the randomisation stage and I have since had to come off the rituximab due to side effects.'

## What are the phases of clinical trials?

Clinical trials involving treatments are divided into different phases, from phase 1 to phase 4. Each phase reflects how much is known about a particular treatment. New treatments or new ways of using existing treatments are tested:

- first, for safety and to identify the optimal dose tolerated
- second, in a small number of people to see if they are likely to work (**efficacy**), whether they are safe and what the potential side effects are
- third, in large number of people to see if they work better than established treatments.

Usually trials involving treatments are done in phases. This is not necessary for other types of trials, eg where only established tests are done, samples are taken or questionnaires are given.

## 2

### Phase 1 trials

Phase 1 is the earliest stage of testing a drug in people. Drugs that have been tested in a laboratory or in animals have shown that they may work in humans with lymphoma and are now ready to be tested in volunteers.

Phase 1 trials usually involve a small number of people (fewer than 20) and are designed to answer questions like:

- Is the drug safe for humans?
- How much of the drug do you need to give?
- What are the short-term side effects?

Although safety and dose optimisation are usually the primary areas of research for phase 1 studies, these studies often look at the response to treatment as well. This is to get an initial idea of whether the treatment will work.

Many drugs don't get past phase 1 because they don't show the same promise in humans as they did in the lab or animal studies, or because they cause troublesome side effects in people.

Phase 1 trials are often only for people with advanced disease that hasn't responded to standard treatment or for people who have relapsed several times and exhausted all other treatment options. This is because it isn't ethical to give you an unknown treatment until all known options have been tried. Phase 1 trials often involve having many blood tests or other investigations. If the trial is designed to find out how much of the drug is needed to see a response, the dose you receive may not be enough for you to see any benefit. Higher doses may be more likely to cause troublesome side effects.



Phase 1 trials usually recruit people slowly so can last for anything from a few months to several years. You will participate only for the duration of your treatment, not the entire trial period, but follow-up normally continues until the end of the entire trial period.

Phase 1 trials are not always about testing a new drug. Sometimes phase 1 trials test whether existing treatments can be used in a different way.

### Phase 2 trials

Phase 2 trials involve more people than do phase 1. They are designed to find out more about how well the treatment works. They continue to record side effects. Phase 2 trials are designed to answer questions like:

- Does the drug work for a particular type of lymphoma?
- How well does it work?
- What else can we learn about its side effects?
- Does the drug work well enough to compare it with standard treatment?
- Can the drug be combined with other treatments?

Some drugs have been approved on the basis of information from phase 2 trials.

Phase 2 trials are not always about testing a new drug. Sometimes phase 2 trials test existing treatments in a new combination. Other times they test treatments developed for one type of lymphoma to measure their ability to treat (**efficacy**) different types of the disease.

### Phase 3 trials

If the results from phase 1 and phase 2 trials suggest that a treatment is safe and effective in lymphoma, then it will be

## 2

compared with the best existing treatment. This is known as a phase 3 trial and allows researchers to look more closely at different aspects of the treatment. Phase 3 trials can also test new ways of using the standard treatment. For example, they might compare standard treatment alone with a combination of standard treatment plus another drug. They might compare different dosing schedules to see if giving a drug more or less frequently or for a different number of cycles than usual affects response. Phase 3 trials also continue to look at the side effects a treatment can cause, including late effects.

← Read Diana's personal experience of a phase 3 clinical trial testing a new way of using an existing treatment on pages 20-21.

Phase 3 trials might be designed to answer questions like:

- Do more people live longer after the new treatment compared with standard treatment?
- Does the new treatment cause fewer long-term side effects than the standard treatment?

Phase 3 trials involve a large number of people – hundreds or even thousands – often in many hospitals in the UK or abroad. Sometimes these trials are quite complicated. They might involve a number of distinct treatment groups called 'arms'.

In most phase 3 trials participants are allocated to treatment arms in a process called '**randomisation**'. If a new treatment is being added to a standard treatment for one group, the other group might have a dummy treatment, known as '**placebo**', instead of the new

treatment. This means that everyone is having a similar number of treatments and volunteers won't know which treatment arm they are in. Doctors often won't know either.

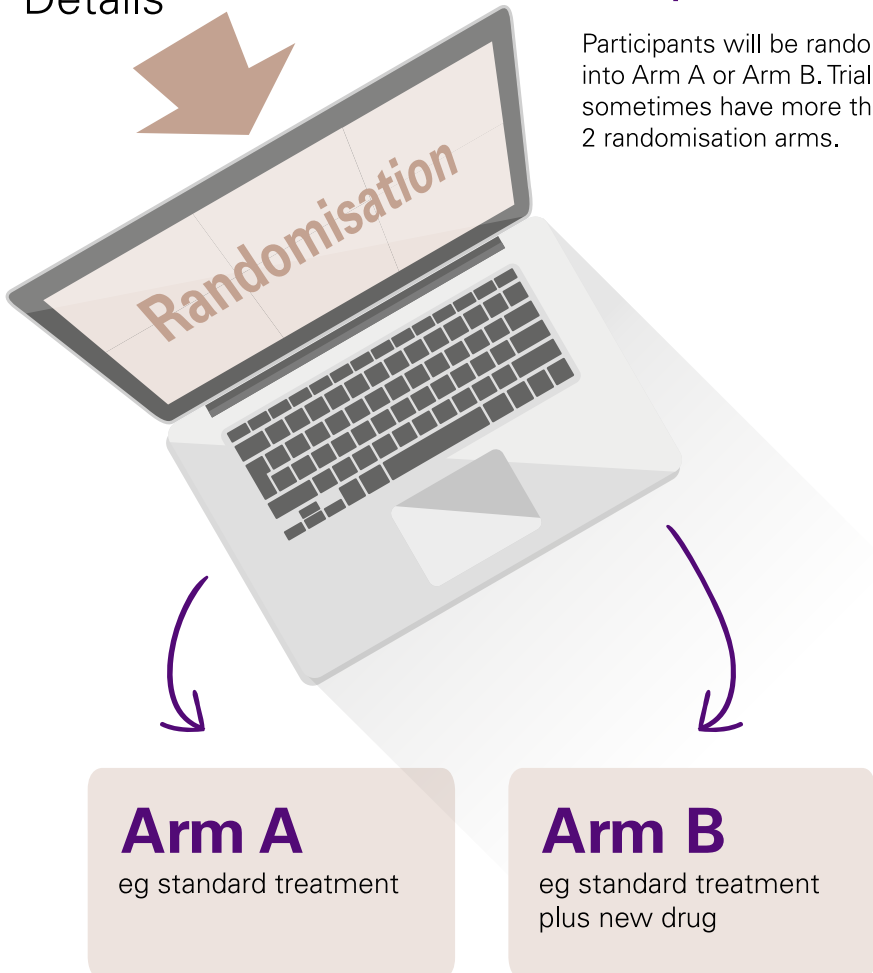
2

# Data

Anonymised  
Details

**Randomisation is usually completed by a computerised service.**

Participants will be randomised into Arm A or Arm B. Trials can sometimes have more than 2 randomisation arms.



2

## **Carol's experience of several clinical trials**

Some people participate in several clinical trials if their lymphoma relapses several times or doesn't respond to treatment.

