Acute leukaemias of ambiguous lineage (ALALs)

Acute leukaemias of ambiguous lineage (ALALs) are very rare types of fast-growing leukaemia that do not fit clearly into the two main types (AML or ALL). Find out more about the different types, symptoms they can cause and how they're treated.

Summary

- Acute leukaemias of ambiguous lineage (ALALs) are extremely rare, fast-growing types of blood cancer.
- There are different types of ALAL, which behave differently. They can affect adults or children.
- We do not know the exact cause of ALALs. It is not because of anything you have or have not done.
- ALALs are diagnosed using blood and bone marrow tests.
- Treatment can vary. Your doctor will suggest the most suitable option for you based on your individual circumstances. This might be:
    - Treatment as part of a clinical trial, if there is one suitable for you
    - Chemotherapy, on its own or with a targeted medicine
    - A stem cell transplant, if you are fit enough to have one
    - Medicines to prevent or treat symptoms or side effects
- Outcomes for ALALs vary from person to person. Your consultant is the best person to tell you what they expect for you.
- **We are here for you if you need support.**

Download our factsheet on ALALs

What are ALALs?

Acute leukaemias of ambiguous lineage (ALALs) are very rare, fast-growing types of blood cancer.

There are different types of acute leukaemia. They are named after the type of cell the leukaemia started in. 'Ambiguous lineage' means doctors can't be sure exactly what cell type this was. The leukaemia cells may have markers of more than one type, or no particular type at all.

ALALs have markers of white blood cells. The markers might be from a mixture of immature white blood cells called:

Myeloid cells

B-lymphocytes or B cells

T-lymphocytes or T cells

Or they might not have markers of a specific cell type.

The markers the leukaemia cells have can change over time, especially during or after treatment.

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Types of ALAL

There are different types of ALAL. They can be grouped in two different ways:

- By the markers on the leukaemia cells
- By the gene changes inside the cells

Your haematology team will tell you what type you have and what it means.

Types by cell markers

Cell markers are proteins on the surface of the leukaemia cells. Using cell markers, there are three main types of ALAL.

Mixed phenotype acute leukaemias (MPALs)

This is when leukaemia cells have markers from more than one cell type. It can happen in two ways:

1. Each leukaemia cell has markers of more than one cell type. You might hear some doctors call this 'biphenotypic' leukaemia.
2. Some leukaemia cells have one type of marker and some have a different type. You might hear some doctors call this 'bilineage' or 'trilineage' leukaemia.

There are four main types of MPAL.

- **B/myeloid MPAL** has a mix of B-cell and myeloid cell markers. About 60 in every 100 people with MPAL have this type.
- **T/myeloid MPAL** has a mix of T-cell and myeloid cell markers. Up to 35 in every 100 people with MPAL have this type.
- **B/T MPAL** has a mix of B-cell and T-cell markers. Around 4 in every 100 people with MPAL have this type.
- **B/T/myeloid MPAL** has a mix of B-cell, T-cell and myeloid cell markers. Around 2 in every 100 people with MPAL have this type.

Acute undifferentiated leukaemia (AUL)

This is when the leukaemia cells do not have markers for any particular cell type.

Acute leukaemia of ambiguous lineage, not otherwise specified (ALAL NOS)

This is the name for acute leukaemias that do not fit into any of the other groups.

Types by gene changes

ALALs can also be grouped by the gene changes in the leukaemia cells.

Gene changes have complicated names so they are usually shortened to their initials.

Types of ALAL based on gene changes are:

- **MPAL with *BCR-ABL1* fusion**. About 10 to 15 in every 100 people with an MPAL have this gene change. It typically affects adults. It is usually linked to T/myeloid MPAL. But it can happen in other types.
- **MPAL with *KMT2A* rearrangement**. About 10 in 100 people with MPAL have this gene change. It is more common in children.

