

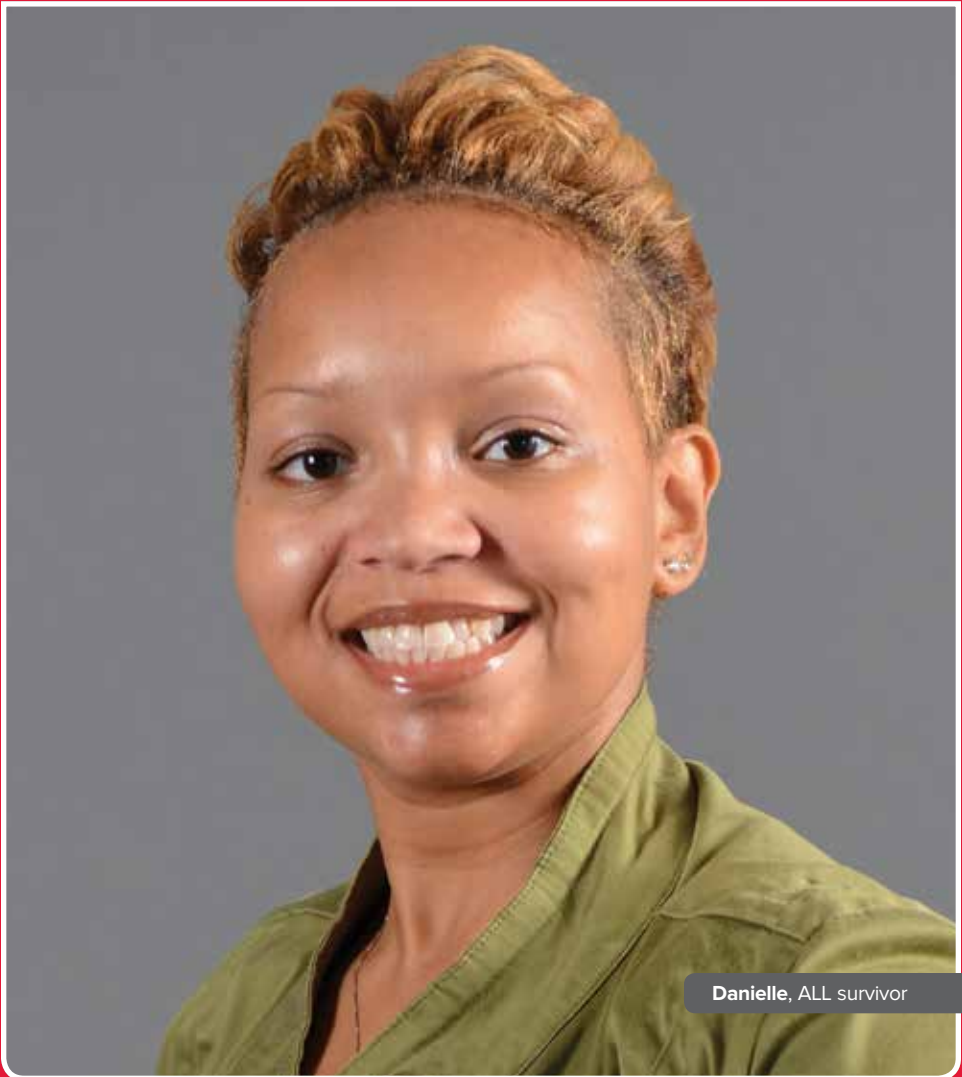


LEUKEMIA &  
LYMPHOMA  
SOCIETY®

fighting blood cancers

**someday  
is today®**

# Acute Lymphoblastic Leukemia



Danielle, ALL survivor

Support for this publication  
provided by

**AMGEN**



**Oncology**

Revised 2016

The Leukemia & Lymphoma Society wants you to have the most up-to-date information about blood cancer treatment. See below for important new information that was not available at the time this publication was printed.

- In April 2017, the Food and Drug Administration (FDA) approved methotrexate (Xatmep™) for the treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as a component of a combination chemotherapy maintenance regimen.

For more information, contact an Information Specialist at (800) 955-4572 or [infocenter@lls.org](mailto:infocenter@lls.org).

## A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Our research grants have funded many of today's most promising advances; we are the leading source of free blood cancer information, education and support; and we advocate for blood cancer patients and their families, helping to ensure they have access to quality, affordable and coordinated care.

Since 1954, we have been a driving force behind nearly every treatment breakthrough for blood cancer patients. We have invested more than \$1 billion in research to advance therapies and save lives. Thanks to research and access to better treatments, survival rates for many blood cancer patients have doubled, tripled and even quadrupled.

Yet we are far from done.

Until there is a cure for cancer, we will continue to work hard—to fund new research, to create new patient programs and services, and to share information and resources about blood cancer.

This booklet has information that can help you understand acute lymphoblastic leukemia (ALL), prepare questions, find answers and resources, and communicate better with members of your healthcare team.

Our vision is that, one day, all people with blood cancers will either be cured or will be able to manage their disease so that they can experience a better quality of life. Today, we hope our expertise, knowledge and resources will make a difference in your journey.



**Louis J. DeGennaro, PhD**

*President and Chief Executive Officer  
The Leukemia & Lymphoma Society*

# Inside This Booklet

- 2** Introduction
- 2** Resources and Information
- 5** Leukemia
- 6** Acute Lymphoblastic Leukemia
- 6** Incidence, Causes and Risk Factors
- 8** Signs and Symptoms
- 9** Diagnosis and Cell Classification
- 14** Treatment
- 29** Follow-Up Care
- 32** Research and Clinical Trials
- 34** Normal Blood and Marrow
- 37** Medical Terms
- 48** More information
- 49** References

## Acknowledgement

The Leukemia & Lymphoma Society gratefully acknowledges, for her critical review and important contributions to the material presented in this booklet,

Elizabeth Raetz, MD  
*Professor of Pediatrics*  
*Pediatric Hematology/Oncology*  
*University of Utah*  
*Huntsman Cancer Institute*  
*Primary Children's Hospital*  
*Salt Lake City, UT*

This publication is designed to provide accurate and authoritative information about the subject matter covered. It is distributed as a public service by LLS, with the understanding that LLS is not engaged in rendering medical or other professional services.

# Introduction

This booklet provides information about acute lymphoblastic leukemia (ALL) for patients and their families. Brief descriptions of normal blood and marrow and the lymphatic system as well as definitions of medical terms are included.

ALL may be called by other names, including “acute lymphocytic leukemia” and “acute lymphoid leukemia.”

About 6,590 new cases of ALL are expected to be diagnosed in the United States in 2016. As of 2012, an estimated 71,898 people are living with or are in remission from ALL. Although ALL can occur at any age, it is the most common cancer found in children and young adults less than 20 years old.<sup>1</sup>

Advances in the treatment of ALL have resulted in improved remission rates. The number of patients who have gone into remission or have been cured is increasing. New therapies are under study in clinical trials.

<sup>1</sup> Source: The Leukemia & Lymphoma Society. facts 2015-2016. Available at [www.LLS.org/booklets](http://www.LLS.org/booklets). Accessed July 29, 2016.

# Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team members’ knowledge and skills.

## For Help and Information

**Consult with an Information Specialist.** Information Specialists are master’s level oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. EST)
- Email: [infocenter@LLS.org](mailto:infocenter@LLS.org)
- Live chat: [www.LLS.org](http://www.LLS.org)
- Visit: [www.LLS.org/information specialists](http://www.LLS.org/information specialists).