Carol was diagnosed with Hodgkin lymphoma in 2004 at the age of 26. The standard treatment given at the time was not successful and after further chemotherapy, an autologous stem cell transplant (using her own cells) and radiotherapy, Carol's lymphoma was still not in remission. She entered a clinical trial of a new treatment (an anti-CD30 antibody) in 2006 and had a partial response. In 2008, her lymphoma began to grow again and she entered another trial, this time using a new radioimmunotherapy drug, which uses an antibody to deliver radiation directly to the lymphoma cells. A scan showed she still had some lymphoma. After some other treatments also didn't put her lymphoma into remission, there were no other treatment options available. In 2011, Carol was offered brentuximab vedotin on a compassionate use basis as a named-patient.

Brentuximab vedotin is a targeted therapy that uses an antibody to deliver strong chemotherapy to the lymphoma cells.

When there is no suitable clinical trial and they have no other treatment options, occasionally a drug company will allow some people access

to experimental drugs on a compassionate use or named-patient basis. This is usually while the drug company is waiting for approval of a drug based on trials that have already been done.

Based on the outcomes for people in phase 2 trials, brentuximab vedotin received a European marketing authorisation in 2012 for the treatment of some people with relapsed or refractory Hodgkin lymphoma.

Carol says: 'I found that if I just took things a day at a time, that I could leave all the worrying to the specialist. I know I am no health expert, so I tried to focus on what I knew about – which in my case was being a freelance musician. It was almost as though responding a little to each treatment so far gave me the time for brentuximab to be available for me. I started treatment with brentuximab in 2011. I still recall being told I was in remission for the first time in 7 years, which was overwhelming. This allowed me to prepare for an allogeneic stem cell transplant (using donor cells).

Decisions on my treatment have always been my own. I'm very close to my parents and brother, and they have been unbelievably supportive in backing me up 100% in every decision I made. Now that I am through treatment, including an allogeneic stem cell transplant, I get a lot more emotional. Before I don't recall crying, and was just focused and determined. Perhaps that was my coping mechanism.'

→ For more information on randomisation and placebos, see pages 29-31

## 2

### **Phase 4 trials**

Phase 4 clinical trials are done after the treatment has been licensed. They can be done to learn more about the side effects of a drug, how to improve combinations of drugs, or how the treatment impacts people's long-term health.

### **Pilot and feasibility studies**

Researchers sometimes conduct pilot studies or feasibility studies before starting a main trial. These are small studies involving a few people. They aim to find out if the main trial can be done and how the parts of the trial work together.

### **Compassionate use programmes**

Occasionally, drug companies make an experimental drug available to an individual or a few people outside of a clinical trial when those people have no other treatment options and there is evidence that the drug might help them. The drug may be supplied through a compassionate use programme or on a named-patient basis. This happens rarely. The decision to supply the drug is made by the drug company, not your doctor.

A compassionate use programme is for patients who may benefit from an experimental medicine but don't meet the eligibility criteria for a clinical trial, or the drug company is waiting for approval of the drug based on existing clinical trials. There will be a central register of people treated in this way so side effects can be recorded.

Doctors can also contact the manufacturer directly to ask if they will provide an experimental drug for an individual patient on a named patient basis. There is no central register of patients treated this way.

← Read Carol's personal experience, including access to a drug via compassionate use, on pages 26-27.

2

## What are randomisation, blinding and placebos?

### What is a 'randomised controlled' trial?

Some phase 2 and most phase 3 clinical trials compare a new treatment with the best standard treatment. People taking part in a trial (participants) are divided into 2 (or more) groups. The people in 1 group will have the current standard treatment and the people in the other group will have the treatment being tested. The group having standard treatment are called the 'control group'.

In most trials, a computer randomly allocates the people taking part to each trial group. Neither the volunteers, nor their doctor, can choose which group they end up in. This is called '**randomisation**'. Your doctor won't know in advance what treatment you will have. These trials are known as '**randomised controlled trials**' and many clinical trials for lymphoma are organised in this way.

← Read Michael's personal experience of a randomised clinical trial on pages 14-15.

← See illustration of the randomisation process on page 25.

## What is meant by 'blind' or 'double blind'?

You may not know which treatment you are having. This is called a '**blind**' or 'single blind' trial. In this case, your doctor will know which treatment you are having but won't be able to tell you.

2

If the trial is 'double blind' neither you nor your doctor will know which treatment you are having. The trial organisers will be able to identify which treatment group you are in and can disclose this immediately if there is any cause for concern.

Blinding is done because knowing which treatment you are having could potentially influence your expectations about it. Your expectations can influence the outcome of your treatment (placebo effect). Blinded trials are intended to remove your expectations from the equation making the trials more scientifically valid.

Trials are 'double-blind' so that your medical team aren't affected by knowing which treatment you are having. This is because knowing which treatment you are having could influence their assessment of your response (observer **bias**).

This doesn't mean that you or the medical team are deliberately affecting the results – people can't help being influenced by knowing which treatment they, or the people they care for, are on.



## What is a placebo?

A **placebo** is a dummy treatment. It is something that looks the same as the trial treatment, but it doesn't contain any active treatment. Placebos can be used where there is no standard treatment to compare the new treatment with. People in a control group who are taking a placebo wouldn't be having any other treatment if they weren't in the trial. It wouldn't be ethical to give a dummy treatment to someone who would be having active treatment otherwise.

Clinical trials for cancer rarely involve giving a placebo alone. Placebos are sometimes used in cancer trials when researchers are adding a new treatment to a standard treatment (see the section on phase 3 trials on page 23). One group of participants in the trial would have the standard treatment and the new treatment being tested. Volunteers in the other group (the control group) would have the standard treatment and a placebo.

## What is a trial 'arm'?

Trials that compare 1 group of people with another refer to these groups as 'arms'. This is because they look like arms when the trial design is turned into a diagram. Most randomised trials have 2 arms, but some have 3 or more.

The people in 1 arm are usually given different treatment to the people in another arm, so the results from each arm can be compared. The drug or combination of drugs could be different. A different treatment pattern may be used for each arm, eg 1 group of people may receive more cycles (a block of treatment that is followed by a rest period) of

treatment than another group. A group of people may also be called a 'cohort'.

← See illustration of trial arms on page 25.

2

## Summary

Cancer treatment trials are divided into phases. Phase 1 and phase 2 trials are done to find out about new treatments or to find how best to use established treatments. Phase 3 are done to compare new treatments with the standard treatment or to find out how to improve the standard treatment. Phase 4 trials are done to collect information on treatments that are already licensed.

Most big lymphoma trials are **randomised controlled trials**. This means that the treatment you have – whether it is a new treatment or a standard treatment – is chosen randomly, usually by a computer. If the people taking part in the trial don't know which treatment group they are in, it is a 'single-blind' trial. If the doctors don't know this either, it is a 'double-blind' trial.

Trials are organised in these ways to answer researchers' questions in a scientifically valid way. They are also designed to be fair and safe for the people who take part.

# 2

# How are clinical trials organised?

3

**How are clinical trials set up?**

**How are trials monitored and where are the results published?**

## How are clinical trials set up?

Clinical trials are set up by individuals or organisations looking for new treatments. The head of the group is called the 'chief investigator'. In cancer trials, these are doctors who are specialists in the type of cancer being studied. Many UK cancer specialists are involved in research as well as clinical practice. Clinical trials are also organised by drug companies.

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Clinical trials take a long time to set up. It can take years before a trial progresses from a question asked in a laboratory or a clinic, through the design stage to recruiting participants. Some trials never get past the planning stages. Some can't get funding so have to be abandoned before they start.

