Clinical trials for lymphoma

What are clinical trials?

What do they involve?

Lymphoma research

Taking part

We are discontinuing this book but will keep this edition available while the content in it stays relevant.
This booklet has been researched and written by Lymphoma Action, the only UK charity dedicated to those affected by lymphoma.

We would like to thank our incredible supporters whose generous donations enable us to offer all our essential support services free of charge. As an organisation we do not receive any government or NHS funding and so every penny received is truly valued. From everyone at Lymphoma Action, and on behalf of those affected by lymphoma, thank you.

To make a donation towards our work, or to get involved with fundraising for us, please visit lymphoma-action.org.uk/Donate
Your diagnosis

Your trial

### Key contact

Name: __________________________________________

Role: __________________________________________

Contact details: __________________________________________

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<tr>
<th>Job title/role</th>
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<tr>
<td>GP</td>
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<td>Consultant haematologist/oncologist</td>
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<td>Research nurse or clinical trial practitioner</td>
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About this book

Clinical trials are vital for testing new treatments for lymphoma and finding out which treatments work best and for which people. This booklet explains what clinical trials are, what’s involved in taking part and why they are important for people with lymphoma. There is space for notes and questions for you to think about.

Important and summary points are written in the chapter colour.

- Lists practical tips.
- Space for questions and notes.
- Lists other resources you might find useful.

The information in this booklet can be made available in large print.
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I feel fortunate to have been given the opportunity to take part in the trial. It encouraged me to find out more about my illness, however scared I was at first. I have no doubt that all cancer patients get excellent care, but the trial nurses are always there if I have any questions.

Roger, who was treated as part of a clinical trial for central nervous system lymphoma
What are clinical trials?

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Clinical trials are medical research studies involving people.

Some trials involve healthy volunteers, but clinical trials for lymphoma treatments involve people with lymphoma.

Clinical trials are the only way to answer key questions about lymphoma.

Clinical trials done in the past underpin the treatments available for people with lymphoma today. They are vital for improving lymphoma treatment, outcomes, and the quality of life of people with lymphoma.

Find out more about how clinical trials are contributing to improving outcomes on page 37.

Types of clinical trials

Many clinical trials for lymphoma test treatments.

New treatments are only tested in clinical trials after they have been tested thoroughly in the lab, on cells and in animal studies.

Treatment trials

Treatment trials can involve testing new treatments or testing existing treatments in new ways.
Trials testing new treatments aim to find out:

• the best doses to use
• if a new treatment is effective and if so, in which people
• what side effects (unwanted effects or ‘toxicities’) it causes.

Treatment trials are also done to improve existing treatments or to find out which treatment is best. For example, they can:

• **Compare treatments** to help researchers find out which is more effective.
• **Find out if giving people less treatment is just as effective but reduces side effects** if this treatment is usually very successful for a type of lymphoma.
• **Identify people who need stronger treatment early**, to give them a better chance of the treatment being successful.

Two or more treatments are also often combined to see if combining treatments can make them more effective without causing too many side effects.
Other types of research

This booklet focuses on treatment trials but not all research involves treatments. There are many reasons for a research study to be carried out, for example:

• To find out more about a disease, which helps with designing new treatments.
• To improve tests that are used to diagnose lymphoma. A study might compare different tests, for example scans, to find out which is best at detecting lymphoma.
• To test different follow-up schedules and recovery packages.
• To find out how your lymphoma has affected your quality of life.

Research studies often only need samples, for example blood samples or a sample of your biopsy. You might not need to have extra tests to collect these samples if you take part in a research study. The samples are sometimes taken at the same time as other tests you are having. Some studies only use samples that have been previously collected (for example, your biopsy).

You might only be asked to complete questionnaires to help researchers learn more about your disease or about your quality of life.
Many treatment trials also collect samples for research as well as samples to monitor your wellbeing and your response to treatment. These samples are sometimes used for future research too.

**Drug development**

Clinical trials are a vital part of drug development. All new treatments have to be thoroughly tested in the people they are designed for before they can be more widely used.

The people in clinical trials are monitored very carefully to make sure any side effects are managed well, to look out for unexpected side effects and to test how well the treatment is working.

A treatment can only be approved for wider use when enough information about it has been gathered. This means drug development can take a long time.
Figure: Drug development process for drugs in general, showing it can take an average of 12 years to develop a drug.
Phases of clinical trials

Clinical trials are usually carried out in phases from 1 to 4 (you might see them in Roman numerals too – I, II, III, IV). More is learnt about a treatment as it goes through the different phases.

