



LCH1V - A trial looking at improving treatment for children and young people with Langerhans cell histiocytosis (LCH-IV)

About

This trial is trying to improve treatment for Langerhans cell histiocytosis (LCH). The trial is for children and young people up to and including the age of 17. We use the term 'you' in this summary, but of course if you are a parent, we are referring to your child.

More about this trial

LCH is a very rare condition that affects both children and adults. Langerhans cells are a type of white blood cell called a histiocyte. They help to fight infection. Langerhans cells are normally found in the skin and the main airways. A person with LCH has too many Langerhans cells and they spread to different tissues and organs in the body, causing symptoms.

Although LCH is not cancer, it can behave in a similar way to cancer and a cancer specialist usually treats people with it. How LCH grows and the treatment people need varies. Some children and young people do not need treatment while others might need chemotherapy, with or without steroids.

Usually, children and young people with LCH are put into 2 groups:

- single system LCH (SS LCH), when LCH is affecting 1 body organ, for example the skin, bone or lungs
- multisystem LCH (MS LCH), when 2 or more body organs have LCH cells. This can include 'high-risk' body organs such as the bone marrow, liver or spleen

The research team are looking at changing the treatment for LCH in several ways. Everyone is put into one of 7 groups (5 treatment and 2 observation groups) based on:

- what your LCH was like at diagnosis, which includes if you have single system or multisystem LCH
- how well treatment is working

The trial team want to see if making changes for each of the 5 treatment groups can improve treatment for children and young people with LCH. You might move between groups at certain points during the trial, depending on how well treatment is working.

The overall aims of the trial are to:

- improve treatment

- make it less likely for LCH to return after treatment
- help with the side effects of treatment

Who can take part

The following bullet points list the entry conditions for this trial. Talk to your doctor or the trial team if you are unsure about any of these. They will be able to advise you.

You may be able to this trial if all of the following apply. You:

- have a diagnosis of Langerhans cell histiocytosis
- are 17 years old or younger
- are willing to use reliable contraception during treatment and for 12 months afterwards if there is any chance you or your partner could become pregnant

Who cannot take part

Who cannot join the trial is different for each of the groups. Your doctor will explain more about this. You might be able to join another group if there is one group you cannot take part in.

How has the trial been designed

This is an international phase 3 trial. It will recruit 1,400 children and young people into group 1.

Some parts of the trial, for some groups, are randomised. Those taking part are put into groups by a computer. Neither you nor your doctor will be able to decide which group you are in.

Your doctor will talk to you about the randomisations and when they are due to happen.

Group 1

This group is for children and young people having first line treatment. First line treatment is the first treatment you have for LCH.

Everyone in group 1 is split into two groups:

- multisystem LCH - there is LCH in more than one organ in your body
- single system LCH - to be in this group the LCH is affecting a bone in your face or more than one bone in your body. You might hear other, more general definitions of single system LCH

The first treatment for everyone in group 1 is the chemotherapy drug vinblastine and the steroid drug prednisolone.

Multisystem LCH

The researchers are looking at:

- adding a chemotherapy drug called mercaptopurine after your course of initial treatment for LCH
- comparing treatment for 12 months with treatment for 24 months

Single system LCH

The researchers are looking at comparing 6 months of treatment with 12 months of treatment.

You cannot join group 1 if you:

- have no active signs of LCH but have permanent problems from LCH such as a bone fracture in your spine (vertebra planar) or scarring and stiffness of your lungs (lung fibrosis)
- have had oral treatment or treatment into a vein (intravenously) for LCH before, apart from steroids for up to 7 days
- are pregnant or breastfeeding

You may be able to join another group and take part in the trial, if you cannot take part in group 1.

Group 2

This group is for children and young people who need to have second line treatment for their LCH. This means you have had first line treatment for LCH and either:

- your LCH is not getting better with treatment
- your LCH has come back

Everyone in this group will have 24 weeks of treatment with the drugs:

- vincristine
- prednisolone
- cytarabine

You go on to have more treatment, if your LCH is improving. The researchers want to look at the difference between continuing treatment with the chemotherapy drugs:

- indometacin or
- mercaptopurine and methotrexate

Group 3

This group is for children and young people who need to have more intensive treatment.

This is because the LCH is in 'high - risk' organs and the LCH hasn't got better with their first treatment. So, they are having problems which can be severe. The problems will depend on which organs the LCH is affecting.

The researchers are looking at how well the combination of the chemotherapy drugs cytarabine and cladribine work for this group.

Group 4

This group is for children and young people who need to have further intensive treatment for their LCH. And their doctor thinks a stem cell transplant is the best treatment option for them.

The trial team want to find out:

- how safe a stem cell transplant is for this group
- how well the treatment works
- what the side effects are

Group 5

Group 5 is for children and young people who have LCH that is affecting their central nervous system (CNS). Doctors might call this CNS- LCH. There is also no LCH in any other parts of the body.