In addition, clinical trials in the UK are governed by strict legislation. This legislation aims to protect the people taking part and helps to ensure that trials are as safe as possible. Making sure that a trial complies with the legislation is a time-consuming process, but a very important one.

### Sponsors

A trial may be sponsored (funded) by a university (academic trial) or by a pharmaceutical company. All studies must be approved by the Medicines and Healthcare Products Regulatory Agency (MHRA) – a governmental organisation that regulates the use of medicines in the UK – and also by an independent ethics committee.

### Starting out – the proposal

The research group in charge of the trial will have an idea that needs to be tested and will come up with a proposal.

Most of the lymphoma clinical trials in the UK are organised through the National Cancer Research Institute (NCRI). The NCRI coordinates cancer research throughout the UK, but doesn't fund trials directly. It is a partnership between the Department of Health, cancer research organisations and drug companies. The NCRI has a specialist Lymphoma Clinical Studies Group (CSG) that concentrates on lymphoma research. This group has subgroups for the different types of lymphoma. The Lymphoma CSG includes many leading UK lymphoma specialists. Researchers with a proposal for a clinical trial can approach the appropriate subgroup and ask for support in developing the trial. Sometimes this happens the other way round – the subgroup can suggest an idea for a clinical trial to researchers.

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### **Funding clinical trials**

Clinical trials are expensive. Funding has to cover research staff, administration and people as well as technology required to analyse the results. The costs of the drugs involved, any tests needed and the cost of additional hospital stays also need to be covered. Clinical trials often follow each participant for a number of years, so the follow-up costs continue long after you've finished treatment.

Funding has to be in place at an early stage or the trial will never get past the planning phase. There are a number of ways of paying for a trial. Many cancer trials in the UK are funded by a drug (pharmaceutical) company, by a national charity or by a governmental organisation.

Often funding comes from a combination of sources:

- **Drug companies** often pay for clinical trials to test new drugs that they have developed. Sometimes a drug company will provide a drug free of charge for a trial organised by another organisation or institution.
- **National charities** – many charities provide funding for cancer research in the UK. Some of them pay for cancer research in general. Cancer Research UK is the largest of these organisations and one of the main providers of cancer research funding in this country. Other organisations pay for research into particular types of cancer. Bloodwise, for example, provides funding for research into all blood cancers, including lymphoma. The Lymphoma Research Trust is a smaller organisation that funds research carried out by the Haematology Trials Group (see page 41). The Lymphoma Association doesn't currently fund research. We feel that our focus should remain on providing information and support for people with lymphoma.
- **Governmental organisations** – government money for research is also made available through various funding streams provided by the National Institute for Health Research (NIHR). The government pays for the coordination of cancer research through the National Cancer Research Institute (NCRI) or Clinical Research Networks (CRNs).

→ For details of these organisations, see page 85-87.

Funders or researchers often approach other researchers who have experience and qualifications in the same field and ask them to review the trial proposal. This is to make sure the trial is scientifically valid and to identify any



issues that may have been overlooked. This process is called **peer review** (or independent scientific review).

## Planning – the protocol

Once the aim of the trial is agreed on and the funding is in place, the group will produce a document called a 'protocol'. The **protocol** describes the study in detail, by:

- providing background information about the disease being researched
- explaining why the research is needed
- discussing how many participants will be needed and who will be eligible
- describing exactly what treatments will be involved and how and when they will be given or what methods will be used if the study does not involve treatment (eg, diagnostic studies)
- specifying how patients will be monitored and for how long
- outlining the timeframes for the trial as a whole and for each participant.

The protocol is an important document. It acts as a set of rules that doctors and nurses have to follow. Participants in clinical trials are treated at hospitals throughout the UK and sometimes abroad. The protocol ensures that everyone involved in a particular trial is treated in the same way, regardless of what the usual practice is at a particular hospital. This helps make sure that the results of the trial are scientifically valid.

Another way of ensuring that the results are scientifically valid is to carefully work out how many people will need to take part. For large phase 3 trials, the studies need to recruit the right number of people to detect any

differences between treatment groups, assuming any differences exist. A trial that is too small could have a result that isn't a real finding but happened by chance.

### Getting the go-ahead

Clinical trials of medicines need to be authorised by the MHRA. This is a government agency that is responsible for ensuring that medicines work and are acceptably safe. The MHRA will focus on how the drug is made and if it is in accordance with strict rules for making a medicine.

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A **Research Ethics Committee** (REC) also has to approve the protocol. RECs are made up of health professionals, academics and members of the public. They might include people with legal experience or a philosophical or theological background, among others. The committee is independent of the researchers and the agencies or companies that are paying for the research.

The members of the REC examine the protocol carefully and in detail to ensure that the researchers are working in the participants' best interest. The REC has to make sure that the trial isn't ethically questionable. For example, the committee will consider whether people would be put at an unacceptable level of risk if they took part in the trial. They will consider whether or not all participants will be treated fairly. The National Health Service (NHS) Health Research Authority's National Research Ethics Service is an example of one such committee.

Ethics committees pay particular attention to the content of the Information Sheet and to the Consent Form that all participants have to read and sign. They

make sure that people can make an informed decision about participating in a trial. Ethics committees are very influential. No change can be made to the trial at any stage without the prior approval of the REC.

→ You can read more about information and consent on pages 60-63.

Once a trial has been approved by the REC, the protocol is examined by local NHS Trusts and research and development (R&D) departments of hospitals that want to take part. They assess whether the hospital has enough staff, equipment and expertise to carry out the trial.

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### **Starting a trial – recruitment**

Once the protocol has been approved by the REC and funding is in place, the investigators can begin. It may take several years for a trial to recruit enough participants. The trial is publicised and discussed at meetings and conferences. Cancer treatment centres are invited to take part. Doctors are asked to mention the trial to anyone who might be suitable. This doesn't mean that you will be signed up for a trial just because your hospital is participating. You might be invited to take part, but you can always choose not to do it. It won't affect the care or treatment your doctor gives you.

### **Coordinating lymphoma trials**

The Haematology Trials Group coordinates many UK clinical trials for people with lymphoma. They promote trials, arrange for hospitals to participate, provide the volunteers with the information they need, and collect the results. The information they collect is kept in a database that is added to each year. This pool of

information is a vital resource for current and future researchers and doctors.

There are several other coordinating groups in the UK, such as the University of Southampton Clinical Trials Unit, the Liverpool Cancer Trials Unit, the Children's Cancer and Leukaemia Group (CCLG) and the Plymouth Lymphoma Trials Unit (which concentrates on research into mantle cell lymphoma).

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→ You can find out where to look for information about current clinical trials on page 49.

## How are trials monitored and where are the results published?

### Keeping an eye on the trial – data monitoring

The final results of a clinical trial might not be ready for some years after the trial has ended. However, the results that come out during the trial – **interim data** – are carefully monitored. This monitoring is done by a committee of experts who are independent of the trial researchers. This is done to ensure that monitoring of the results is objective.

Trial monitoring is important for the safety of the people participating in the trial. It provides a 'big picture' of all the participants, not just the people being treated at a given hospital. Monitoring ensures that trial organisers are aware of any significant differences between groups as soon as possible, eg when people in either group are doing much better or much worse than expected.

## Stopping trials early

In some instances, a trial will close early. Sometimes this will be because it is difficult to recruit enough people. Slow recruitment means that a trial will take too long to reach its conclusion. It is unethical to invite people to take part in a trial that is likely to never come up with a result.