**Free Information Booklets.** LLS offers free education and support booklets that can be downloaded and read online or ordered in hard copy. For more information, please visit [www.LLS.org/booklets](http://www.LLS.org/booklets).

**Telephone/Web Education Programs.** LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit [www.LLS.org/programs](http://www.LLS.org/programs).

**Co-Pay Assistance Program.** LLS offers insurance premium and medication co-pay assistance for eligible patients. For more information, please

- Call: (877) 557-2672
- Visit: [www.LLS.org/copay](http://www.LLS.org/copay)

## Community Resources and Networking

**LLS Community.** LLS Community is an online social network and registry for patients, caregivers, and supporters of those with blood cancer. It is a place to ask questions, get informed, share your experience, and connect with others. To join, visit [www.LLS.org/community](http://www.LLS.org/community).

**Online Blood Cancer Discussion Boards and Chats.** Online discussion boards and moderated online chats can provide support and help cancer patients to reach out and share information. For more information, please visit [www.LLS.org/discussionboard](http://www.LLS.org/discussionboard) and [www.LLS.org/chat](http://www.LLS.org/chat).

**LLS Chapters.** LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: [www.LLS.org/chapterfind](http://www.LLS.org/chapterfind)

**Other Helpful Organizations.** LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, locating summer camps and other needs. For more information, please visit [www.LLS.org/resourcedirectory](http://www.LLS.org/resourcedirectory).

**Clinical Trials (Research Studies).** New treatments for patients are under way. Patients can learn about clinical trials and how to access them. For more information, please call (800) 955-4572 to speak with an LLS Information Specialist who can help conduct clinical-trial searches.

**Advocacy.** The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: [www.LLS.org/advocacy](http://www.LLS.org/advocacy)

**Sign Up for an e-Newsletter.** Read the latest disease-specific news, learn about research studies and clinical trials, and find support for living with blood cancer. Please visit [www.LLS.org/signup](http://www.LLS.org/signup).

### **Additional Help for Specific Populations**

**Información en Español (LLS information in Spanish).** For more information, please visit [www.LLS.org/espanol](http://www.LLS.org/espanol).

**Language Services.** Let your doctor know if you need a language interpreter or other resource, such as a sign language interpreter. Often, these services are free.

**World Trade Center (WTC) Survivors.** People who were involved in the aftermath of the 9/11 attacks and then subsequently diagnosed with a blood cancer may be eligible for help from the World Trade Center (WTC) Health Program. People eligible for help include

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area, lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: [www.cdc.gov/wtc/faq.html](http://www.cdc.gov/wtc/faq.html)

**People Suffering from Depression.** Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a two-week period. For more information, please

- Call: National Institute of Mental Health (NIMH) Resource Center at (866) 615-6464
- Visit: NIMH at [www.nimh.nih.gov](http://www.nimh.nih.gov). Enter “depression” in the search box

**Children’s Concerns.** A family that has a child diagnosed with ALL is thrown into an unfamiliar world of treatment and follow-up care. The child, parents and siblings will all need support. Help is available. Do not hesitate to ask for assistance for your child, yourself or other family members, even if you are already working with a psychologist, social worker or child-life specialist. For practical guidance on how to support your child and other family members, deal with your own concerns, share the news with extended family and friends and make the transition to life after treatment ends, see the free LLS booklet *Coping With Childhood Leukemia and Lymphoma*.

**The Trish Greene Back to School Program for Children With Cancer.** This program is designed to increase communication among healthcare professionals, school personnel, parents and patients to assure children with cancer a smooth transition back to school. For more information about these and other programs

- Call: (800) 955-4572
- Visit: [www.LLS.org/chapterfind](http://www.LLS.org/chapterfind)

**Feedback.** To give suggestions about this booklet, visit [www.LLS.org/publicationfeedback](http://www.LLS.org/publicationfeedback).

## Leukemia

Leukemia is a cancer of the marrow and blood. The four major types of leukemia are acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL).

Acute leukemias are rapidly progressing diseases. They affect cells that are not fully developed. These cells cannot carry out their normal functions. Chronic leukemias usually progress more slowly and patients with chronic disease have greater numbers of mature cells. Generally, the more mature cells can carry out some of their normal functions (see *Normal Blood and Marrow* on page 34).

With lymphoblastic leukemia, the cancerous change begins in a marrow cell that would normally develop into a lymphocyte (a type of white blood cell). With myeloid leukemia, the cancerous change begins in a marrow cell that normally forms red blood cells, some types of white blood cells and platelets.

The four main types of leukemia are further classified into subtypes. Knowing the subtype of your disease is important because your treatment approach may be based on that subtype (see *Subtypes of ALL* on page 11).

More general information about ALL is provided in the free LLS booklets, *Understanding Leukemia* and *The ALL Guide—Information for Patients and Caregivers*.



# Acute Lymphoblastic Leukemia

**How ALL Develops.** ALL results from either an acquired or a genetic injury to the DNA (genetic material) of a developing cell in the marrow. Once the marrow cell becomes a leukemic cell, that cell multiplies uncontrollably into billions of cells. These cells are known as “lymphoblasts” or “leukemic blasts.” They fail to function as normal blood cells but are able to grow and survive better than normal cells.

The presence of the leukemic blasts blocks the production of normal cells. As a result, when ALL is diagnosed, the number of healthy blood cells (red blood cells, white blood cells and platelets) is usually lower than normal.

## The medical term for a

Low red blood cell count

Low platelet count

Low neutrophil count

## Is

Anemia

Thrombocytopenia (“thrombocyte” is another word for platelet)

Neutropenia (a neutrophil is a type of white blood cell)

## Incidence, Causes and Risk Factors

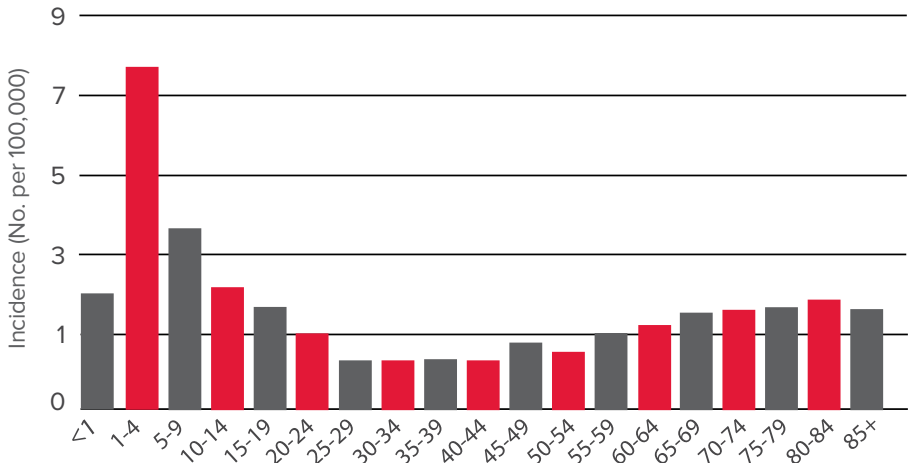
**Incidence.** ALL is the most common childhood acute leukemia. It represents about 75 to 80 percent of acute leukemias among children. The median age at diagnosis is 15 years and about 52 percent of the patients diagnosed are younger than 20 years.