The LCH in this case can be:

- a tumour
- neurodegenerative - the LCH starts to affect the brain, this usually makes movement more difficult for children

LCH as a tumour

The trial team are looking at how well the chemotherapy drug cladribine works for this group.

Neurodegenerative CNS LCH

The trial team are looking at how well the chemotherapy drug cytarabine works for this group.

Group 6

This group is for children and young people who have a new diagnosis of single system LCH.

The trial team are interested in looking at how well children and young people do in this group if they have:

- no treatment - also known as the 'watch and wait' approach
- local treatment - such as surgery, steroid cream or a steroid injection into the area where the LCH is

Group 7

Everyone who has had treatment in this trial can join group 7. The researchers want to find out:

- the long-term effects of having LCH and LCH treatments
- if the LCH comes back after treatment.

The trial team want to follow up the children and young people for as long as possible. This is to help LCH treatment in the future.

Samples

The trial team will ask if you would be happy for a tissue sample of LCH to be stored for future research into LCH.

Your doctor takes this sample at the same time as the biopsy which they use to confirm the LCH diagnosis.

You do not have to agree to this if you don't want to. Your care will not be affected in any way.

Biology study

The trial team will ask you if you would be happy to give extra samples of:

- blood
- urine
- bone marrow

And part of the sample from your biopsy, if you had one at diagnosis.

You usually won't have any extra procedures to give these samples. The trial team will let you know if an extra procedure needed.

The researchers hope that information they get from these samples will help children with LCH in the future.

Hospital visits

When you are first diagnosed with LCH and before you start treatment, you have some tests. These are not the same in every hospital and depend on your symptoms.

Some of these tests are similar to ones you have to find out if you have cancer, or to check whether treatment is working.

You might have:

- a physical examination - including measuring your height and weight
- a physical examination that measures how well your brain and nerves are working - this includes your speech and what your balance is like
- blood tests
- urine tests
- a tummy (abdominal) ultrasound
- a chest x- ray
- an MRI scan
- tests which measure the effect of LCH on your brain and attention (neuropsychological testing)
- heart trace (ECG)
- heart scan (echocardiogram)
- Bone marrow test

How often you go to the hospital for treatment and what kind of tests you have during this time depends on your treatment group. Your doctor will let you know what to expect.

Some of the more intensive treatments mean you stay in hospital as an inpatient. You usually stay in hospital for over a month if you are having a stem cell transplant.

You see your doctors and other members of the trial team regularly while taking part.

Whichever group you join, when you finish the trial treatment, you see the trial team again, as part of the long term follow up. This is explained in the trial as it's own group, group 7.

You see the team or have some tests:

- at least every 3 months during the first 12 months
- at least every 6 months after 1 year for 5 years

You might be seen once a year after 5 years. You and your doctor will talk about your follow up together after 5 years.

At some follow up visits, you might have:

- a physical examination - including your height, weight and to see if you have gone through puberty
- blood tests
- urine tests
- hearing tests (audiology)

- an MRI scan, CT scan or ultrasound scan
- lung function tests
- a dental examination
- tests which measure the your brain and attention (neuropsychological testing)

Side effects

The possible side effects depend on the treatment you have.

Group 1

Possible side effects of prednisolone include:

- irritation of the stomach lining
- increased appetite and weight gain
- a skin problem (acne)
- increased risk of infection
- behaviour changes and mood swings
- damage to your bone
- changes in blood sugar levels - this usually goes back to normal after treatment
- increase in blood pressure – this usually goes back to normal after treatment

Possible side effects of vinblastine include:

- a drop in blood cells causing an increased risk of infection, bleeding problems, tiredness and breathlessness
- feeling or being sick
- constipation
- hair loss
- jaw or bone pain

Possible side effects of mercaptopurine include:

- a drop in blood cells causing an increased risk of infection, bleeding problems, tiredness and breathlessness

Rare but serious side effects of mercaptopurine include:

- a second cancer, some time after treatment
- liver damage

Chemotherapy might affect your ability to have children (fertility). Your doctor will talk with you about options to try to help preserve fertility for the future.

Other groups

We have more general information about the short and long term side effects of chemotherapy.

The intensive chemotherapy and supportive medicines you might have with a stem cell transplant can have serious side effects.

These might include:

- a drop in blood cells causing an increased risk of infection, bleeding problems, tiredness and breathlessness. Infections may be life threatening

- a sore mouth
- difficulty eating and drinking
- fever and chills
- diarrhoea
- skin problems

Your doctor will give you more detailed information depending on what treatment you have.

The trial team will monitor you during the time you have treatment and you will have a phone number to call them if you are worried about anything.

Where are the Trial locations

Aberdeen
Belfast
Birmingham
Bristol
Cambridge
Edinburgh
Glasgow
Leeds
Leicester
Liverpool
London
Manchester
Newcastle upon Tyne
Nottingham
Oxford
Sheffield
Southampton

Recruitment start: 09/08/2016

Recruitment end:01/12/2025

How to join a clinical trial

Please note: In order to join a trial you will need to discuss it with your doctor, unless otherwise specified.

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