In some cases, trials will close early if 1 group of people is clearly doing much better than the others. If this happens, where possible, participants will be swapped to the better treatment.

Occasionally trials are closed early because people are having serious side effects. If this does happen, it is more likely in phases 1 and 2. A drug is only tested in phase 3 trials if the results from earlier phases suggest it is safe to proceed. Therefore it is rare for a phase 3 or 4 trial to close early due to side effects. If unexpected side effects are detected as late as phase 4, when the drug has already been marketed, the drug may be withdrawn.

## Publication of trial results

Recruiting participants, running the trial and analysing the results can take several years. Once the trial has finished, the researchers will aim to publish the results of their work. There are many weekly and monthly professional and academic journals that publish information from various areas of medical research. Journals usually publish research from all over the world so that doctors can learn about developments elsewhere. Ask your research team about their publication policy.

Results are also likely to be discussed at conferences attended by doctors and nurses working in cancer

treatment. These conferences are held regularly in the UK and internationally. The conferences are an important opportunity for doctors to hear about each other's work, to challenge each other, and to gain from each other's experience.

→ For more information on trial results and what they mean, see pages 66-67.

### 3

#### **How will trial results affect people with lymphoma?**

The results of clinical trials often influence how doctors and nurses who specialise in lymphoma do their work.

Trial results can:

- improve the way people with lymphoma are diagnosed, treated and cared for, in the short-term and in the long-term
- allow new drugs to be marketed for a particular condition
- identify areas that need more research
- provide evidence that guides how treatments are used and funded in NHS hospitals.

## Summary

Clinical trials are organised by people or organisations looking for new therapies. They usually work with a national organisation, the National Cancer Research Institute (NCRI), which coordinates cancer research in the UK.

Trials can be paid for by drug companies, cancer research charities, governmental organisations, or a combination of these organisations.

Clinical trials start with a plan known as a '**protocol**', which undergoes careful examination by a **research ethics committee** before the trial is allowed to go ahead. This is done to make sure that the trial will be run in an approved way and that the people taking part in it will be safe.

Trials are monitored and can be changed if necessary during the course of the trial; trials can be stopped early if necessary.

Trial results are usually published and discussed in professional journals and at medical conferences. Trial results influence medical practice, allow new products to be licensed and provide evidence to make treatments available on the NHS.

# 3



# Taking part in a clinical trial

## 4

**Who can take part in a clinical trial?**

**What are the advantages and disadvantages of taking part in clinical trials?**

**What is 'informed consent'?**

**Who has access to trial data?**

**What happens if you change your mind?**

**What should you do if you are unhappy?**

**What is follow-up and what do trial results mean?**

## Who can take part in a clinical trial?

4 There are clinical trials for people who are newly diagnosed and trials for people whose lymphoma has come back (**relapsed**) or has not responded to previous treatment (**refractory**). Some trials research the most common lymphomas and some are set up to look at more unusual types of the disease. This doesn't mean that there is a clinical trial for everyone. Clinical trials only enrol people who meet certain criteria (**eligibility criteria**). Those are made up of **inclusion** and **exclusion criteria**, which allow researchers to compare like with like. If the researchers know that the participants are roughly the same to start with, then any differences in outcome are more likely to be the result of the treatment, not of some other factor. This gives the trial the best chance to answer the questions it sets out to answer and it ensures that the results are scientifically valid.

### Inclusion criteria

**Inclusion criteria** set out who can join the trial. For example, the exact type of lymphoma participants must have, the stage of their lymphoma and whether they have already had treatment or not. The criteria might also give an age range that the participants must be within.

### Exclusion criteria

**Exclusion criteria** set out who can't join the trial. For example, people who have had certain previous treatments might be excluded if that treatment could influence how the body reacts to the treatment under investigation. Or people with early-stage lymphoma might be excluded if the researchers want to know how good a treatment is for more advanced-stage lymphoma.

**Exclusion criteria** are also important to ensure that the trial is safe. Pregnant and breastfeeding women are usually excluded from trials in case the new medicine could harm an unborn baby or be transmitted in breast milk. People who've had other medical conditions may also be excluded. For example, if the treatment being tested can affect the heart, people who've had any type of heart disease may not be allowed to join the trial.

Making **eligibility criteria** as specific as possible ensures the researchers are comparing like with like. These criteria also make the trial as safe as possible for the people involved.

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### Finding the right trial

If you are interested in taking part in a clinical trial, talk to your consultant or clinical nurse specialist (CNS). They might be able to suggest a trial that is suitable for you. If no trial is available where you are being treated, your doctor may be able to refer you elsewhere. There are also sources of information on the internet to help people find out about clinical trials:

- The Cancer Research UK website has a database of cancer trials that are recruiting in the UK and explains them in plain English ([www.cancerresearchuk.org/about-cancer/find-a-clinical-trial](http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial)).
- The UK Clinical Research Network ([www.crn.nihr.ac.uk](http://www.crn.nihr.ac.uk)) also has a searchable database of trials ([www.public.ukcrn.org.uk/search](http://www.public.ukcrn.org.uk/search)).
- The UK Clinical Trials Gateway ([www.ukctg.nihr.ac.uk/default.aspx](http://www.ukctg.nihr.ac.uk/default.aspx)) has a database of UK trials for all medical conditions.

If you find information about a trial that interests you, it is important to talk to your consultant or clinical nurse specialist. The trials you read about might be happening in other parts of the country or world. The information you find online could be out of date and the trial mentioned may have already closed. Even if the information is current and local, you still may not be able to take part. You might not meet the **eligibility criteria**. For example, there might be aspects of your health, or previous treatment, which exclude you from certain trials.

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Don't be disappointed if you can't find a clinical trial that is suitable for you. You will still be offered the best available treatment. Let your consultant know that you are interested in principle and they will keep this fact in mind as they plan your treatment.

### **Why isn't there a trial that is right for you?**

Although doctors and researchers are keen to get people into clinical trials, the number of participants is still small. There are many thousands of people living with lymphoma in the UK, but only a very small proportion of these people are taking part in a trial at any given time. There are a number of reasons for this.

- There are relatively few trials taking place at any one time. Clinical trials are complicated and time-consuming to set up. A clinical trial will only be established when there is enough evidence to justify it and this evidence can take years to gather.
- Trials are only open for a limited period of time, usually a few years, depending on how long it takes to recruit the required number of people. So you might find that enrolment on a suitable trial has already closed by the time you learn about it.

- Even if you find out about a trial for your type of lymphoma, you might not be eligible to take part. You might have the right type of lymphoma, but be at a different stage in your treatment. Or you might have already had the type of treatment that excludes you from taking part. You may be in the wrong age bracket for the trial. Or you may have another medical condition that excludes you from the trial.
- Some consultants might not want to enter their patients into clinical trials because they feel sceptical about a new treatment until they have clinical evidence that it works better than the treatment already available. Their professional opinion and a desire to do what is right by their patients may make them reluctant to get you involved with a particular trial.

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**What can you do if your hospital is not involved?**


You might know about a clinical trial that you believe you could be eligible for, but find that your treatment hospital is not participating. Discuss this with your medical team. Ask why your hospital is not taking part.

If you want to be considered for inclusion in a clinical trial you may want to think about having treatment at a hospital that is running a trial. It might be difficult to talk to your current team about this, but do raise the subject with them. They will be used to requests like this one and won't be offended. Your consultant is best qualified to give you advice about other hospitals and will be able to check the **eligibility criteria** for the trial and enquire whether you may be suitable. If you do go ahead with the trial, your consultant will also need to share information about your care with the other treatment centre. If you feel unable to discuss participating in a

trial with your current specialist, then talk to your GP.