About 36 percent of cases are diagnosed in people ages 45 years and older and only 11 percent of the patients diagnosed are ages 20 to 44. See Figure 1 on page 7 for age-specific incidence rates.

ALL is most common in whites and Hispanics.

Approximately 6,590 new cases of ALL are expected to be diagnosed in the United States in 2016.

## Acute Lymphoblastic Leukemia: Age-Specific Incidence Rates (2009-2013)



**Figure 1.** | The horizontal axis shows five-year age intervals. The vertical axis shows the frequency of new cases of ALL per 100,000 people, by age-group. Note that the risk of ALL is greatest in the first five years of life. An increase in occurrence is also seen in older individuals.

Data derived from Surveillance, Epidemiology and End Results (SEER) Program. National Cancer Institute, 2016.)

**Causes and Risk Factors.** The exact cause of ALL is not known but there are a few factors that have been associated with an increased risk of developing ALL.

- Exposure to radiation
- Exposure to chemotherapy
- Some genetic disorders

Exposure to high doses of radiation (carefully studied in atomic bomb survivors in Japan) is one factor associated with developing ALL. A child who has had multiple diagnostic x-rays may be at a slightly increased risk for ALL but more studies need to be done to confirm these research findings. Previous chemotherapy and radiotherapy may be a cause of ALL in adults.

ALL occurs at different rates in various settings. Higher leukemia rates are reported in more developed countries and in higher socioeconomic groups. These and other findings have led to the hypothesis that reducing children's exposure to bacterial infections during the first year of life may have increased the risk of childhood ALL. Other life-saving benefits from avoidance of bacterial infections during infancy have been found.

Infants born with Down syndrome (also called trisomy 21) are at increased risk (about 40-fold between birth and 4 years) of developing acute leukemia. Although rare, other genetic conditions have been categorized as risk factors for ALL. These include neurofibromatosis, Klinefelter syndrome, Fanconi anemia, Schwachman syndrome, Bloom syndrome and ataxia telangiectasia.

Scientists continue to explore possible relationships to lifestyle or environmental factors. Research supports the view that a number of complex factors may be involved.

Some cases of ALL relate to a mutation in a lymphocyte that occurs during the prenatal period (in utero). Usually the leukemia is diagnosed in infancy or in the first few years after birth. However, in some cases, years may pass before the disease appears. With ALL, it seems that additional genetic abnormalities can occur after birth and allow the unregulated cell growth that triggers the disease, because there are more mutations found in utero than there are cases of childhood ALL.

## Signs and Symptoms

A person who has signs or symptoms that suggest the possibility of leukemia is usually referred to a doctor who is a specialist in disorders of the blood and cancer. This type of doctor is called a hematologist/oncologist. The signs and symptoms of ALL are also associated with a number of other less serious diseases. The specialist will order additional tests in order to make an accurate diagnosis.

It is common for someone with ALL to feel a loss of well-being because of the underproduction of normal bone marrow cells. This person may tire easily and have shortness of breath during normal physical activities.

To determine the reason for these signs and symptoms, your doctor will want to examine your blood by doing a blood test called a “complete blood count”(CBC). Low numbers of red blood cells, white blood cells and platelets are common in patients with newly diagnosed ALL.

Other signs and symptoms of ALL include

- A pale complexion from anemia
- Signs of bleeding caused by a very low platelet count, including
  - Black-and-blue marks or bruises occurring for no reason or because of a minor injury
  - The appearance of pinhead-sized red spots on the skin, called “petechiae” (peh tee’ key uh)
  - Prolonged bleeding from minor cuts
- Fever
- Fatigue
- Frequent minor infections
- Discomfort in bones or joints

- Enlarged spleen, liver or lymph nodes
- Pain or feeling of fullness below the ribs
- Shortness of breath
- Weight loss or loss of appetite

Leukemic cells can also collect in the testes in a small number of male patients.

**Bleeding.** A low platelet count predisposes patients to bleeding. Frequent or severe nosebleeds, bleeding gums, blood in the urine, and bruising easily are common symptoms of ALL. Bleeding in the brain or lungs is serious and can be fatal. (see *Low Blood Cell Counts* on page 26).

**Infection.** Severe infection usually does not occur at the time of diagnosis. If the neutrophil count becomes or remains low because of ALL or its treatment, serious infections may occur and can be life-threatening. However, if proper precautions are taken during therapy, most patients do not develop life-threatening infections (see *Infection* on page 26).

## Diagnosis and Cell Classification

An accurate diagnosis of the type of leukemia is important. The exact diagnosis helps the doctor to

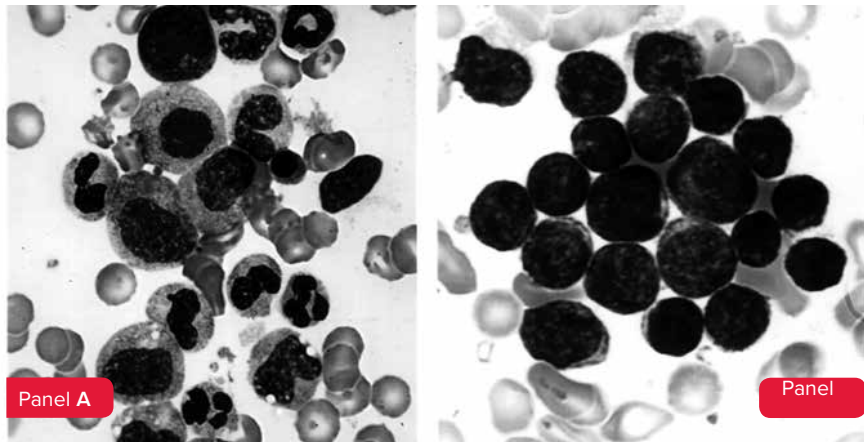
- Estimate how the disease will progress
- Determine the appropriate treatment

### Talk to your doctor about

- The diagnostic tests that are being done
- What the results mean
- Getting copies of the test results

**Blood and Bone Marrow Tests.** Blood and bone marrow cells are examined to diagnose ALL and identify the ALL subtype (see *Subtypes of ALL* on page 11). A change in the appearance and number of cells helps make a diagnosis. An examination of the stained (dyed) blood cells with a microscope will often show the presence of leukemic blast cells (immature cells that do not function like normal, mature white blood cells). A bone marrow examination is preferred to diagnose ALL because some patients do not have leukemic blast cells in their bloodstream at the time of diagnosis (see Figure 2 on page 10).

## ALL Blast Cells



**Figure 2.** | Panel A shows a photograph of developing cells in healthy marrow. The variation in the appearance of the cells is characteristic of normal marrow. Panel B shows a photograph of marrow cells from a patient with acute lymphoblastic leukemia. An unvaried appearance characterizes the leukemic blast cells.

**Blood and Marrow Samples.** In order to complete blood tests, blood samples are generally taken from a vein in the patient’s arm. Samples of marrow cells are obtained by bone marrow aspiration and bone marrow biopsy. The cells from the blood and marrow samples are examined under a microscope. Your doctor will work with a hematopathologist, a specialist who studies blood diseases by looking at the samples of blood and marrow cells and other tissues.