**Phase 1**

A phase 1 trial is often the first time a treatment is tested in people (‘first-in-man’ studies). These early-phase trials test treatments in a small number of people, usually those who have run out of standard treatment options.

Phase 1 trials might include only people with lymphoma or people with lots of different types of cancer. Many phase 1 trials aim to:

- find the most effective safe dose of the treatment for a certain disease
- find out what the treatment’s side effects are.
Phase 2 trials find out more about how well a treatment works in a larger number of people.

Phase 2 trials also continue to find out about treatment side effects. They are often for people with certain types of lymphoma. Sometimes they test a new treatment in combination with an existing treatment.

Phase 3 trials often compare the new treatment with the best standard treatment available. They can also test new ways of using existing treatments.

Phase 3 trials involve lots of people, often in many different countries. They can take years to complete.
New medicines are usually approved (given permission to be used for certain people with a certain disease) in the UK based on the results of phase 3 trials. This is often called ‘licensing’. The results of phase 2 trials might be used as evidence for licensing if they are significant enough, or if the condition under investigation is rare and there are not enough people to do a phase 3 trial.

After a drug has been licensed, clinical trials might still be done to find out more about it, for example about its side effects or how it impacts on people’s long-term health. These are phase 4 clinical trials.

**Other types of clinical trial**
There are other types of trial, too, for example pilot studies or feasibility studies. These are small studies done before a main trial to test how the main trial is going to work.
Randomisation and blinding

In many trials, everyone has the same treatment. Some larger trials are randomised.

Randomisation is where you are put into groups (often called ‘arms’) that have different treatment. For example, one group might have standard treatment and the other group might have the new treatment. You are put into a group at random using a computer. This is the same as tossing a coin to see who goes into which group. You can’t choose which group you are in and neither can your doctor.
At the start, I wanted to know which treatment pattern I would have, but once the decision had been made, it didn’t really matter as long as it worked. Sue, treated in a randomised trial for follicular lymphoma

Some randomised trials are also blinded.

**Blinding** is where you can’t tell the difference between each treatment, so you don’t know which treatment group you are in. Blinding helps to stop the ‘placebo effect’ where people think a new treatment is helping them because they expect it to.

**Could I get a placebo?**

Many people considering a clinical trial worry that they won’t get a treatment that actually works and will instead get a dummy treatment – a placebo.

It is not ethical to give you a dummy treatment if you need active treatment for your lymphoma.
In lymphoma clinical trials, placebos are sometimes used alongside other treatments, for example, if a new treatment is being added to standard treatment. In this case, everyone in the trial has standard treatment, but:

- one group of people has the new treatment with standard treatment
- another group of people have a placebo as well as standard treatment.

The new treatment and the placebo look the same so you can’t tell which treatment you are having.

**Treatment for arm 1**
- Standard treatment
- New treatment

**Treatment for arm 2**
- Standard treatment
- Placebo

*You will always be given active treatment in a clinical trial if you would be having active treatment outside of a clinical trial.*
It seemed as if the worst that would happen if I joined the trial was that I’d have the standard treatment but more blood tests and oversight, which might help my treatment and recovery. If I was put into the experimental treatment group, it might work better and be easier to deal with.

Michael, who is on an ongoing clinical trial for small lymphocytic lymphoma (SLL)/chronic lymphocytic leukaemia (CLL)
What do clinical trials involve?

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# Process of a clinical trial

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<th>Step</th>
<th>Description</th>
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<tr>
<td>Proposal</td>
<td>Organisations or drug companies want to answer a question about lymphoma. Experts in the field discuss ideas and a proposal is made.</td>
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<tr>
<td>Getting funding</td>
<td>The organisers apply for funding – drug companies, national charities and governmental organisations fund research.</td>
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<tr>
<td>Planning</td>
<td>A document describing the study in detail is produced – a 'protocol'. The protocol is reviewed and approved by authorities and ethics committees.</td>
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<td>Hospital facilities are assessed to make sure they are suitable for them to take part.</td>
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<td>Recruiting</td>
<td>The study doctors at each hospital start asking people if they would like to take part – recruitment can take years.</td>
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<tr>
<td>Follow-up and results</td>
<td>Data (results of tests) are monitored during the trial. Participants have check-ups to see how they do. Results of the trial are published (often many years later).</td>
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It can take a long time to set up and carry out a clinical trial. Before a trial starts, it is very important that the plan for the trial (the protocol) has been thoroughly reviewed to make sure the trial is ethical. The trial is ethical if it is as safe as possible for the people taking part and it is in the best interests of people with lymphoma that the trial goes ahead. The UK Medicines and Healthcare products Regulatory Agency (MHRA) and ethics committees have to approve the trial before it can go ahead.