Of course involvement in clinical trials is not the only consideration when deciding where to have treatment. There will be other issues to consider if you are thinking of changing hospitals, particularly travel, if the other hospital is far from where you live, and other practical implications. It is also important to remember that the vast majority of patients will do very well with standard treatment that is not part of a clinical trial.

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 For more information about where to have your treatment and how to seek a second opinion, please call our helpline on 0808 808 555.

## **What are the advantages and disadvantages of taking part in clinical trials?**

There is no way to tell if taking part in a trial will benefit you. The Information Sheet will describe the possible risks and benefits of taking part in the trial. But the trial treatment is being tested so there is no way to tell how it will affect you. The trial team are not allowed to persuade you to take part.

In fact, the people who run clinical trials are obliged to give you all the information they have and tell you about all the possible drawbacks. They have to tell you about the risks before you agree to take part. It may feel as if people are trying to talk you out of participating, but this is a necessary part of informing you about the trial and what it could mean for you.

→ Read Sue's experience of some of the advantages and disadvantages of taking part in a clinical trial on page 54-55.

## **What are the advantages of taking part in a trial?**

It is important to realise that many of the benefits of taking part in a trial – access to expert staff, good-quality information and careful follow-up – are part of good medical care. You don't need to take part in a trial to get good medical care.

### **Access to expert support and advice**

People taking part in clinical trials will be treated by health professionals with extensive up-to-date knowledge about recent developments in lymphoma treatment. Doctors and nurses following the trial protocol will be acting on the most current information about someone in your situation. Being part of a trial means that your local team becomes part of a wider network for exchange of information and professional support.

You will have access to experienced research nurses or a CNS with a research interest. These nurses are dedicated to the support of patients involved in the clinical trial. They can help you to discuss any worries with your team.

### **Close monitoring and detailed follow-up**

Clinical trials for lymphoma are usually concerned with the effects of a new treatment or a change in standard treatment. For this reason, clinical trials pay particular attention to side effects and to your response to treatment. Of course standard therapy will include monitoring and observation, too, but clinical trials often involve having more tests to see how you are getting on.

## **Sue's experience of a randomised trial adding a new drug to standard treatment**

Many trials look at the effects of adding a new drug to the standard treatment.

Sue was diagnosed with follicular lymphoma in 2007 at the age of 61. She relapsed in 2010 and was offered the choice of standard treatment or entering a clinical trial testing the safety and effectiveness of adding a new drug to chemotherapy.

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GAUDI was a phase 1 study investigating the safety and effectiveness of adding different doses of obinutuzumab to chemotherapy. Obinutuzimab is an antibody that targets CD20 on B cells. It works in a similar way to rituximab, which is often used to treat people with follicular lymphoma. The investigator decided which chemotherapy regimen each participant would receive based on their individual circumstances. Participants were randomised to determine which dose of obinutuzumab they would receive. People who responded to treatment were offered obinutuzumab maintenance every 3 months for up to 2 years.

The results of the trial suggest that obinutuzumab is safe and effective for people with follicular lymphoma. These results guided the design of larger, phase 3 clinical trials of obinutuzimab and chemotherapy to treat follicular lymphoma.



Sue says: 'It was clearly explained to me that the drug was being trialled and that it was impossible to know at that stage if it was the best course of treatment, although the clinical team seemed to think it would be. But they stressed it had to be my decision.

Although the information I was given was easy enough to read and understand, I took it to my GP to discuss. She pointed out that my progress would be well monitored, in terms of the number of check-ups, blood tests and opportunities to see the treating team.

I entered the trial, which was a randomised trial. At the start I wanted to know which treatment pattern I would have, but once the decision had been made it really didn't matter as long as it worked. I received obinutuzumab with CHOP chemotherapy, which put my lymphoma into remission. I then had 8 doses of maintenance obinutuzumab. I am still in remission nearly 5 years after starting on the trial.

Part of the follow-up of the trial involved having scans at 6-monthly intervals. These scans are for the purpose of the trial, not specifically for my own benefit. It was always stressed that I could leave the trial at any time. After 8 scans that I would not have had if I had not been on the trial, I have asked to have no more scans unless I need one. My check-ups now follow the same pattern as for anyone else – that is annually, or when I feel there may be a problem and ask for one. I feel happy with that decision.'

Phase 3 and some phase 2 clinical trials are also concerned with your health in the long-term. This means that as well as wanting to know what happens to your lymphoma, the researchers may want to assess any potential **late effects** of the treatment. This is why people in clinical trials are often followed up for longer periods than they would be otherwise. Ask your medical team how trial follow-up will be different from usual practice. Ask if there are any risks associated with having extra tests needed for the trial, eg some types of scans expose you to radiation.

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### Access to the latest treatments

Clinical trials provide you with an opportunity to have an experimental treatment, which might work better than the current standard treatment. However, if you are taking part in a randomised trial, you won't be able to choose which treatment you have. If you don't have the new treatment, you will have the best available standard treatment. Both arms of the trial will receive the same monitoring and follow-up.

Clinical trials offer access to another treatment after all standard options have been tried.

← There is an explanation of the process of randomisation on pages 25 and 29.

### Access to information

Providing good quality information for trial participants is crucial in the approval process of a clinical trial. You will receive information about your situation, your treatment, its possible risks and benefits. Staff dedicated to answering your questions will be available. You are likely

to receive more information than you would have got in routine practice.

### Helping others

People who have lymphoma now benefit from clinical trials that have taken place over the last 30 years. Clinical trials have resulted in important changes in the treatment of lymphoma. It is thanks to past participants of clinical trials that lymphoma treatment is now safer and more effective than it used to be. By taking part in a clinical trial you will help other people diagnosed with lymphoma in the future, even if the trial doesn't benefit you directly.

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'I joined the trial because it sounded worthwhile, and it is good to be involved with something that might help other people.'

### What are the disadvantages of taking part in a trial?

People can find some aspects of taking part in a trial difficult. The uncertainty about the outcome, the lack of control over treatment choice, additional appointments and tests, coping with all the information given and the decisions needed to be made can be stressful.

You do not have to enter a clinical trial even if your doctor asks you if you would like to. It will not affect your standard of care if you say no. If you are afraid to say no, talk to your research nurse. Your research nurse can help you to discuss your fears and assist you in deciding whether a clinical trial is suitable for you.

## Uncertainty about the outcome

Taking part in a clinical trial will involve uncertainty. Clinical trials are set up to provide answers to questions, so uncertainty is hard to avoid. You may not know which treatment you will have. You will not be able to choose the treatment. You won't know whether the trial treatment is better than standard treatment. You could be allocated to a group that ends up doing less well in the longer term. You may experience unexpected side effects.

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The degree of uncertainty will depend on the phase of the trial (see pages 21-28), what it is looking at and how it is designed. The trial team will give you information about the treatments involved and what is already known about them. Remember that clinical trials don't get off the ground if there is any suggestion that participants will be at a disadvantage. The treatments being tested in clinical trials must be considered to be potentially better, and no worse, than the best standard treatment for someone in your situation. As described on page 40-41, all trials must be approved by the governmental regulatory body, the MHRA, and an independent **research ethics committee**. These committees have to be satisfied that the trial is asking a worthwhile question and is safe for the participants.