**Bone Marrow Aspiration and Biopsy.** These tests are used to examine marrow cells to find abnormalities, and both tests are generally done at the same time. For both procedures, the patient is given medication to numb the area, or given a general anesthesia, and the sample is taken from the hip bone. For a bone marrow aspiration, a special needle is inserted through the hip bone and into the marrow to remove a liquid sample of cells. For a bone marrow biopsy, a special needle is used to remove a core sample of bone that contains marrow. Both types of samples are examined under a microscope to look for chromosomal and other cell changes.

**Other Tests.** “Karyotyping” (to detect chromosome abnormalities) and “cytogenetic analysis” (study of cells, especially chromosomes) are processes used to identify certain changes in chromosomes and genes. Laboratory tests called “fluorescence in situ hybridization” (FISH) and “polymerase chain reaction” (PCR) assays may be done, in which cells in a sample of marrow are studied to look for certain changes in the structure or function of genes. In some cases, other special tests may also be used.

**Immunophenotyping.** This process, used to identify cells based on the types of proteins (antigens) on the cell surface, is necessary to establish the diagnosis of

B-cell ALL, T-cell ALL or acute myeloid leukemia (AML). “Flow cytometry” is the name of one test that may be used to do immunophenotyping.

The diagnosis of ALL is confirmed by identifying

- Leukemic blast cells in the bone marrow samples
- The percentage of blast cells in the bone marrow. Blast cells normally comprise 1 percent to 5 percent of marrow cells.
- The presence of at least 20 percent blast cells in the bone marrow from the biopsy material.

All male patients should be evaluated to see if there is any disease in the testes; while testicular involvement is generally rare in ALL, it is more common in the subtype T-cell ALL.

An echocardiogram (a cardiac ultrasound) should be considered for all patients due to the potential use of anthracyclines. Anthracyclines are drugs that are commonly used in ALL therapy and they are known for their potentially toxic effects to the heart and other organs. Assessment of cardiac function is particularly important for patients who have a history of heart problems, prior exposure to anthracyclines or symptoms that indicate heart dysfunction.

For patients with neurologic signs or symptoms at diagnosis, imaging studies, for example a computerized (or computed) tomography (CT) scan or a magnetic resonance imaging (MRI) scan of the head, should be considered.

See the free LLS booklet *Understanding Lab and Imaging Tests* for more comprehensive information about these tests.

**Subtypes of ALL.** ALL has many subtypes. They can be identified and classified by immunologic, cytogenetic and molecular genetic tests. Some of these tests may be repeated during and after therapy to measure the effects of treatment. Depending on the subtype, the doctor will determine which drugs or drug combinations, drug dosages, and duration of treatment are most appropriate for the patient, and whether other types of treatment, such as a stem cell transplant, may be needed to achieve the best results.

ALL is divided into three major subtypes based on the physical characteristics and the level of development of the leukemia cells. This basic classification helps the treatment team to start planning the best course of treatment for the patient. The principal ALL subtypes are

- Precursor B-cell ALL
- Mature B-cell ALL
- T-cell ALL.

The phenotype or physical characteristics of the leukemia cell determine whether the cells are of B-cell or T-cell origin. The B-cell subtype is identified by finding cell surface markers on the leukemic blast cells that are the same as those that develop on normal B lymphocytes. The T-cell subtype is identified by finding cell surface markers on the leukemic blast cells that are the same as the ones that develop in normal T lymphocytes.

Not all B-cell disease is treated in the same way. Mature B-cell leukemia is also known as “Burkitt leukemia/lymphoma.” It accounts for 2 percent to 3 percent of patients who have acute lymphoblastic leukemia. The treatment for Burkitt leukemia is based on therapy for non-Hodgkin lymphoma and is completely different from the treatment used for ALL. For more information, see the free LLS booklet *Non-Hodgkin Lymphoma*.

The genetic classification of ALL cells is also important (See Table 1 on page 13). About 75 percent of adult and childhood cases can be classified into subgroups based on the chromosome number or DNA analysis, specific chromosomal rearrangements and molecular genetic changes.

Examination of leukemic cells by cytogenetic techniques allows for identification of chromosome or gene abnormalities. Translocations are the most common type of DNA change associated with ALL. In a translocation, the DNA from one chromosome breaks off and becomes attached to a different chromosome. Other chromosome changes such as deletions (part of the chromosome is lost) and inversions (rearrangement of the DNA within part of a chromosome) can also lead to the development of ALL, but these changes are less common. In many cases of ALL, the genetic changes are not known. Not all patients who have ALL exhibit the same chromosome changes. Some changes are more common than others and some have a greater impact on the patient’s projected outcome, called “prognosis.”

Other features that are important in guiding the treatment approach include

- The patient’s age
- The white blood cell count (WBC)
- Involvement of the central nervous system

**Table 1. Common Chromosomal and Molecular Abnormalities in ALL**

Abnormality	Gene(s) Associated	Frequency in Adults (%)	Frequency in Children (%)	Associated Prognosis
<b>Hyperdiploidy</b> More than 50 chromosomes	—	7	25	Favorable prognosis
<b>Hypodiploidy</b> Fewer than 44 chromosomes	—	2	1	Poor prognosis
Translocation between chromosomes 12 and 21	<i>ETV6-RUNX1 (TEL-AML1)</i>	2	22	Favorable prognosis
“Philadelphia” or “Ph” chromosome Translocation between chromosomes 22 and 9	<i>BCR-ABL1</i>	25	2-4	Favorable prognosis with contemporary therapy
“Ph-like” or “ <i>BCR-ABL1</i> -like” ALL ( <i>BCR-ABL1</i> -negative)	<i>IKZF1</i> and others	10-30	15	Poor prognosis
Translocation between chromosomes 1 and 19 (associated with central nervous system [CNS] leukemia)	<i>TCF3-PBX1 (E2A-PBX1)</i>	3	6	Favorable prognosis with contemporary therapy
Translocation between chromosomes 4 and 11, translocation between chromosomes 9 and 11, translocation between chromosomes 11 and 19 (associated with infant and older adult groups, CNS leukemia)	<i>MLL</i>	10	8	Poor prognosis
Translocation between chromosomes 8 and 14	<i>c-MYC</i>	4	2	Favorable prognosis with short-term intensive therapy
ETP (early T-cell precursor)	various	2	2	Poor prognosis
Ikaros	<i>IKZF1</i>	50	12-17	Poor prognosis
<p>Other Abnormalities and Their Associated Prognoses</p> <ul style="list-style-type: none"> <li>• <i>CRLF2</i> and Janus Kinase (<i>JAK</i>) mutations—Poor prognosis</li> <li>• <i>NOTCH1</i> mutations—Favorable prognosis</li> <li>• <i>HOX11</i> overexpression—Favorable prognosis with chemotherapy alone</li> <li>• Chromosome 21 amplification—Requires intensive therapy to avert poor prognosis</li> </ul>				

Adapted from NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia, 2016.



# Treatment

A diagnosis of ALL is associated with a wide range of outcomes. It is essential to seek treatment in a center where doctors are experienced in the care of patients with acute leukemia. Patients who have ALL need treatment as soon as possible after diagnosis. The approach for treating each patient is based on an individual's subtype, risk factors and treatment goals. Generally treatment can last between one and a half to three years.

**Treatment Planning.** A number of factors affect the choice and outcome of treatment, including

- The ALL subtype
- The type of leukemic lymphocytes as determined by their immunophenotype and chromosome composition
- Whether the patient has received chemotherapy in the past to treat another type of cancer
- Whether ALL is present in either the central nervous system or other sites outside of the bone marrow
- Whether the ALL has not responded to treatment or the patient has relapsed
- The presence of systemic infection at diagnosis
- The patient's age and general health.