Clinical trials are very expensive, so it can take time to get funding to go ahead – the funders also have to be sure that the trial is a good idea and the research questions it aims to answer are important. Funding has to cover everything needed for the trial, including staff, facilities, treatments, and collecting and analysing the results.

Treatments tested in clinical trials are often very expensive but they are not funded by the NHS. The costs of the new drugs are covered by funding for the trial, for example by a pharmaceutical company.
Who can take part?

There are clinical trials suitable for all sorts of situations:

- For your first treatment, or if you need more treatment because your lymphoma has come back or didn’t respond to treatment.
- For many different types of lymphoma, both common and rare.
- For all age groups – children, adults, younger people or older people.

However, there is not a clinical trial for everyone at any one time. You have to meet the strict eligibility criteria of a clinical trial to be able to take part.

What are eligibility criteria?

The eligibility criteria are lists of requirements that you have to meet to be able to take part in a clinical trial. They include inclusion and exclusion criteria.

Eligibility criteria keep you safe and make sure the results of the trial give the researchers as much information as possible.

Researchers have to make sure they are comparing like with like – if all the people in the trial have similar characteristics, any differences in outcomes are more likely to be due to the treatment in the trial. They also have to make sure it is safe
for you to take part in the trial. Each clinical trial has its own set of eligibility criteria.

You must meet all the eligibility criteria to be able to enter a clinical trial. Even if there is only one requirement that you don’t meet, it is unlikely that you will be able to take part.

**Inclusion criteria: who can join the trial**

*Inclusion criteria are the characteristics you or your lymphoma must have in order to take part.*

They include what type of lymphoma you must have, what previous treatment, if any, you must have had, and what age range you need to be in.

**Exclusion criteria: who can’t join the trial**

*Exclusion criteria are important in keeping you safe.*

People with certain other conditions might be excluded if the trial treatment could be more dangerous for them. People who’ve had certain other treatments might also be excluded as it could be difficult for researchers to tell if an effect is due to the treatment that is being investigated in the trial or a previous treatment. Pregnant and breastfeeding women are usually excluded from clinical trials in case an experimental treatment could harm an unborn baby or could be passed to a baby in breast milk.
Finding clinical trials

Your consultant or clinical nurse specialist (CNS) might talk to you about taking part in a clinical trial. You can ask them if they can suggest a trial that might be suitable for you.

Your consultant might be able to refer you to another hospital that is running a clinical trial if it isn’t running at your hospital.

Don’t be worried about asking to be referred to another hospital. Your consultant is used to that type of request.

Ask about clinical trials – they might give you other treatment options.
There are sources of information on the internet to help you find out about clinical trials.

**Tips for finding information about trials**

- Search reliable sites so that the information is most likely to be accurate (see page 48).
- Be aware that clinical trials change quickly – the information you find might be out-of-date.
- Some trials recruit very slowly as they monitor patients carefully. Even if you are suitable, there might not be a slot for you.
- Take any information you find to your consultant so you can discuss whether it would be an option for you.
• Our clinical trials information service, Lymphoma TrialsLink, includes a database of lymphoma trials for people in the UK, with brief summaries of each trial to help you find out what’s involved and whether you might be able to take part. Visit lymphoma-action.org.uk/TrialsLink

• The UK Clinical Trials Gateway has a database of UK trials for all medical conditions. However, the language is often scientific. Visit ukctg.nihr.ac.uk

• Some lymphoma trials are listed on Cancer Research UK’s database of cancer clinical trials, and their summaries aim to explain what’s involved for the people who take part. Search ‘find a trial’ at cancerresearch.org.uk

Not everyone can take part in a clinical trial as there are only a limited number of trials at any one time. Let your consultant know that you are interested in trials in case there is a suitable trial for you.

Remember that most people do very well on standard treatment for lymphoma and a clinical trial may not benefit you.
What should I consider?

If you are considering taking part in a clinical trial, it is important that you have all the information you need to make a decision on whether it is right for you.

A trial treatment is being tested, so no-one can tell you whether or not it will benefit you.

The trial team are not allowed to persuade you to take part in a clinical trial. You have to be told about all the possible risks and benefits.

You do not have to take part in a clinical trial to get good medical care. If you decide not to take part, you still have expert care, good quality information about your treatment, and careful follow-up after treatment.

