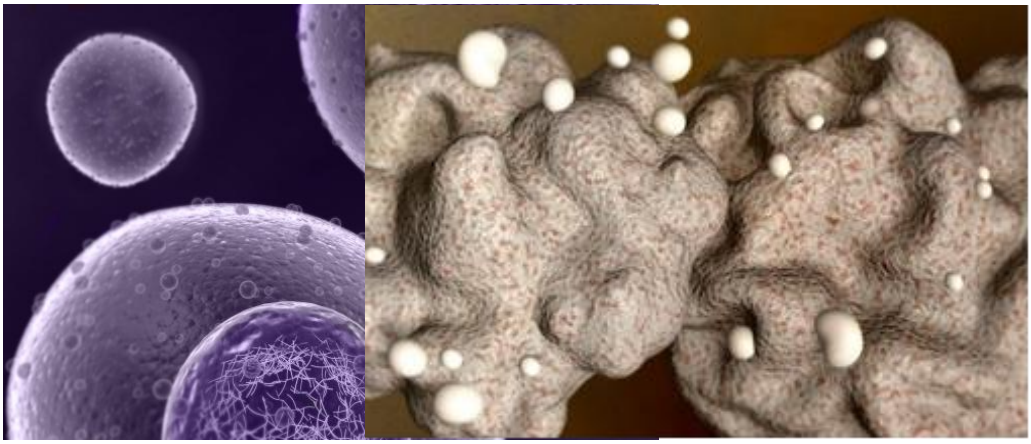

Acute Lymphoblastic Leukaemia (ALL) EU Fact Sheet

Overview

Acute lymphoblastic leukaemia (ALL) is a rare and rapidly progressing cancer of the blood and bone marrow — the spongy tissue inside bones where blood cells are made.[1,2] The disease originates from immature blood cells, rather than mature ones.[2]

ALL occurs when a bone marrow cell develops mutations or errors in its DNA and instructs the cell to continue growing and dividing. Patients with ALL have abnormal white blood cells (lymphoblasts) that crowd out healthy white blood cells, red blood cells and platelets.[2]

In Europe, 7,000 cases of ALL are diagnosed each year.[3] However, there are several subtypes of ALL, and among each subtype the projected incidence is even smaller.[4] For example, it is estimated that the incidence of adults with Philadelphia chromosome-negative (Ph-) relapsed or refractory B-precursor ALL in the European Union is approximately 900 patients per year.[5] Adult patients diagnosed with Ph- ALL are particularly young, with a median age of 34 to 39 years.[6,7]

Fast Facts

- *In Europe, 7,000 cases of ALL are diagnosed each year.[3]*
- *The prognosis for adult patients with ALL who are refractory to treatment or experience relapse is poor – in adult patients with relapsed or refractory ALL, median overall survival is just three to five months.[8]*
- *The type of treatment ALL patients receive and the treatment outcome depends on the ALL subtype and individual risk factors.[9,10]*

Symptoms

In general, signs and symptoms of ALL may include:[2]

- Frequent infections
- Bleeding from the gums
- Fever
- Frequent or severe nosebleeds
- Lumps caused by swollen lymph nodes in and around the neck, underarm, stomach or groin
- Pale skin
- Shortness of breath
- Weakness, fatigue or a general decrease in energy

Risk Factors

Physicians are not certain what causes the DNA mutations that ultimately lead to the production of abnormal lymphoblasts and ALL, but they do know that most cases of the disease are not inherited.[2] Factors that may increase the risk of ALL are:[2]

- Previous cancer treatment
- Exposure to radiation
- Genetic disorders
- Having a brother or sister with ALL

Diagnosis

Tests and procedures used to diagnose ALL include:[2]

- **Blood tests:** Blood tests may reveal abnormal blood counts, such as too many white blood cells, not enough red blood cells and not enough platelets. A blood test may also show the presence of blast cells — immature cells normally found in the bone marrow but not circulating in the blood.
- **Bone marrow test:** During bone marrow aspiration, a needle is used to remove a sample of bone marrow, from the hip bone to look for leukaemia cells. Physicians in the lab will classify blood cells into specific types based on their size, shape and other features. They also look for certain changes in the cancer cells and determine whether the leukaemia cells began from B lymphocytes or T lymphocytes.
- **Imaging tests:** Imaging tests such as a chest X-ray, a computerised tomography (CT) scan or an ultrasound scan may help determine whether cancer has spread to the brain, spinal cord or other parts of the body.
- **Spinal fluid test:** A lumbar puncture test, also called a spinal tap, may be used to collect a sample of spinal fluid. The sample is tested to see whether cancer cells have spread to the spinal fluid.