## Talk to your doctor about

- Your treatment options and the results you can expect from treatment
- The results you might expect with standard therapy
- Participating in a clinical trial

**Pretreatment Considerations.** Adults of childbearing age and parents of children diagnosed with ALL should ask the doctor for information about addressing the risk for infertility.

See the free LLS fact sheet *Fertility Facts* for more details.

**Chemotherapy.** There are three parts to the treatment for ALL. These are induction, consolidation (also called “intensification”) and maintenance. Consolidation and maintenance are therapies given after remission, also called “postremission” therapies.

**Induction Therapy.** The initial phase of chemotherapy is called “induction.” The specific drugs, the dosages used, and timing of administration, depend on several

factors, including the patient's age, the specific features of the leukemia and the overall health of the patient.

The goal of induction therapy is to achieve remission, which means all signs and symptoms of leukemia have disappeared from the blood and marrow, although there may still be some in the body. A remission is not a cure but it is a very important part of the process because it allows normal marrow cells to develop and the patient's blood counts to return to normal levels. Generally, if blast cells are still evident after the first course of induction chemotherapy, a second course of chemotherapy, usually using different drugs, is given.

Induction regimens for ALL generally use a combination of drugs that include

- Vincristine
- Anthracyclines (daunorubicin, doxorubicin)
- Corticosteroids (prednisone, dexamethasone) either with or without
- PEG-L-asparaginase and/or cyclophosphamide

This well-established regimen is known as hyper-CVAD. It is given as hyperfractionated therapy. This means that the total dose of the drugs is divided into small doses that are given more than once a day.

Other drugs such as methotrexate, cytarabine, and/or 6-mercaptopurine (6-MP) may be also included at the same time as induction therapy, especially if there is involvement of the central nervous system.

Imatinib mesylate (Gleevec®) is often included in the treatment plan for patients with Philadelphia chromosome positive (Ph+) ALL. For more information on this type of ALL and its treatment, please see page 20.

Typically, the severity of the disease and the side effects of this initial therapy result in an initial hospital stay of four to six weeks. Some patients who live with a caregiver and near the medical facility may be safely discharged sooner. This depends on the policies of the treatment center and the status of the patient.

To give medications and perform other functions, a central line (indwelling catheter) is placed surgically in a vein in the patient's upper chest. The catheter is tunneled under the skin of the chest so that it stays firmly in place. The external end of the catheter (port) can be used to administer medications, fluids or blood products or to withdraw blood samples for cell counts and chemical tests. An alternative is a peripherally inserted central venous catheter (PICC or PIC line), which can be placed in a vein of the upper arm.

A child with ALL is usually admitted to the hospital to start the induction treatment as soon as the diagnosis is known. Most children go into remission after the first month of therapy.

For some children, the hospital stay is the first time they have been away from home for an extended period of time. Providing age-appropriate information to your child about the illness and treatment will help him or her build trust in you and the members of the treatment team. It will also help them feel more comfortable talking about their fears and concerns.

For practical guidance about how to support your child and other family members, deal with your own concerns, share the news with extended family and friends and make the transition to life after treatment, see the free LLS booklet *Coping With Childhood Leukemia and Lymphoma*.

**Table 2. Some Drugs Used for Treatment and/or in Clinical Trials for ALL**

Most antileukemic drugs interact with the cell's genetic material, the DNA.

### **Antitumor Antibiotics**

- daunorubicin (Cerubidine<sup>®</sup>)
- doxorubicin (Adriamycin<sup>®</sup>)
- mitoxantrone (Novantrone<sup>®</sup>)
- idarubicin (Idamycin<sup>®</sup>)

### **DNA-Repair Enzyme Inhibitors**

- etoposide (VP-16; VePesid<sup>®</sup>, Etopophos<sup>®</sup>)
- teniposide (VM-26; Vumon<sup>®</sup>)
- topotecan (Hycamtin<sup>®</sup>)

### **DNA Synthesis Inhibitor**

- carboplatin (Paraplatin<sup>®</sup>)

### **DNA-Damaging Agents**

- cyclophosphamide (Cytosan<sup>®</sup>)
- ifosfamide (Ifex<sup>®</sup>)

### **Enzymes That Prevent Cells From Surviving**

- Asparaginase *Erwinia chrysanthemi* (Erwinaze<sup>®</sup>)
- pegaspargase (PEG-L-asparaginase; Oncaspar<sup>®</sup>)

### **Tyrosine Kinase Inhibitors**

- imatinib mesylate (Gleevec<sup>®</sup>)
- dasatinib (Sprycel<sup>®</sup>)
- nilotinib (Tasigna<sup>®</sup>)

### **Antimetabolites**

- azacitidine (Vidaza<sup>®</sup>)
- cladribine (2-CdA; Leustatin<sup>®</sup>)
- clofarabine (Clolar<sup>®</sup>)
- cytarabine (cytosine arabinoside, ara-C; Cytosar-U<sup>®</sup>; DepoCyt<sup>®</sup>)
- fludarabine (Fludara<sup>®</sup>)
- hydroxyurea (Hydrea<sup>®</sup>)
- 6-mercaptopurine (Purinethol<sup>®</sup>)
- mercaptopurine (Purixan<sup>®</sup>)
- methotrexate
- nelarabine (Arranon<sup>®</sup>)
- 6-thioguanine (thioguanine; Tabloid<sup>®</sup>)

### **Drug That Prevents Cells From Dividing**

- vincristine (Oncovin<sup>®</sup>)
- liposomal vincristine (Marqibo<sup>®</sup>)

### **Synthetic Hormones**

- prednisone
- prednisolone
- dexamethasone

### **Immunotherapies**

- alemtuzumab (Campath<sup>®</sup>)
- rituximab (Rituxan<sup>®</sup>)
- ofatumumab (Arzerra<sup>®</sup>)
- blinatumomab (Blinicyto<sup>®</sup>)
- inotuzumab ozogamicin
- chimeric antigen receptor (CAR) T cells

## Postremission Therapy (Consolidation and Maintenance Therapy).

Because residual leukemia cells that are undetectable by blood or marrow examination remain after remission, the optimal treatment for patients who have ALL requires additional intensive postremission therapy. As in the induction phase, individual factors such as the age of the patient, the ability to tolerate intensive treatment, cytogenetic findings, the availability of a stem cell donor and other considerations may influence the treatment approach.

- **Consolidation.** Consolidation, also known as “intensification,” therapy is usually given in cycles for four to six months. The goal of this phase of treatment is to reduce the number of leukemic cells still remaining after induction therapy. Generally, several chemotherapy drugs are combined to help prevent the leukemia cells from developing drug resistance. When necessary, drugs may be administered directly into the spinal canal using what is called intrathecal therapy, and treatment is continued.

Some of the drugs used in the consolidation stage of treatment include

- High-dose methotrexate
- Cytarabine
- Vincristine
- 6-mercaptopurine
- PEG-L-asparaginase (a long course)
- Corticosteroids (prednisone, dexamethasone)

Treatment protocols may include one or two intensified treatments similar to the ones used during induction. These intensified treatments are also known as “re-induction” or “delayed intensification” treatments.