You can say ‘no’ at any stage. You do not have to take part and even if you agree to take part, you can change your mind. You will still get the best available treatment and care.
What are the possible advantages of a trial?
The possible advantages of a trial are:

- **Access to support and advice from experts** for you and the trial staff.
- **Dedicated research staff**: nurses or other staff with a research interest can answer your questions and support you in addition to your usual team.
- **Comprehensive information** about the treatments and their risks and benefits.
- **Close monitoring and detailed follow-up**: you have more tests and often longer follow-up than usual to keep a close eye on any side effects and your response to treatment.
- **Access to the latest treatments**: a new treatment could benefit you, or experimental treatment could be available when you have run out of other treatment options.
- **Helping others**: even if the trial doesn’t benefit you directly, it gives researchers important information that helps drive forward improvements in lymphoma treatment and care.
What are the possible disadvantages?
Most of the possible disadvantages of a trial are around uncertainty. A clinical trial is an experiment, so no-one knows what the results will be. Uncertainty is greatest for phase 1 trials, where very new treatments are tested. These trials are usually restricted to people who have no other treatment options. This can feel daunting. Don’t be afraid to ask questions and share your worries.

- **Uncertainty about the outcome:** no-one can say whether the treatment you get as part of a trial will be better than the treatment you would have got if you didn’t take part. However, remember that clinical trials do not go ahead if the experimental treatment is not thought to be as good as, or, potentially better than, standard treatment for someone in your situation.
- **Extra hospital visits and tests:** these can be reassuring, but some people find them stressful or inconvenient. Talk to your team to make sure you are comfortable with the tests you need to have as part of the trial.
- **Too much information:** you might find some of the information you are given worrying or difficult to understand. Ask your team to explain it to you.
Will I 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 might get your expenses paid, such as travel costs. Ask your trial team if your travel or any other expenses will be covered as part of the trial.

Do I have to pay?
No, you do not have to pay to take part in a clinical trial.

The drugs involved in clinical trials can be very expensive as drug development is a long and expensive process. However, clinical trials can give people access to expensive drugs outside of the NHS. The NHS does not pay for drugs that are part of the clinical trial; they are funded by the pharmaceutical company or other funders.

Informed consent
You have to give informed consent to take part in a clinical trial. This means that the researchers have to make sure you have information about the trial and the treatments, and that you fully understand it. They must give you a chance to ask questions and to discuss the information they give you with them. You can discuss it with other people too: your family, friends, and other health professionals like your GP.
You are given information that you should be able to take away with you and read in your own time. You can make notes and highlight anything you don’t understand so that you can discuss it with the research team.

Don’t be worried about asking questions – ask as many questions as you need to make sure you are comfortable with your decision. You might find it helpful to take someone with you to appointments so they can help you remember what you are told or can make notes for you.

The clinical team stressed that it had to be my decision whether to take part. Although the information I was given was easy enough to read and understand, I took it to my GP to discuss.

Sue, who was treated for relapsed follicular lymphoma as part of a clinical trial

If you decide to take part in the trial, you are asked to sign a consent form, so both you and the research staff have a record of your agreement.

You can change your mind at any time – you do not have to continue to take part in a clinical trial even if you have signed a consent form.
Tips for asking questions

• Ask as many questions as you need to make sure you understand what’s involved in the trial and what is expected of you.
• If you think a question is silly, ask it anyway. Your research team will be expecting all sorts of questions.
• If you don’t understand the answer to a question, ask it again.
• Make a note of questions you’d like to ask so you don’t forget them.
• Note down the answers or ask to record the conversation; when you are given lots of information, it can be very difficult to remember the bits that are important to you.
• Take someone with you to appointments to take notes or help you remember the answers you are given.

There are lists of questions you might find helpful to ask, and space for notes, at the back of this booklet on pages 63 to 69.
An experimental drug put my classical Hodgkin lymphoma into remission for the first time in the 7 years since I was diagnosed. I still remember being told I was in remission. It was overwhelming.

Carol, who took part in several clinical trials and went into remission after having brentuximab vedotin, which has since been approved to treat some people with Hodgkin lymphoma.

Photo credit: Magi Haroun
Research in lymphoma

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Lymphoma research is bringing about big changes in the management of some types of lymphoma. Progress has been greater for some types of lymphoma than others, and it is vital that clinical trials are conducted for rare and difficult-to-treat lymphomas so that outcomes can be improved for people with those types of lymphoma too.

Some of the key advances from recent years are described below. This is not a comprehensive list and research continues to drive forward progress in developing and testing new treatments.

**Targeted drugs**

Targeted drugs affect processes in cells. They work in different ways:

- to stop cancer cells growing or dividing
- to cause cancer cells to die
- to use your own immune system to help your body get rid of cancer cells.