Some phase 1 trials might involve very new treatments being tested on a small number of people. In such a case, there will be greater uncertainty about the treatment and its side effects. These trials are usually restricted to people who have no other treatment options. This can be daunting even if you do not have any other treatment options. Share your worries with your team and discuss with them whether a clinical trial is right for you.

## Not being able to choose the treatment

Many clinical trials for lymphoma compare a group of people having a new treatment with a **control group** of people who are having the standard treatment. People are randomly put into these groups by a computer. This is called '**randomisation**'. If you are taking part in one of the **randomised controlled trials** you won't be able to choose what treatment you have. Neither will your doctor.

← There is more information about randomisation and randomised controlled trials on page 29.

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You might be disappointed if you are in the control group. Remember that the control group will have the best standard treatment for someone in your situation and it may turn out to be just as good as – or perhaps better than – the newer treatment.

One group of people might have poorer results in the longer term. This might not be obvious for a long time because results of clinical trials are measured over many years and some measurable effects can take a long time to show up. You and people close to you can find this difficult to deal with. If it becomes obvious early on that one group is doing much better than the other, then the trial will close early and all patients will switch to the better treatment, if possible.

← Stopping trials early is discussed on page 43.

## Extra hospital visits and tests

Some people find the extra tests and follow-up needed in a clinical trial to be reassuring. However, the need for extra

hospital visits and tests might be stressful or inconvenient for you. Talk to the medical team if you think you might have difficulty with the extra visits. Discuss the risks of any additional tests, eg extra scans could increase your exposure to radiation. The risks of these tests will have been assessed by a radiation expert but talk to your team to make sure you are comfortable with them.

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‘Some people might think the number of extra hospital visits is a disadvantage. As part of the follow-up, I had 8 scans that I wouldn’t have had if I hadn’t been on the trial. It was always stressed that I could leave the trial at any time, so I did not have to have those extra scans. It was my decision.’

### Worrying about the information you are given

Information can be a good thing or a bad thing, depending on your perspective. Taking part in a trial will mean dealing with a lot of information. You may find some of it worrying. Talk to your medical team if anything you hear, or any of the information you get, is troubling you or is difficult to understand.

## What is ‘informed consent’?

The law requires you are well informed about the trial. Researchers must make sure that you fully understand the trial before you agree to take part. They must give you a chance to ask questions and to talk about the information they have given you.

→ See pages 72-77 for some questions you could ask about clinical trials.

## The Information Sheet

The hospital will give you an Information Sheet, which usually runs for several pages. It will provide detailed information about aspects of the trial, including some or all of the following:

- the purpose of the trial
- who will be involved and why the trial might be suitable for you
- how many people will be recruited
- when it will start and finish and what the timescale for the research is (if possible)
- what is known about trial treatments
- what side effects to expect and how to manage them
- what the potential risks and benefits are
- what the trial design is – whether participants are randomised into groups, when **randomisation** takes place and how it is done
- what tests you'll need to have, what they will involve and when they will be carried out
- how the trial will be funded and any possible conflicts of interest (for example, whether the researcher in charge of the trial is being paid by the company that makes the drug)
- what institutions the researchers are part of, eg hospitals or universities
- how long you will be part of the trial, and what will be expected of you
- what will happen to your personal information
- what your rights are to withdraw from the trial and what happens if you do
- what to do if you are unhappy
- what happens if new information about your disease or treatment becomes available while the trial is going on
- what to do if you have questions or concerns.

You will have time to look at all this information carefully. You should be able to take it away with you and might find it helpful to share it with someone close to you.

'The information I was given was excellent and I was able to ring and discuss any queries before signing up.'

## 4

Be sure to talk to your specialist, research nurse or another member of your team. Talk to them about anything in the Information Sheet that worries you, or anything you don't fully understand. Go through the document and highlight the parts you want to ask about. The research team will expect you to ask questions. They should give you time to talk about your concerns and they should make sure that you understand what is involved. You can discuss the Information Sheet with your GP as an independent, unbiased professional who may know you well.

### **Consent Form**

Once you have had the time to read the Information Sheet and ask questions, you will be asked to sign a Consent Form. Signing the Consent Form will indicate that you:

- have read and understood the Information Sheet
- have had the chance to ask questions and that you understood the answers
- understand that the trial is voluntary and that you can withdraw from it at any time you choose
- agree that information about you can be shared, with whom it can be shared and that you understand what



kind of information this will be. A pharmaceutical company may constantly analyse the information and data coming from a trial; however, all of your data will be anonymised before the pharmaceutical company can analyse it

- agree to take part in the trial.

Once you have agreed to take part in the trial, you and a member of the research team will sign and date the Consent Form. They will give you a copy to keep.

You can withdraw from the trial at any time. Signing the Consent Form doesn't prevent you from changing your mind in the future. Some people might feel under pressure to sign up for a trial. You might feel that you owe it to your doctor to take part. You may worry that saying 'no' will mean you don't get the treatment you need. You might be in a rush to start treatment.

**Remember: you are not obliged to take part in a trial. It is your decision. Turning down an offer to take part in a trial won't influence the standard of care you receive.**

### Will you be paid for taking part?

Clinical trials for cancer are nearly always done with people who have cancer and so don't usually involve any payment. In some commercial trials, you may be reimbursed for your expenses, such as travel. Ask your trial team about this.

## Who has access to trial data?

### Confidentiality

Personal and medical information about you will remain

4

confidential. The team looking after you will keep the usual hospital medical records about your care. These records will remain confidential to your medical team. If your trial is sponsored by a pharmaceutical company, someone from that company will have access to your data, but only in the presence of your medical team. Regulatory authorities, such as the MHRA, may inspect trial sites to ensure trials are being run according to regulatory guidelines. They will look at participants' notes but are also bound by confidentiality agreements. No information from your notes will be taken from the hospital without first being anonymised.

In commercial trials, clinical research associates (CRAs) monitor the trial and make sure it is being conducted correctly and that your information is accurate and confidential. Non-commercial trials are also monitored but this may be less frequent and could be done by a member of the trial team, rather than a dedicated CRA.

Information about you that is collected and recorded as part of the trial will have a code number attached to it instead of your name. The results of clinical trials are published in professional journals but neither patient names nor assigned code numbers are included. Sometimes individual responses are mentioned, eg '1 patient had this side effect ...', but no names or personal details are ever published.

### **Storage of tissue and blood samples**

Sometimes trials involve storage of tissue samples from a **biopsy** or blood samples for future use, either as part of the trial you are in or as part of a biobank of cancer

samples for use in future research. You will be told if this will happen to your samples and, in some trials, you will have the option to opt out of having your tissue or blood stored. You may be asked to enter a trial that only asks for tissue samples or blood samples for research. Tissue samples are usually referred to by code so won't be labelled with your personal details. You are not usually told the results of any tests done on these samples.

## What happens if you change your mind?

# 4

You can withdraw from the trial if you wish, but you might not be able to continue with the same treatment you have been having. If your treatment has not yet been completed, you will probably then have the standard treatment for someone in your situation. Before you decide to take part you should be aware of what happens if you withdraw from a trial. Ask your doctor or research nurse what treatment will be available to you if you do withdraw.

Treatments you have during the trial can influence the treatment you can switch to after you withdraw. For example, you may not be able to switch halfway through from one chemotherapy regimen to another. Make sure you ask your medical team about the possible consequences of changing your mind before you sign up.