- **Maintenance.** Maintenance therapy usually lasts for about two years for adults and two to three years for children. The goal of maintenance is to prevent disease relapse after induction and consolidation therapy. In some cases, postremission chemotherapy also includes drugs that were not used during induction treatment. Most maintenance regimens include
  - 6-mercaptopurine (administered daily)
  - Methotrexate (administered weekly)

Some types of high-risk ALL—such as T-cell ALL or ALL infants or in adults—are usually treated with higher doses of drugs during induction, consolidation and maintenance therapy.

**Central Nervous System (CNS) Prophylaxis.** Although the presence of CNS involvement at diagnosis is not common (only 3 to 7 percent of cases), a large

percent of patients (50 percent or more) may eventually develop central nervous system leukemia without the routine administration of CNS-targeted therapy, also called “central nervous system prophylaxis.”

ALL cells often collect in the covering of the spinal cord and brain, called the “meninges.” If not treated, meningeal leukemia can occur. Areas of the body that are less accessible to oral or intravenous chemotherapy are sometimes referred to as “sanctuary sites.” Central nervous system prophylaxis is directed at those sites. Intrathecal treatment involves injecting drugs, such as methotrexate, into the spinal column.

In most doctors’ practices, cranial radiation for pediatric patients (except in patients who have CNS leukemia or a CNS relapse) is not used. Treatment without radiation decreases the patient’s chances of experiencing long-term and late effects, such as organ damage, the development of second cancers and neurocognitive impairment.

### ALL Treatment Overview

#### Treatment Phase

#### Features

#### Goal

**INDUCTION**  
(4-6 weeks)

- Multiagent chemotherapy (may include vincristine, anthracyclines, corticosteroids, PEG-L-asparaginase, cyclophosphamide, other agents)
- CNS\* prophylaxis (intrathecal therapy)

- Achieve remission

**CONSOLIDATION/  
INTENSIFICATION**  
(4-6 months)

- Given in cycles
- Drug combinations used may be similar to induction
- Intrathecal therapy may be continued
- Consider HSCT\*\* for certain high-risk patients

- Eliminate any leukemic cells that remain after induction therapy
- Presymptomatic CNS\* treatment

**MAINTENANCE**  
(2 years—adults)  
(2-3 years—children)

- Drug combinations given in 1 or 2 intensified treatments
- May include daily mercaptopurine, weekly methotrexate, periodic vincristine, corticosteroids and intrathecal therapy

- Prevent disease relapse

\*CNS, central nervous system

\*\*HSCT, hematopoietic stem cell transplantation

Based on NCCN Guidelines.

**Figure 3.** | The figure above provides general information. There are many different ALL treatment approaches. Speak to your doctor to develop a specific treatment plan for either you or your child.

**Philadelphia Chromosome Positive (Ph+) ALL.** About 25 percent of adults and only about 3 percent of children who have ALL have a subtype called “Ph-positive ALL” (also known as either “Ph+ or Philadelphia chromosome positive ALL.”) Patients with this subtype of ALL have a chromosome alteration that results in a specific mutation of the *BCR-ABL* gene.

These patients are treated with the tyrosine kinase inhibitor (TKI) drugs imatinib mesylate (Gleevec®), dasatinib (Sprycel®), nilotinib (Tasigna®) or ponatinib (Iclusig®), in addition to other multidrug chemotherapy. TKIs specifically block the leukemia-causing effects of the *BCR-ABL* gene mutation in many patients. Gleevec treatment with chemotherapy is effective for some Philadelphia chromosome positive (Ph+) ALL patients. Sprycel and Tasigna are used to treat Ph+ ALL patients who do not tolerate, do not respond to, or who develop resistance to Gleevec. Iclusig is used to treat Ph+ ALL adult patients with the T315I mutation.

TKIs given alone would not result in cures for Ph+ ALL patients, so these drugs are combined with chemotherapy. This combination has become the standard of care for Ph+ ALL patients. New combinations of drugs are being studied in clinical trials for the treatment of Ph-positive ALL.

Allogeneic stem cell transplantation had been considered a standard of care for adolescent and young adult (AYA) patients with Ph+ ALL. However, its role has become less clear with the advent of TKI-targeted therapies. Several clinical trials are evaluating the role of transplantation for this disease subtype.

**Philadelphia chromosome-like (Ph-like) ALL.** Philadelphia chromosome-like ALL is a subgroup of B-cell ALL that has genetic features similar to ALL but lacks the *BCR-ABL1* fusion gene that defines Ph+ ALL. This subtype of ALL is more likely to be seen in males and patients with Down syndrome and occurs four to five times more frequently in children and young adults than Ph+ ALL. It is associated with an unfavorable prognosis. Recent studies that analyzed the genetic profile of Ph-like ALL have suggested that using tyrosine kinase inhibitors (TKIs) such as imatinib or dasatinib and other targeted therapies may significantly improve patient outcomes. In current clinical trials, the drugs ruxolitinib and dasatinib are being studied in combination with several chemotherapy drugs for the treatment of children with Ph-like ALL and cytokine receptor-like factor 2 rearrangements and/or JAK or ABL kinase pathway activation.

For more information about clinical trials, see page 32.

**Older Adolescents and Young Adults (AYA).** Older adolescents and adults younger than 40 years are termed the “adolescent and young adult (AYA)” group. Traditionally, treatment protocols for this group have been similar to protocols for adult treatment. However, researchers in clinical trials started looking into the use

of a variety of pediatric protocol options. The AYA group with ALL was treated with pediatric protocols and the outcomes were reported to be better than those of similar patients who were treated with adult protocols.

Some of these treatment options include combination chemotherapy using different dosing amounts; combination chemotherapy including rituximab (Rituxan<sup>®</sup>) and intensified doses of nonmyelotoxic drugs, such as prednisone, vincristine (Oncovin<sup>®</sup>) or PEG-L-asparaginase. Asparaginase *Erwinia chrysanthemi* (Erwinaze<sup>®</sup>) is offered as an alternative when the patient is allergic to PEG-L-asparaginase. Speak to your doctor or call an Information Specialist to learn about the different clinical trials that may be available to you or your child.

**Childhood Versus Adult Forms of ALL.** ALL has an unusual pattern of age distribution. The risk of developing ALL peaks between the ages of 1 to 4 years and then decreases until about age 55. At age 55, the incidence increases again, especially among men. As with other types of leukemia, incidence increases again as a person gets older.

The adult form of ALL is more resistant to treatment than the childhood form; however, over the past few years, several factors have contributed to longer remissions and prolonged survival for adult patients who have ALL. These include

- Improved outcomes with allogeneic stem cell transplantation
- Use of tyrosine kinase inhibitors (TKIs) for Philadelphia chromosome positive (Ph+) ALL
- Use of intensified pediatric-like therapy for adolescents and young adults

For ALL patients older than 60 years, patient performance status, other health issues and ALL risk features are taken into consideration when a treatment plan is being developed. Age alone is not a reason to withhold treatment. However, older patients may have a poorer response to therapy because

- The leukemic cells of older ALL patients have a higher occurrence of unfavorable cytogenetic and molecular abnormalities.
- Older patients may have other medical problems including heart, lung or kidney disease or diabetes mellitus. The doctor may have to select less toxic drugs or decrease the dosage and frequency of treatment.