Targeted drugs often have fewer side effects than chemotherapy as they target cancer cells more precisely. Chemotherapy drugs kill healthy cells as well as cancer cells, which causes many of the side effects of this type of treatment.
The first targeted drugs for lymphoma were antibody treatments. Your body makes antibodies naturally to fight infection. Each antibody sticks to a target (a certain protein or ‘antigen’) on cells, such as bacteria, and tells your body to get rid of those cells. Laboratory-made antibodies work in the same way and attach to a specific target to tell your body to destroy it. Laboratory-made antibodies are ‘monoclonal’, which means they are exactly the same, and target the same antigen.

Figure: Monoclonal antibodies locking on to antigens on a cell

Antibodies can also be combined with other treatments, such as chemotherapy drugs, to help deliver these treatments directly to the lymphoma cells. This reduces the effects of these treatments on healthy cells and therefore reduces side effects.
Many targeted drugs used for lymphoma affect the activity of important processes that keep cancer cells alive. Targeting these processes can stop cancer cells growing or cause them to die.

Find out more about targeted drugs and how they work at lymphoma-action.org.uk/TargetedDrugs. We have webpages on many of the targeted drugs used to treat people with lymphoma.

New options for people with difficult-to-treat classical Hodgkin lymphoma

Although first-line treatment is usually successful for Hodgkin lymphoma, newer targeted treatments are improving outcomes for those who have lymphoma that is more difficult to treat. For example:

- brentuximab vedotin, which is an antibody–drug conjugate, consisting of an antibody joined to a strong chemotherapy drug
- checkpoint inhibitors (pembrolizumab and nivolumab), which are a type of drug that allows your immune system to recognise and kill cancer cells.
New treatment pathways for low-grade (slow-growing) lymphomas

There are several targeted drugs already being used routinely to treat people with some types of low-grade non-Hodgkin lymphoma. Some new treatments are being used as a first treatment (first-line) for groups of people who don’t respond well to standard chemo-immunotherapy (chemotherapy with antibody therapy) or who are not fit enough for stronger treatments. These drugs are also offering options for people whose lymphoma has come back.

Importantly, some of these drugs are putting low-grade lymphomas into deeper remissions – they leave behind fewer lymphoma cells, which means remission is likely to last longer, or the lymphoma might never come back. These drugs also offer a lower risk of serious side effects compared with other treatments such as chemotherapy.

Targeted drugs for low-grade lymphoma include:

- ibrutinib
- venetoclax
- idelalisib
- newer antibodies that work in a similar way to rituximab (obinutuzumab and ofatumumab).
These drugs are often used alone but are also being tested or used in combination to improve outcomes further.

Research is moving quickly. There are lots of other new drugs in development that work in different ways.

Find clinical trials of new drugs at lymphoma-action.org.uk/Find-a-Trial

Possible treatment options are finally emerging for some people with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

There is a lot of interest in CAR T-cell therapies, which harness the power of your own immune system to get rid of lymphoma. CAR T-cell therapy involves having your own T cells (a type of white blood cell) collected and genetically modified so that they can recognise and kill lymphoma cells. The modified cells are called ‘CAR T cells’. When they have been made, the CAR T cells are given to you as a treatment for your lymphoma. You also have chemotherapy to reduce the number of white blood cells in your body and make room for the CAR T cells to grow.
CAR T-cell therapies might put DLBCL that has repeatedly failed to respond to chemotherapy into remission, as these treatments work in a different way to chemotherapy. This type of treatment is considered a breakthrough for some circumstances, but it can have serious side effects and is only suitable for people who are fit enough to have it.

Read more about CAR T cells at lymphoma-action.org.uk/CARTcells
Other targeted drugs like polatuzumab vedotin, an antibody–drug conjugate, could also be effective for people who previously had few treatment options.

**Reducing long-term problems**

Treatment for some types of lymphoma is generally very successful, but research still continues to drive forward improvements. A key focus is on reducing treatment so people have fewer side effects without reducing the effectiveness of the treatment.

**Response-adapted treatment for classical Hodgkin lymphoma**

Recent clinical trials aim to reduce late effects of treatment for Hodgkin lymphoma.

Doctors are now using PET scans part-way through treatment (interim PET) to tell them how your lymphoma is responding. They can then avoid giving you more treatment than you need, which reduces the risk of you developing problems in the future. They may also decide to change your treatment if your lymphoma doesn’t respond as well as expected.

Far fewer people with Hodgkin lymphoma now receive radiotherapy and many receive less bleomycin, which is a chemotherapy drug that may cause lung problems in some people.
Replacing radiotherapy with other treatments

Radiotherapy can be very effective but might also cause long-term problems depending on how much you are given and what part of your body is being treated. Research has shown that a self (autologous) stem cell transplant could be as effective but cause fewer long-term brain problems than whole-brain radiotherapy for people with lymphoma in their central nervous system.