## **What should you do if you are unhappy?**

Your Information Sheet will include contact details for people who can help you if you are unhappy about your care during the trial. It will also include information about what to do if you feel that you have been harmed as a result of trial treatment.

# 4

## **What is follow-up and what do trial results mean?**

### **Follow-up**

Clinical trials can involve a long period of follow-up. Researchers (and, of course, doctors) are usually interested in long-term results as well as in the initial effect of a treatment. The Information Sheet should include details about your follow-up, what tests might be involved and how often you will have them.

### **What do the researchers measure?**

Researchers have different ways of measuring how well a treatment works. The Information Sheet you are given will explain what measure the researchers will use. For example, they might use scans before, during and after treatment to see how you respond. Make sure you understand any risks associated with extra tests, eg some scans expose you to radiation.

Researchers are looking at outcomes or 'end points', such as:

- **Response rates:** measure how many people have lymphoma that shrinks due to the treatment. A response can be a
  - **complete response** (CR), which means that the lymphoma has disappeared for a time
  - **partial response** (PR), which means that the lymphoma has shrunk by at least half (when it stays the same, it is called **stable disease**).
- **Duration of response:** the time between treatment and the lymphoma coming back (relapsing) or starting to grow again (**disease progression**). You might hear this being called the '**progression-free interval**' or 'event-free interval' or '**progression-free survival**' (PFS).
- **Survival rates:** measure how many people are alive at a given point after treatment (usually 5 or 10 years). This might be:
  - **disease-free survival**, the percentage of people in the trial who are alive and free of lymphoma after a certain number of years, or
  - **overall survival** (OS), the percentage of people who are alive after a certain number of years, with or without signs of lymphoma.

### When will the trial results be available?

Trials can continue to recruit participants for many years. Researchers often want to record outcomes of participants 5 or 10 years after their treatment has finished. So it might take many years for the results to be reported. Results are usually reported at major medical conferences and in journals.

← Publication of trial results is discussed on page 43.

## Summary

Clinical trials have **eligibility criteria** to determine who can take part. These criteria are there to ensure that the trial is safe and scientifically valid.

Not all hospitals take part in clinical trials. If you are interested in taking part in a trial, talk to your doctor or clinical nurse specialist as you may be able to be referred to a trial site.

4

There is no way to tell how taking part in a trial will affect you. You will have access to a lot of information and there will be a dedicated research nurse to answer your questions. Clinical trials often give you an opportunity to try the latest treatment and usually involve more monitoring and follow-up than does routine clinical practice.

You don't have to take part in a clinical trial. Some people find it difficult to deal with the uncertainty of trying a new treatment and of not being able to decide which treatment they will have. This might be particularly difficult in a **blinded** trial where you do not know which treatment you are receiving.

You will be given very detailed information about the trial procedures. It might seem overwhelming, but researchers have to make sure you know what is involved before you agree to take part. If you have any questions, ask your research team before you agree to take part.

Withdrawing from a trial may affect the kind of treatment you can get in the future. Make sure you understand what happens if you change your mind beforehand.

It might take several years after the trial has completed before the final results are reported. Results are usually reported at medical conferences and published in specialist journals.

# 4



# Questions to ask

**Questions to ask your specialist about clinical trials**

**Questions to ask yourself about taking part in a clinical trial**

**5**

## Questions to ask your specialist about clinical trials

You should have plenty of time to ask questions about a trial. Write your questions down beforehand. You might find it helpful to take someone with you to the appointments. They might be able to better remember what you are told because they will be less anxious, or they could note the answers you get. You should feel free to ask about anything that is on your mind. There is no such thing as a silly question.

It might help to ask some of these questions:

- How will this trial help people?
- What will the trial involve?
- How can it benefit me? Will it benefit me?
- What is known about the trial treatment?
- What are the risks?
- How do you know the trial is safe?
- Will I be able to choose the treatment if I am in the trial?
- Will the trial take longer compared with standard treatment?
- Where will I have treatment?
- Will I have to stay in hospital?
- How often will I have treatment?
- Will I have more tests than I would in routine care?  
What are the risks associated with having these extra tests?
- Will I have to fill in questionnaires about how I am feeling? How many? How often?
- How will the trial affect my day-to-day life?
- How many extra hospital visits will be involved?
- Will I be reimbursed for extra travel costs?







## Questions to ask yourself about taking part in a clinical trial

Taking part in a clinical trial is an opportunity to be a part of an important process. You will be taking part in something that many people are investing in. The outcome of your involvement could have real impact on people who have lymphoma in the future. It isn't a decision to be taken lightly. You should carefully consider what you have been told.

5

You might want to ask yourself some of the following questions to help you make a decision:

- Do you understand what is involved in taking part in the trial?
- Do you understand the risks?
- Do you understand that you may not benefit from the trial?
- Have you had an opportunity to ask questions?
- Have your questions been answered well enough?
- Do you feel comfortable with the people who will be treating you? Do you feel you will be able to ask them questions?
- If the trial is randomised, are you happy with it?
- If the trial is blinded, do you understand that you will not know what treatment you are receiving?
- Are you aware of the implications for further treatment if you decide to withdraw?
- Are there any practical implications to take into account, such as travel and an increased number of visits to hospital? How will you manage them?



# Conclusion

Whatever your situation, we hope that this booklet has helped you better understand clinical trials – why they are done, how they are organised and what they involve.

Deciding to take part in a trial can be difficult. You need to understand why the trial is being done, what it involves and how it will affect you. Do ask your medical team questions until you feel sure you understand what will happen and why.

If you would like further information on anything you have read in this booklet or if you have any concerns about any aspect of your lymphoma, please call our free, confidential helpline on 0808 808 5555 or email us on [information@lymphomas.org.uk](mailto:information@lymphomas.org.uk)



# Glossary

<b>Bias</b>	accidental or intentional distortion of the truth. Bias can result when the way a trial is designed or the way data are analysed favour a particular outcome
<b>Biopsy</b>	a test that takes some tissue so that the cells can be looked at under a microscope
<b>Blind or Blinding</b>	blinding means that people taking part in a trial do not know which treatment they are receiving. If the doctor or researcher doesn't know this either, this is 'double-blinding'
<b>Complete response</b>	the lymphoma has disappeared for a time
<b>Control group</b>	a comparison group of trial participants who are not treated with the treatment that is being investigated (they might receive no therapy, a different therapy or a placebo)
<b>Disease-free survival</b>	the percentage of people in the trial who are alive and free of lymphoma after a certain number of years

<b>Disease progression</b>	continued growth of the lymphoma (researchers define this as growth of more than a fifth while you are having treatment)
<b>Efficacy</b>	the ability of the drug to produce a beneficial effect
<b>Eligibility criteria</b>	a list of characteristics that describe the entry conditions for people joining a trial (eg the type and/or stage of lymphoma they must have)
<b>End point</b>	a way of measuring how well a treatment works. Common end points used in trials are partial and complete response rates, progression-free interval and survival rate. End points are also sometimes called 'outcomes'
<b>Exclusion criteria</b>	a list of characteristics that would prevent someone from taking part in a trial
<b>Inclusion criteria</b>	a list of characteristics needed to allow someone to take part in a trial (eg disease stage, age range)
<b>Informed consent</b>	an agreement people make to take part in a trial after being told all the important facts about the trial and after having their questions answered satisfactorily