The main goal of therapies targeting patients older than 60 years is to maintain efficacy while minimizing toxic side effects. It is important to know that even in otherwise healthy patients aged 75 years or older, the principal cause of treatment failure is not toxicity, but failure of the treatment to eliminate the ALL cells. A large number of patients in this group relapse.



For patients with ALL that is resistant to treatment or who have relapsed, allogeneic stem cell transplantation may be the best option if they are able to achieve complete remission before transplantation. Likewise, patients with high-risk disease are recommended for transplantation if it is unlikely that they will achieve remission with chemotherapy alone.

A new type of immunotherapy called “chimeric antigen receptor (CAR) T-cell therapy” uses the patient’s own immune cells to target and eliminate cancerous cells. It is being studied in the treatment of refractory and relapsed ALL in both children and adults. For more information on this therapy, see page 34 and see the LLS fact sheet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts*.

There are new treatments under study for ALL patients of all ages and for all stages of the disease.

### **Talk to your doctor about**

- Whether treatment in a clinical trial is right for you or your child

**Minimal Residual Disease (MRD).** Sensitive testing techniques permit the identification of small amounts of residual leukemia cells, known as “minimal residual disease (MRD),” at times when blood and marrow appear normal. This approach can be used if the leukemia cells have a detectable molecular abnormality or immunophenotype. It can also permit more sensitive follow-up of patients in remission and can help determine whether additional treatment is necessary.

Studies in both children and adults with ALL have shown that persistence or reappearance of MRD after induction chemotherapy is the most powerful prognostic indicator for both children and adult patients with ALL, even in patients who have low-risk features at diagnosis. Most patients who have persistent MRD after chemotherapy experience a relapse despite continued chemotherapy treatment.

**Stem Cell Transplantation.** Some patients may benefit from intensive chemotherapy alone followed by standard or reduced-intensity stem cell transplantation.

The decision to undergo a transplant should be discussed with your doctor. Most children treated for ALL will not need a transplant but allogeneic stem cell transplantation is an option for children with very high-risk or persistent disease. Cord blood stem cells may also be a source of donor cells for the transplant. For children who do undergo transplantation, the use of unrelated human leukocyte antigen (HLA)-matched donors appears to be just as successful as it is for related HLA-matched donors (for example, siblings), making more donors available through stem cell transplantation registries.

For an adult, the decision depends on the features of the leukemia and the patient's general health and age.

Which patients are likely to benefit from transplantation after their first complete remission is a question under study in clinical trials. Some of the main factors that influence the approach used are

- Patient age
- Ability to tolerate intensive treatment
- Cytogenetic and molecular characteristics of the ALL cells
- Availability of an HLA-matched related or unrelated stem cell donor.

**Allogeneic Stem Cell Transplantation.** This treatment uses donor stem cells to restore a patient's marrow and blood cells. For standard-risk patients in first remission, the choice between a transplant (either standard or reduced-intensity) and continued chemotherapy is not clear.

For high-risk patients, an allogeneic transplant is an option for those patients in first remission who have a matched related or matched unrelated donor. Cord blood stem cells may be an alternative source for donor stem cells if an appropriate sibling or unrelated donor is not available. Allogeneic stem cell transplantation is a curative treatment option for some high-risk ALL patients in first remission.

Children who relapse less than six months following initial treatment or while in chemotherapy have a lower chance of a second remission. For these children and for children with refractory disease, transplantation with a matched related or matched unrelated donor may be considered. Cord blood stem cells may also be a source of donor cells suitable for the transplant. For children who do undergo transplantation, the use of unrelated human leukocyte antigen (HLA)-matched donors appears to be just as successful as it is for related HLA-matched donors (for example, siblings).

**Reduced-Intensity Allogeneic Stem Cell Transplantation.** The benefits and risks of reduced-intensity allogeneic stem cell transplantation have not yet been clearly established for ALL patients. Patients who are either too old or too ill to have a standard allogeneic stem cell transplant may be candidates for a reduced-intensity transplant if a suitable donor is available. The conditioning therapy used for a reduced-intensity transplant is not as strong as that for a standard allogeneic stem cell transplant; it does not completely inactivate the patient's immune system or treat the ALL as aggressively.

Reduced-intensity allogeneic stem cell transplantation is based on the following two considerations:

- Much-improved immunosuppressive therapy prevents the patient from rejecting the donor's stem cells, even though the patient's immune system has not been fully suppressed by the lower-intensity conditioning therapy.
- The anticipated attack of the donor's immune cells successfully suppresses the patient's leukemia cells. This attack is referred to as a "graft-versus-leukemia effect" or "GVL." Over time, if the transplant is successful, the donor's stem cells replace the patient's immune cells. The engrafted donor immune cells recognize minor tissue antigens on the patient's leukemia cells and continue to suppress their growth.

The risk of graft-versus-host disease (GVHD) is an important consideration and a potentially disabling side effect.

#### **Talk to your doctor about**

- Whether a stem cell transplant is an option for you or your child

**Autologous Stem Cell Transplantation.** This procedure uses the patient's own stem cells to restore blood cell production. This type of transplant is not commonly used to treat ALL.

**Refractory Leukemia or Relapsed Leukemia.** Most patients achieve an initial remission. However, some patients have residual leukemic cells in their marrow even after intensive treatment. This is referred to as "refractory leukemia." Other patients achieve remission but then have a decrease number of normal blood cells and a return of leukemia cells in the marrow. This situation is called a "relapse."

With refractory leukemia, different drugs from those used in the first course of treatment may be administered in an effort to induce remission. Stem cell transplantation may be an option following remission and it may result in a more durable remission. In patients who relapse, the duration of the remission, the patient's age and the cytogenetic findings in the leukemia cells influence the approach to therapy. Drugs similar to those administered initially, different drugs or stem cell transplantation may be used to treat the relapsed leukemia.

There are several drugs approved by the FDA to treat patients who have relapsed or refractory ALL.

- Nelarabine (Arranon<sup>®</sup>), a type of antimetabolite drug, is approved for patients with relapsed T-cell ALL.

- Liposomal vincristine (Marqibo®) is approved for adult patients with Ph chromosome-negative ALL who have relapsed two or more times, or whose leukemia has progressed following two or more regimens of therapy.
- Blinatumomab (Blinicyto®) is a bispecific, anti-CD19, CD3 T-cell engager, approved for the treatment of relapsed or refractory Ph chromosome-negative B-cell precursor ALL.
- Clofarabine (Clolar®) is approved for patients between 1 and 21 years old with relapsed or refractory ALL after they have received at least two prior chemotherapy regimens.
  - Although treatment with clofarabine alone is not curative, it may lead to a temporary remission.
  - Clofarabine is also being studied (in combination with other drugs) in clinical trials for the treatment of children, adolescents and adults with relapsed or refractory ALL.

Once the disease is in remission, an allogeneic stem cell transplantation, which may result in a cure, can be considered.

**Risk Factors.** The following factors may increase the risk for relapse after initial treatments:

- Older age (greater than 60 years)—for adult patients
- Infancy or being older than 10 years—for childhood ALL patients
- Microscopic evidence of leukemia (minimal residual disease) that persists a certain number of days after the start of therapy (this number is specific to disease subtype)
- A high white blood cell count at the time of diagnosis
- Disease that has spread beyond the bone marrow to other parts of the lymphatic system, such as the spleen
- Certain genetic abnormalities, such as the presence of the Philadelphia chromosome, JAK mutations or *MLL* (mixed-lineage leukemia) gene translocations
- The need for treatment beyond induction chemotherapy in order to achieve a first complete remission

Patients with one or more of these risk factors may be candidates for stem cell transplantation once they are in first remission. Talk to your doctor for more information.