Research is also testing whether stronger chemotherapy can reduce the need for radiotherapy in some lymphomas, such as Hodgkin lymphoma.

Answering questions about maintenance for follicular lymphoma

People with follicular lymphoma often have maintenance treatment, where they have regular doses of an antibody treatment after their main course of treatment. Maintenance helps keep the lymphoma under control for longer. However, questions remain over who benefits from maintenance, how long it should be given for, and which antibody is best to use. Clinical trials are answering these questions and many more to help clinicians improve outcomes for people with lymphoma and avoid giving them more treatment than they need.
Intensifying treatment

Clinical trials often offer new treatment options for people whose lymphoma has come back or hasn’t responded to standard treatment but some trials aim to improve first treatment to reduce the number of people who need other options. Giving more intensive (stronger) treatment often comes with disadvantages such as more serious side effects or effects on fertility. Clinical trials are helping to pick out who would benefit from stronger treatment at the outset.

Testing new combinations and comparing treatments

Using existing treatments in new combinations can improve outcomes. The chemotherapy regimen (combination of drugs) CHOP is still widely used for people with T-cell lymphoma but recent trials have shown that other regimens are more effective for certain types of T-cell lymphoma, and this has changed standard treatment.

Combinations of newer targeted drugs are also being used for low-grade lymphomas as they can be more effective in combination than they are alone. However, some combinations cause more side effects as your immune system takes a greater hit. Clinical trial participants are monitored closely for serious or unexpected problems and these trials are helping researchers work out which combinations are safe and effective.
Learning more about lymphoma

Research studies often run as part of treatment trials but can also be done as separate studies. Collecting samples from people with lymphoma allows a wealth of research to be conducted to find out more about lymphoma. This research is helping to answer questions such as:

• What genetic changes in the lymphoma cells can predict which treatment will work best?
• Can features of the lymphoma help clinicians work out who needs stronger treatment and who is likely to respond to less treatment?
• What markers can be measured to predict if someone might relapse in the near future?
Tips for finding out about lymphoma research

• Keep an eye on our news section at lymphoma-action.org.uk/News for the latest news on drug approvals, trial results, conference updates and more.

• Look at the news sections of major cancer charities, like Cancer Research UK at cancerresearchuk.org/cancer-news

• Sign up to receive our magazine, which features clinical trials news in every issue. Visit lymphoma-action.org.uk/LymphomaMatters

• Don’t believe everything you read in the papers – they can sensationalise and exaggerate results. Find the facts behind the headlines at nhs.uk/news

• Look out for reports from major conferences, such as the International Conference on Malignant Lymphoma (ICML), the British Society of Haematology (BSH), or the American Society of Haematology (ASH), among others.
Soon after my treatment ended, I received a letter telling me that there had been no difference between the two treatments in the trial I was on. Although this was a little disappointing, I was glad to have been able to do my bit. John, who had treatment as part of a clinical trial for his diffuse large B-cell lymphoma
Taking part in a clinical trial

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Trial results 60
What happens in a clinical trial?

Consent
Your medical team and research staff explain the trial and give you information to take away and read.
You are asked if you agree (consent) to take part – you have to sign the consent form before the next stage.

Screening
You have tests to see if you meet the eligibility criteria (see page 24).
The research team look at your medical records and test results.

Allocation
You are enrolled in to the trial and are put into a treatment group (if there is more than one).

Treatment
You have the treatment and tests described in the information you were given.
You are monitored carefully to see how you respond and to check for side effects.

Follow-up
You have regular check-ups and tests after treatment to see how you are doing.
The trial team

Many trial centres have dedicated research staff who look after people taking part in clinical trials.

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<thead>
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<th>Job Title</th>
<th>What they do</th>
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<tr>
<td><strong>Research nurse</strong>*</td>
<td>• Act as your key contact.</td>
</tr>
<tr>
<td>An experienced nurse trained in</td>
<td>• Explain the trial to you and answer your questions.</td>
</tr>
<tr>
<td>clinical research</td>
<td>• Arrange your tests and carry out some tests and treatments.</td>
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<td></td>
<td>• Look after you during the trial.</td>
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<tr>
<td><strong>Clinical trial practitioner</strong></td>
<td>• Your key contact might be a clinical trial practitioner instead of a nurse.</td>
</tr>
<tr>
<td>(CTP)</td>
<td>• CTPs do a similar job to research nurses but don’t do your tests.</td>
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<tr>
<td>Usually a scientist trained in</td>
<td></td>
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<tr>
<td>clinical research</td>
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<tr>
<td><strong>Principal investigator (PI)</strong></td>
<td>• The consultant in charge of the trial at your hospital. This is usually a lymphoma consultant with a research interest.</td>
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<td>• Other doctors might also be involved.</td>
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*In some centres, these are lymphoma specialist nurses with a research interest.
There are other staff who are crucial to the running of a clinical trial but act behind the scenes so you might not meet them. For example, a data manager oversees the collection of data (such as results from tests) for the trial and makes sure the data is accurate so the results of the trial will be valid.