There are subtypes of ALL, which play a key role in helping the physician plan a patient's treatment and are an important part of diagnosis.[9,10] Physicians mostly use the World Health Organisation system of classification, which is based on the type of lymphocyte that has become cancerous.[10] There are three main ALL subtypes:[10]

- Pre (precursor) B cell ALL - the most common type in adults
- Mature B cell ALL (sometimes called Burkitt type ALL) - this type is identified by particular genetic changes
- Pre (precursor) T cell ALL - more likely to affect young adults and is more common in men

Treatment

Treatment for ALL is typically conducted in phases:[2]

- **Induction therapy:** Induction therapy is also known as the initial cycle of therapy. The purpose of the first phase of treatment is to kill most of the leukaemia cells in the blood and bone marrow and to help restore normal bone marrow cells.
- **Consolidation therapy:** Consolidation therapy is also called post-remission therapy. This phase of treatment is aimed at destroying the undetectable leukaemia cells remaining somewhere in the body.
- **Maintenance therapy:** Maintenance therapy, the third phase of treatment, is intended to help prevent leukaemia cells from recurring. The treatments used in this stage are often given at much lower doses.
- **Preventive treatment to the spinal cord:** Patients with ALL may receive treatment to kill leukaemia cells located in the central nervous system during each phase of therapy. In this type of treatment, chemotherapy drugs are injected directly into the fluid that covers the spinal cord. This treatment is designed to kill cancer cells that can't be reached by chemotherapy drugs given by mouth, by injection just under the skin (subcutaneous) or through an intravenous line.

Adult patients with ALL respond to treatment in different ways within each phase, and approximately 60 percent of patients will relapse following frontline therapy.[11] Also during the frontline phase, approximately 11 percent of patients fail to respond to treatment and have what is called refractory disease.[11,12] The average five-year survival rate for adult patients with ALL after first relapse is seven percent.[13]

As a result of these complexities and depending on the progression of the disease, treatment for ALL can span two to three years and may include the following:[2]

- **Cytotoxic chemotherapy**: Cytotoxic chemotherapy uses drugs to kill cancer cells and is typically given as a form of induction therapy in children and adults, and is also used in the consolidation and maintenance phases.
- **Targeted drug therapy:** Targeted drugs attack specific abnormalities present in cancer cells that help them grow and thrive.
- **Radiation therapy:** Radiation therapy uses high-powered beams, such as X-rays, to kill cancer cells.
- **Stem cell transplant:** A stem cell transplant may be used as consolidation therapy in people at high risk of relapse or for treating relapse when it occurs. The goal of this procedure is for someone with leukaemia to re-establish healthy stem cells by replacing cancerous bone marrow with leukaemia-free marrow.
- **Clinical trials:** Clinical trials are studies that test new cancer treatments or new ways of using existing treatments. While clinical trials give patients a chance to try the latest cancer treatment, treatment risks and benefits are still being evaluated. Patients should discuss the potential risks and benefits of clinical trials with their physician before signing an informed consent in order to be included in a clinical trial.

The goal of treatment is complete remission (CR). Remission occurs when there is no evidence of ALL and the patient's blood and marrow cells return to normal levels.[14] In ALL, CR is often defined as less than five percent blasts in the bone marrow, an absolute neutrophil count of more than 1,000/µL and platelets of more than or equal to 100,000/µL.[15]

Other endpoints of treatment include:[15,16]

- **CRh*:** CR with only partial haematological recovery; no evidence of circulating blasts or extramedullary disease, partial recovery of peripheral blood counts.
- **CRi*:** CR with incomplete blood count recovery; all criteria for CR met except for residual neutropaenia (<1,000/µL) or thrombocytopaenia (<100,000/µL).
- **CRp:** CR with incomplete platelet recovery; all criteria for CR met except for residual thrombocytopaenia (<100,000/µL)
- **Partial remission (PR):** A decrease of at least 50 percent in percentage of blasts to five percent to 25 percent in the bone marrow aspirate.
- **Molecular complete response (molecular CR)*:** Also known as complete MRD response or MRD negativity, a molecular CR is defined as the presence of less than one leukaemic blast cell in 10,000 normal cells (10^{-4} or 0.01 percent).

**Definition may vary*

MRD Testing

After reaching CR, a small amount of leukaemia cells may still be within the body even if they aren't seen with a microscope. This is called minimal residual disease (MRD), it is a state of disease in which the microscopic analysis does not show leukaemia, but more sensitive techniques still detect remaining malignant cells.[17]

MRD tests may be used to ascertain the prognosis of individual ALL patients and also may guide treatment decisions. Assessment of MRD has acquired a prominent position in European treatment protocols for patients with ALL, on the basis of its high prognostic value for predicting outcome and the possibilities for implementation of MRD diagnostics in treatment stratification.[18]

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