- **MPAL with *ZNF384* rearrangement**. About 20 in every 100 people with an MPAL have this gene change. It is more common in children with B/myeloid MPAL. But it can happen in adults too.
- **MPAL with *BCL11B* rearrangement**. About 10 to 15 in every 100 people with an MPAL have this gene change. It is more common in people with T/myeloid MPAL.

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Who gets ALALs?

ALALs are extremely rare. We think fewer than 25 people are diagnosed with ALALs each year in the UK.

ALALs can affect adults or children. They are slightly more common in males than females.

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What causes ALALs?

> **We do not know the exact cause of ALALs. It is not because of anything you have or have not done.**

People with ALALs have genetic changes in their blood-forming cells. These make the cells grow out of control. We do not know why the changes happen.

The genetic changes can affect whole chromosomes or individual genes. Changes can affect more than one gene.

The gene changes can help doctors work out the type of ALAL you have. This can help them decide on the best treatment option for you.

More about genes and chromosomes

- DNA is the genetic code that tells your cells how to grow and behave.
- A gene is a section of DNA that tells your cells how to make a protein.

- Chromosomes are long, coiled strands of DNA that contain lots of different genes.

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Signs and symptoms of ALALs

ALALs can cause many symptoms. You might get some of these symptoms but not others:


Feeling exhausted or worn out, even after resting.


Swollen lymph nodes (glands) that don't go down within a few weeks.


Fever for no obvious reason.


Bruising easily, or for no reason at all.


Infections that last a long time or keep coming back.


Unusual bleeding, like nosebleeds or bleeding gums.


Tummy pain, bloating or feeling full quickly after eating.


Looking pale. If you have black or brown skin, this may be easier to see on your palms, gums or the insides of your eyelids.


Feeling breathless.

Joint or bone pain.

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Diagnosis of ALALs

It can be difficult to diagnose ALALs. Test results can be similar to other types of blood cancer. It may take time to work out exactly what type of leukaemia you have. You might start treatment before you know the exact type you have.

You'll have blood and bone marrow tests. The samples go to the lab for specialist testing.

Blood tests

You will have blood tests to:

- Measure your numbers of red blood cells, white blood cells and platelets
- See how your blood cells look under a microscope
- Check what proteins your blood cells have on their surface
- Look for chromosome and gene changes in your blood cells

Bone marrow tests

You may also have a bone marrow test. This involves taking a sample of your bone marrow, usually from the back of your pelvis, with a local anaesthetic.

Bone marrow is the spongy centre of your larger bones. It's where blood cells are made.

Lumbar puncture

Depending on your symptoms, your team might do a lumbar puncture to check if you have leukaemia cells in your brain or spinal cord. If you need a lumbar puncture, you have an injection to numb a small area of your lower back. Then your doctor puts a needle between the bones in your spine to collect a sample of fluid.

Genetic tests

Your doctor will send your samples to the lab for genetic tests.

Other tests

Depending on your symptoms and test results, you may need other tests or scans. This might include X rays, MRI scans, PET/CT scans or biopsies.

If you need these tests, your doctor or nurse will explain them to you.

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Treatment for ALALs

ALALs are very rare, so it is difficult for researchers to carry out trials to work out the best treatment options. Different types can also respond differently to treatments. Because of this, there are no standard treatment approaches. Your medical team will suggest the most suitable treatment for you based on:

- Your symptoms and blood counts
- The markers or gene changes in your leukaemia cells
- Your age and overall fitness
- Any other medical conditions you have
- Your preference on how you wish to be treated

The main options are:

A clinical trial

A clinical trial could let you access treatments that would not be available otherwise. Your haematology team might suggest a clinical trial, if there is one suitable for you.

If so, they should explain what it would involve, and the risks and benefits of taking part. They will give you the information you need to decide if it's something you'd like to do. It is your choice whether or not to take part.

Chemotherapy

Your team might recommend a combination of chemotherapy medicines. If so, they will tell you exactly what combination they recommend for you. They will explain what the treatment is, how you have it, and what side effects you might get.