Watch our video *The people involved in lymphoma clinical trials* to learn more about trial teams at lymphoma-action.org.uk/ClinicalTrialsVideos

**What do I need to do?**

When you take part in a clinical trial, you have to agree to the conditions of taking part. The trial team should give you clear information but do ask questions if you are not sure about something. You should be given numbers to call at any time in case you have an urgent question or problem.
Tips for taking part in a trial

• Continue to ask questions throughout the trial if you are unsure of anything.
• Report any changes in your health as soon as possible.
• Keep a clear record of all your appointments.
• Tell your GP and anyone else treating you that you are taking part in a clinical trial.
• Find out if you are able to take your usual medicines and don’t take any new medicines or supplements without checking with the trial team.
• If you are taking medicines at home as part of the trial, make sure you have clear instructions on what you need to do.
• Check if there is anything you can’t eat or drink as they could interact with the drugs you are taking.
• Follow any rules about contraception to avoid putting your partner or an unborn child at risk.
• Remember to complete any diaries or questionnaires that are part of the trial.
Confidentiality

Clinical trials have strict rules about keeping your personal and medical information confidential. They have to follow general data protection regulations (GDPR) to keep your information safe. Your medical team keep your medical records. Data for the clinical trial is collected separately. All information about you that is collected for the trial has a code number attached instead of any details that can identify you.

The organisation running the trial and regulatory authorities, such as the Medicines and Healthcare products Regulatory Agency (MHRA), can inspect trial sites and look at your information but they are bound by confidentiality agreements.

Names, code numbers and personal details are not published as part of the results. If individual responses are mentioned, they are made anonymous; for example, ‘one patient had this side effect’.

Storage of blood and tissue samples
Many trials involve storage of samples, for example blood samples or tissue samples from a biopsy. These samples are used as part of the trial but might also be stored for use in other research in the future. Your trial team tell you how your samples will be used, but you are not usually told the results of future research. For some trials, it may be possible
to opt out of having your samples used for research. Blood and tissue samples are usually referred to by code rather than by identifying details.

What happens if I change my mind?
You can change your mind and withdraw from the trial at any time and you do not have to give a reason if you don’t want to. You might not be able to continue to have the trial treatment if you withdraw. Ask the trial team what happens if you withdraw and what treatment might be available to you. There might be some alternative treatments that you can’t have once you have had the trial treatment, so be aware of what your options are if you change your mind.

What should I do if I am unhappy?
You should be given information that includes details of what to do and who to contact if you are unhappy with your care in the trial. The organisers have to make sure you get the best possible care throughout the trial and if you have any problems as a result of taking part in the trial. It is very important that you tell your trial team about any problems you are experiencing as soon as possible.
Data monitoring
The results from all of the participants’ tests and any side effects are monitored carefully throughout the trial to make sure no unexpected problems develop. For example:

- If unexpected side effects develop, recruitment might be put on hold while the data is reviewed to make sure it is safe to continue to treat people in the trial.
- Data can be reviewed and the protocol might be altered if one group of people is clearly doing much better than another.

Stopping trials early
Trials can be stopped earlier than planned if necessary. Often, this is because not enough people are being recruited. There have to be enough people in a trial to identify differences between groups and to draw conclusions. It is not worth continuing a trial if it is obvious it will not recruit enough people to give meaningful results. If you are already in the trial but it isn’t recruiting anymore, you can still complete the treatment as long as there are no safety concerns.

Sometimes, trials close early because one treatment is clearly better than another. It is not ethical to continue to give you a treatment if the researchers know it is not as good as another treatment. If this happens, you are switched to the better treatment if possible.
Occasionally, trials close early because people are having serious side effects. This is most likely in early-phase trials when not much is known about a treatment before the trial. A drug is normally only tested in phase 3 trials when there is enough evidence that it is safe. If it is unsafe for you to continue the trial treatment, your doctor will discuss other treatment options with you.