<b>Interim data</b>	results that come out during the trial. They are analysed before the end of the trial by an independent data monitoring committee to check for bias and for the safety of the participants.
<b>Late effects</b>	health problems that occur months or years after treatment has ended
<b>Maintenance therapy</b>	treatment to keep lymphoma in remission (no evidence of the disease) after successful treatment
<b>Mechanism of action</b>	the way or ways in which the drug produces its effect
<b>Monoclonal antibody</b>	a manufactured protein that targets malignant cells, triggering the body's own immune system to kill them
<b>Open trial</b>	a trial that is still recruiting participants
<b>Overall survival</b>	the percentage of people who are alive after a certain number of years, with or without having any signs of lymphoma. Often measured 5 years and 10 years after the treatment has ended
<b>Partial response</b>	lymphoma (or other cancer) that has decreased by at least a half for a time

<b>Participant</b>	someone who is taking part in a clinical trial
<b>Peer review</b>	review of a clinical trial by independent experts in the same medical field. They examine the scientific merit, participant safety and ethical aspects of the proposed trial
<b>Pharmacodynamics</b>	the effects of drugs on the body and how the drug causes those effects
<b>Pharmacokinetics</b>	what the body does to a drug – the movement of the drug into, through and out of the body
<b>Placebo</b>	an inactive or 'dummy' treatment designed to resemble the drug being tested if there is no standard treatment to compare a new treatment with. Used to rule out any psychological effects of taking a treatment
<b>Progression-free interval</b>	the time between treatment and the lymphoma starting to increase again. Sometimes called the 'event-free interval'
<b>Progression-free survival</b>	the time someone lives without their lymphoma starting to increase again

<b>Protocol</b>	the plan for a research trial that includes information on the research question being asked by the trial, the eligibility criteria, investigations required and follow-up requirements
<b>Randomisation</b>	a method that ensures that each participant has the same chance of being put into the different treatment groups
<b>Randomised controlled trial</b>	a randomised trial that has a control group
<b>Refractory</b>	lymphoma that does not respond to cancer treatment
<b>Relapsed</b>	lymphoma that has returned after treatment and after a period of time during which the cancer could not be detected
<b>Research Ethics Committee</b>	an independent committee made up of healthcare professionals and lay people that reviews proposed clinical trials in order to make sure that they are conducted ethically and safely
<b>Risk/benefit ratio</b>	the ratio of the risk of an action to its potential benefits; used to decide whether the risks outweigh the benefits

**Stable disease** disease (eg lymphoma) that has stayed the same (ie neither gone away nor progressed)

**Trial arms** the groups which trial participants are assigned to in a randomised controlled trial. The people receiving the current standard treatment are in the 'control arm'; people having new treatment/s are in the 'treatment arm/s'

**Trial phases** clinical trials of treatments are conducted in 4 phases. Phase 1 and 2 test safety and basic effectiveness of new treatments. Phase 3 and 4 trials compare new treatments with standard treatments and monitor side effects in large numbers of people

# Useful organisations and further information

This is a short list of useful organisations, but there are many others. If the right organisation isn't listed here, please call our helpline on [0808 808 5555](tel:08088085555).

## **Cancer Research UK**

A charity that provides information and statistics on all types of cancer, treatment, prevention, screening and research, in addition to maintaining a database for patients of all cancer trials taking place in the UK.

Angel Building, 407 St John Street  
London EC1V 4AD

Phone: 0808 800 4040 (freephone helpline staffed by nurses)

[www.cancerresearchuk.org](http://www.cancerresearchuk.org)

Email: via website

## **Haematology Trials Group**

Part of Cancer Research UK & UCL Cancer Trials Centre. The Haematology Trials Group has been running clinical trials for patients with lymphoma since 1970.

Cancer Research UK & UCL Cancer Trials Centre  
90 Tottenham Court Road

London W1T 4TJ

Phone: 020 7679 9898

[www.ctc.ucl.ac.uk](http://www.ctc.ucl.ac.uk)

Email: [ctc.enquiries@ucl.ac.uk](mailto:ctc.enquiries@ucl.ac.uk)

### **Bloodwise**

Funds research into the causes and treatment of leukaemia, lymphoma and related diseases. Provides a range of publications, including information about clinical trials.

39-40 Eagle Street  
London WC1R 4TH  
Tel: 020 7504 2200  
[www.bloodwise.org.uk](http://www.bloodwise.org.uk)  
Email: via website

### **Lymphoma Research Trust**

Supports research into the treatment of lymphoma. It makes grants to medical researchers at the Lymphoma Trials Office.

Trustees Department  
5th Floor East, 250 Euston Road  
London NW1 2PG  
Tel: 020 3447 9931  
[www.lymphoma-research-trust.org.uk](http://www.lymphoma-research-trust.org.uk)  
Email: [carron.lindsay@uclh.nhs.uk](mailto:carron.lindsay@uclh.nhs.uk)

### **Macmillan Cancer Support**

Provides practical, medical, emotional and financial support to people living with cancer.

89 Albert Embankment  
London SE1 7UQ  
Tel: 0808 808 0000  
[www.macmillan.org.uk](http://www.macmillan.org.uk)  
Email: via website



### **National Cancer Institute (NCI)**

NCI at the National Institutes of Health is an American organisation that carries out cancer research and funds clinical trials for cancer patients in the US and around the world.

BG 9609 MSC 9760  
9609 Medical Centre Drive  
Bethesda, MD 20892-9760  
[www.nci.nih.gov](http://www.nci.nih.gov)  
Email: via website

### **National Cancer Research Institute (NCRI)**

A partnership between the government, charities and the industry used by the main research organisations to plan future cancer research. It monitors the progress of all cancer research initiatives in the UK.

Angel Building, 407 St John Street  
London EC1V 4AD  
Phone 020 3469 8460  
[www.ncri.org.uk](http://www.ncri.org.uk)  
Email: [info@ncri.org.uk](mailto:info@ncri.org.uk)

## **National Institute for Health and Care Excellence (NICE)**

Provides independent, evidence-based guidance on the most effective ways to prevent, diagnose and treat disease and ill health. It appraises clinical trial evidence in the development of their guidance, which underpins prescribing in England and Wales.

10 Spring Gardens  
London SW1A 2BU  
Phone: 0300 323 0140  
[www.nice.org.uk](http://www.nice.org.uk)  
Email: [nice@nice.org.uk](mailto:nice@nice.org.uk)

# Selected references

The full list of references is available on request. Please email us at [publications@lymphomas.org.uk](mailto:publications@lymphomas.org.uk) or call us on 01296 619409 if you would like a copy.

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**'Details of a clinical trial I could enter were clearly explained by the research nurse. Although I left that meeting feeling I wanted to enter the trial, being able to read information about my lymphoma and treatments was really helpful. It enabled me to formulate questions and once I had discussed these with my medical team, I felt confident in going ahead with the trial.'**

Michael, diagnosed with lymphoma in 2010



This booklet will help you understand what clinical trials are, why they are done, how they are organised and what they involve for those who take part. It will also give you useful guidance on how to find out more about trials that might be suitable for you.

The Lymphoma Association provides specialist information and emotional support to anyone affected by lymphatic cancer. Get in touch today to see how we can help you.

Lymphoma Association

3 Cromwell Court, New Street, Aylesbury, Bucks HP20 2PB

General enquiries 01296 619400

**Freephone helpline 0808 808 5555**

**information@lymphomas.org.uk**

**www.lymphomas.org.uk**

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LYM0059/ClinTrialsBk/2015ed4

4th edition produced: December 2015

Next planned review: December 2018

ISBN 978-0-9929362-7-3