Chemotherapy for ALALs is usually based on treatments that have been successful in:

- Acute lymphoblastic leukaemia (ALL). This is the most common approach.
- Acute myeloid leukaemia (AML). Your team might suggest this if your leukaemia cells have myeloid markers or no specific markers.

These treatments are quite intensive, and they are only suitable for people who are fit enough to have them. If you are older, or have other medical conditions, your team might suggest gentler options.

Targeted medicines

Targeted medicines block proteins or genes in leukaemia cells. They aim to kill leukaemia cells with as few effects as possible on healthy cells.

Some targeted treatments used to treat other blood or bone marrow cancers might be helpful for people with ALAL. But there is not much evidence to support their use. Your haematology team might suggest one based on the markers and genes in your leukaemia cells. You usually have it alongside chemotherapy.

Medicines your team might suggest include:

- A type of targeted treatment called a TKI. These target the *BCR*::*ABL1* gene. Examples that might be used as part of your first treatment include imatinib, nilotinib or dasatinib.
- A type of targeted treatment called a JAK inhibitor. These might be helpful in people with a change in the *BCL11B* gene. Examples include ruxolitinib, momelotinib and fedratinib.
- Blinatumomab. This might be helpful in people with a cell marker called CD19.
- Venetoclax. This does not target a specific ALAL marker. But there are some case reports that suggest it might be useful alongside chemotherapy.

Your team might suggest a different targeted treatment. They will explain why they think it might be suitable and give you information about it.

These medicines are not approved to treat ALAL, but your haematology team might use them off-label. This is when a doctor prescribes a medicine that's approved for one condition to treat a different condition.

Some of these treatments might be funded by your hospital, but some might not. Speak to your doctor about what treatments they recommend, and how you can access them.

A stem cell transplant

If your leukaemia responds well to treatment, your team might recommend a stem cell transplant. This is to reduce the risk of leukaemia coming back.

Stem cell transplants are very intensive and they are not suitable for everyone. You must be fit enough for treatment and have a suitable stem cell donor.

Children with ALAL might be cured after chemotherapy alone and may not need a stem cell transplant. But the evidence is not clear.

Gentler treatments

If intensive treatment options are not suitable for you, your team might suggest gentler treatments. This could include a less intensive chemotherapy medicine called azacitidine. It might be used alongside a targeted medicine.

Supportive care

Whatever treatment you have, you might also have medicines to prevent or treat symptoms or side effects. This is called supportive care. It does not treat ALAL itself, but it helps you feel better. It aims to reduce your symptoms and improve your quality of life.

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If treatment is not successful

If ALAL does not respond to treatment, or comes back after treatment, your haematology team will talk to you about your options. These depend on what treatment you've already had and how you responded to it. They might suggest:

- Treatment as part of a clinical trial, if there is one suitable for you.
- Swapping from an ALL treatment to an AML treatment.
- Swapping from an AML treatment to an ALL treatment.
- A targeted medicine.
- Medicines to treat your symptoms and improve your quality of life. Your team might call this palliative care.

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Outcomes of ALALs

Different types of ALAL behave differently and outcomes vary from person to person. They depend on lots of factors, including:

- The exact type of ALAL you have
- The gene changes in your leukaemia cells
- Your age
- Your blood test results
- How well the leukaemia responds to your first treatment

Because ALALs are so rare and do not all behave the same, there is very little reliable data about outcomes. We know:

- ALALs can be difficult to treat, and they can come back after treatment.
- People with the *BCR*::*ABL1* fusion gene usually do better than people with other gene changes.
- Children usually have better outcomes than adults.

Your consultant is the best person to advise you on what they expect for you. They know your individual circumstances and test results.

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Need support?

You are not alone. We're here for you whether you have a diagnosis yourself or know someone who has. If you'd like advice, support, or a listening ear, call our freephone helpline on 08088 010 444 or send a WhatsApp message to 07500 068 065.

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Page last reviewed: 20 April 2026
Updated April 2026
Next review due: 30 April 2029

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