**Follow-up**

Most trials involve a follow-up period of several years after the trial treatment has finished. Follow-up is very important in finding out:

- how well the treatment works long-term
- how well you recover from the treatment
- whether you suffer any late effects (side effects that develop months or years after treatment, for example heart or lung problems).

You might have extra tests to allow the research team to check your response and your recovery during follow-up. Make sure you understand any risks associated with these extra tests, for example radiation from scans.

**Follow-up gives important information about the treatment being tested but remember you can still withdraw from the trial at any time.**
Trial results

The data about your response (for example your scan results) is collected together with that of everyone else in the trial so that the researchers can see how each group or the group as a whole responded to treatment.

Response rates measure how many people have lymphoma that shrinks due to the treatment. There are different levels of response:

- **complete response**: lymphoma has disappeared
- **partial response**: lymphoma has shrunk by at least half
- **stable disease**: lymphoma has stayed the same
- **progressive disease**: lymphoma has got worse.

Response rates can give researchers an idea of how effective a treatment is in the short-term but the information collected during follow-up allows them to find out whether the treatment effects last long-term.

There are various measures that might be reported but the most common for lymphoma clinical trials are:

- **progression-free survival**: the time between treatment and relapse (the lymphoma coming back or starting to grow)
- **overall survival**: how many people are alive at a certain time after their treatment.
The researchers also look in detail at the side effects of any treatment.

It can take many years before the results of a trial are published. This is because it can take years to recruit enough people, and years to then follow them up and find out what happens in the long term.

- Read our news section for regular reports on the results of clinical trials at lymphoma-action.org.uk/News
- Visit our dedicated lymphoma clinical trials information service at lymphoma-action.org.uk/TrialsLink
- If you have a question and can’t find the answer, get in touch by emailing trialslink@lymphoma-action.org.uk
I was very happy being on the trial as I hoped it would help me and also enable me to give something back. I would encourage anyone offered a clinical trial to consider it seriously.

Diana, who was treated as part of a clinical trial for relapsed follicular lymphoma
Questions to ask

Questions to ask the trial team  
Questions to ask yourself  

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Questions to ask the trial team

• How will this trial help people?
• What will the trial involve?
• How might 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 than 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? If so, 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?
• Who will be in charge of my care?
• How long will the follow-up be?
• What will happen if my lymphoma gets worse while I am in the trial?
• What will happen if I change my mind?
• What treatment can I have if I withdraw from the trial?
• Is there anything I can or can’t do while I am taking part in the trial?
• Can I take my usual medications?
• When will the trial results be published?
• How can I find out the trial results?
Questions to ask yourself

• Do I understand what is involved in taking part in the trial?
• Do I understand the risks?
• Do I understand that I may not benefit from the trial?
• Have I had an opportunity to ask questions?
• Have my questions been answered well enough?
• Do I feel comfortable with the people who will be treating me? Do I feel I will be able to ask them questions?
• If the trial is randomised, am I comfortable about not being able to choose which treatment I have?
• If the trial is blinded, do I understand that I will not know what treatment I am receiving?
• Am I aware of the implications for further treatment if I decide to withdraw?
• How will I manage any extra hospital visits and travel?
Information and support

If you’d like to talk to someone about anything to do with lymphoma, get in touch.

Call our Helpline freephone Monday to Friday on 0808 808 5555. You can also use Live Chat on our website

Come to one of our support groups. Find one near you at lymphoma-action.org.uk/SupportGroups

Join our online forum to chat with others who are affected by lymphoma

Get in touch with a buddy, someone affected by lymphoma

Visit lymphoma-action.org.uk/TrialsLink to find clinical trials that might be suitable for you

Like us on Facebook

Follow us on Twitter

Check out our YouTube channel

Follow us on Instagram
How you can help us

We continually strive to improve our resources for people affected by lymphoma and are interested in any feedback you might have about this booklet. Please visit our website at lymphoma-action.org.uk/Book-Feedback or email us at publications@lymphoma-action.org.uk with any comments. You can also call our Information and Support team on 0808 808 5555.

We produce many other publications that give information about lymphoma. Visit our website at lymphoma-action.org.uk or call 0808 808 5555 for more information.

References

The full list of references is available on request. Please email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

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Check our website for the most up-to-date details of our services, including opening times.
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This booklet explains what clinical trials are, why they are important for people with lymphoma, and what’s involved in taking part.

Lymphoma Action is a charity that has been providing information and support to people affected by lymphoma for over 30 years. We’re here for you.

Helpline freephone 0808 808 5555 (Mon to Fri, 10am to 3pm)
Email information@lymphoma-action.org.uk
Visit www.lymphoma-action.org.uk
Live Chat via our website (Mon to Fri, 10am to 3pm)