Relapsed or refractory acute lymphoblastic leukaemia (ALL)

Find out about relapsed or refractory ALL: what it is, how it is diagnosed and treatment options available.

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What is relapsed and refractory ALL?

- Relapsed acute lymphoblastic leukaemia (ALL) is when you achieve remission after treatment, but then the disease returns.
- Refractory acute lymphoblastic leukaemia (ALL) Is when the ALL cells do not respond to treatment and you do not achieve remission.

Remission

The definition of relapsed and refractory ALL are closely related to the concept of remission.

Remission is achieved when:

- Blood cell counts return to normal
- Less than 5% of leukaemia cells are present in the bone marrow
- There are no leukaemia cells detectable elsewhere in the body

Frontline treatments for patients with ALL should enable remission to occur. These may include chemotherapy drugs or targeted immunotherapy drugs such as blinatumomab and inotuzumab ozogamicin.

Measurable residual disease

Measurable residual disease (MRD) measures leukaemia in the body at a molecular level rather than at cellular level. It counts the very small amount of leukaemia present in your body that might have been missed when your blood was viewed under a microscope.

- MRD is said to be positive if leukaemia cells are still present in the body
- MRD is said to be negative if no disease are detectable in your body

MRD gives a very accurate assessment of remission and an early detection of relapse. It can be measured during or after treatment. Measurement of MRD after treatment will let your haematology team about your risk of relapse. The risk of relapse and treatment not working is called a prognosis.

Your haematology team will measure your MRD using either a blood or bone marrow sample.

Common tests for measuring MRD that take place in a laboratory include:

- Flow cytometry
- Polymerase chain reaction (PCR) tests

Any test results should be properly explained to you.

Relapsed ALL

Relapsed ALL is when you achieve complete remission but afterwards your ALL returns.

Patients with relapsed ALL achieve remission with treatment, but later their number of normal blood cells decrease and there is a return of the leukemia cells in the bone marrow. This is called a 'relapse' of their ALL.

Between 15 and 20% of children and around 40% of adults treated for ALL will experience a relapse of their ALL.

A relapse happens in patients who have residual leukaemia cells in their bone marrow even after they have received intensive treatment. Studies have shown that persistence of measurable residual disease (MRD) after induction chemotherapy is predictive for ALL relapse further disease recurrence.

Refractory ALL

Refractory ALL occurs when your complete remission is not achieved because the treatment administered did not destroy enough leukaemia cells. Some patients have

residual leukaemia cells in their bone marrow even after they receive intensive treatment. In both these cases, the leukaemia is called 'refractory'.

Approximately 20% of ALL patients will not respond to treatment and are said to display primary resistant disease. For patients fit enough to receive standard induction therapy, about 60-80% of younger adults and 40-50% of older adults achieve a complete remission, leaving a large number of patients who are refractory to initial induction therapy.

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Symptoms of relapsed ALL

Patients with relapsed ALL have the same symptoms as those for newly diagnosed ALL. These include:

- Anaemia
- Bone and joint pain
- Bruising or petechiae (small red spots on the skin)
- Fever
- Recurrent infections
- Abdominal pain
- Swollen lymph nodes
- Dyspnoea or difficulty breathing

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Treatment for relapsed and refractory ALL

If you have relapsed or refractory ALL you will need further treatment. The main treatment for an ALL relapse is chemotherapy. This is called "reinduction chemotherapy" and is often more intensive than first-round chemotherapy.

Your multi-disciplinary team will discuss and select the treatments that are most appropriate for you. They have knowledge of the details of your ALL and your past medical history.

Multi-disciplinary teams (MDTs) bring together the skills of lots of different types of doctors and nurses. Options for your treatment are discussed at your MDT meeting and

the best treatment for you is selected. Doctors within your MDT will provide the expertise in managing relapsed/refractory ALL.

Treatments options for relapsed or refractory ALL include:

- Chemotherapy
- Targeted therapy
- Immunotherapy
- Radiation therapy
- Central nervous system treatment
- Stem cell transplant
- CAR T-cell therapy

If chemotherapy is used, the combinations FLAG (fludarabine, cytarabine, granulocyte colony-stimulating factor) or FLAG-IDA (FLAG and idarubicin) are the preferred choice.

Combination chemotherapy with or without targeted therapy is an option. A targeted treatment called TKI will be included for Philadelphia-positive patients.

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Prognosis of relapsed ALL

The prognosis for patients with relapsed ALL depends on a number of factors, including:

- The site of relapse (i.e., bone marrow, CNS, testicles)
- The length of time between the initial diagnosis and relapse
- Age at initial diagnosis
- Response after the first month of reinduction treatment
- How many relapses have occurred (first, second, and so on)

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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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