**Clinical Trials.** Several drugs and drug combinations that can be used to treat relapsed and refractory ALL are being studied in clinical trials. LLS Information Specialists offer guidance on how patients can work with their doctors to find out if a specific clinical trial is an appropriate treatment option. Information Specialists conduct clinical-trial searches for patients, family members and healthcare professionals.

### Talk to your doctor about

- Therapies under study in clinical trials for refractory or relapsed ALL

**Disease and Treatment Side Effects.** Most ALL treatment side effects are temporary and subside once the body adjusts to therapy or when therapy is completed. During the course of treatment and at the end of therapy, healthy new cells will begin to grow and develop. Severe side effects are treated on an inpatient basis.

**Low Blood Cell Counts.** ALL decreases the production of normal blood cells. In addition, chemotherapy can be toxic to both normal blood cells and ALL cells. The normal blood cells are eliminated from the marrow along with ALL cells. For the patient, this results in a severe deficiency in the number of

- Red blood cells (anemia)
- Platelets (thrombocytopenia)
- White blood cells called “neutrophils” (neutropenia) and “monocytes” (monocytopenia)

Transfusion of red blood cells and platelets is almost always needed for several weeks during treatment. After that, the blood cell counts usually return to normal levels. It is recommended that only irradiated blood (blood treated with radiation to prevent transfusion associated graft-versus-host disease) products be used.

Growth factors may be given to the patient to stimulate the marrow to make new white blood cells. The growth factors used most frequently are G-CSF (granulocyte-colony stimulating factor; filgrastim [Neupogen®] and pegfilgrastim [Neulasta®]) and GM-CSF (granulocyte-macrophage colony-stimulating factor; sargramostim [Leukine®]). Children are prescribed these agents only in special circumstances.

**Infection.** During treatment for ALL, the deficiency of white blood cells called neutrophils and monocytes can lead to infection from bacteria and fungi normally present in the environment, on the skin, in the nose and mouth, on the gums, or in the colon. The risk of infection may be increased because chemotherapy damages the lining of the mouth and intestines, making it easier for bacteria to enter the bloodstream. When the white blood cell count is low and infection risk is increased, antibiotics are given to prevent or treat infection.

Because the patient has an increased risk of developing an infection, the medical staff, family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents. Caregivers for patients with central lines or ports need to be meticulous in the cleaning of catheters.

Patients at home should not delay in seeking medical attention if any signs of infection develop. A rise in temperature to 101°F or higher, or the onset of chills, may be the only sign of infection in a patient with a very low white blood cell count. Other signs of infection may include persistent coughing; tenderness at a site prone to infection, such as the area surrounding the anus or the facial sinuses; sore throat; pain during urination; or frequent loose stools.

ALL patients are advised to receive certain vaccinations. It is recommended that children receive an annual influenza (“flu”) vaccine. Adult patients are advised to receive vaccinations for pneumococcal pneumonia and influenza. There are two types of pneumococcal vaccines available for adults: a pneumococcal polysaccharide vaccine (PPSV23, Pneumaovax®) and a pneumococcal conjugate vaccine (PCV13, Prevnar 13®). Immunizations using live organisms or with high viral loads, such as the herpes zoster or shingles vaccine (Zostavax®), should not be administered. If a family member or a friend receives the live vaccine, the patient should not go near him or her for a period of time. Your doctor can give you more information.

**Steroids.** The use of corticosteroids such as prednisone and dexamethasone is a main component of virtually every ALL induction regimen. These drugs are frequently incorporated into consolidation and maintenance regimens. Acute side effects of steroids may include hyperglycemia and steroid-induced diabetes. Patients should be monitored for glucose control. Another potential side effect of steroid therapy is the development of gastric ulcers. Use of proton-pump inhibitor drugs to reduce stomach acid is recommended during steroid therapy to reduce these risks.

**Tumor Lysis Syndrome.** Patients with ALL may be at high risk for developing a condition called acute tumor lysis syndrome (TLS), especially those who have very high white blood cell counts before induction therapy. TLS is characterized by metabolic abnormalities caused by the sudden release of the cellular contents of dying cells into the bloodstream, which is induced by chemotherapy. If untreated, TLS can lead to heart arrhythmias, seizures, loss of muscle control, acute kidney failure and even death. Patients are constantly monitored for the development of this condition and are given preventive therapy.

**Other Side Effects.** Chemotherapy affects tissues that normally have a high rate of cell turnover. Thus, the lining of the mouth, the lining of the intestines, the skin and the hair follicles may be affected. Common side effects may include

- Mouth ulcers (canker sores)
- Diarrhea
- Temporary hair loss
- Rashes
- Itchy skin
- Nausea and vomiting
- Headaches
- Loss of appetite
- Fatigue

Fortunately, drugs that counteract nausea and vomiting can be given to prevent or relieve these distressing side effects. Some ALL patients find that acupuncture treatments relieve chemotherapy-associated nausea and vomiting.

In some ALL patients, the concentration of uric acid in the blood may build up as a result of a very high white blood cell count. Chemotherapy may also increase uric acid levels. Uric acid is a chemical in the cell. It enters the bloodstream and is excreted in the urine. If many cells are killed simultaneously, the amount of uric acid in the urine can be so high that kidney stones can form. This may seriously interfere with the flow of urine. Drugs such as allopurinol (Zyloprim®) or rasburicase (Elitek®) and medications to alkalinize the urine can be given to minimize the buildup of uric acid in the blood.

There are drugs and other supportive therapies to prevent or manage many side effects. For more information see the free LLS booklets *Blood Transfusion*, *Cancer-Related Fatigue Facts* and *Understanding Side Effects of Drug Therapy*.

Sometimes, a drug or a drug combination causes side effects that continue for a period of time after treatment ends. Some effects may be long-lasting (see *Long-Term and Late Effects of Treatment* on page 30).

**Talk to your doctor about**

- Possible side effects and follow-up care

# Follow-Up Care

Some of the tests that were done to diagnose ALL may be repeated to

- Follow the effects of treatment
- Make decisions about whether to continue, intensify, change or stop treatment.

After treatment, a patient who is in remission and has completed therapy continues to be examined regularly by his or her doctors. Careful periodic assessment of the patient's health, blood cell counts and, if indicated, marrow is required. As time goes on, less frequent testing and check-ups may be called for, but scheduled assessments should be continued indefinitely.

The National Comprehensive Cancer Network (NCCN) recommends this follow-up during the first three years after the end of treatment:

- First year after completion of therapy
  - Complete physical examination (including testicular exam for males) and blood tests (CBC with differential) on a monthly basis
  - Liver function tests every two months until normal values are achieved
  - Bone marrow aspiration and echocardiogram, if indicated
- Second year after completion of therapy
  - Complete physical examination and blood tests every two to three months
- Third year after completion of therapy and beyond
  - Complete physical examination and blood tests every six months or as directed by the specialist

It is important to keep a record of your cancer treatment so that your doctor can follow up on specific late effects that may be associated with those treatments. This information includes your diagnosis, the names of chemotherapy drugs taken, radiation treatment information, surgeries performed, transplantation history, details about any other treatments, and the names and dates of any significant complications and the treatment received for those complications. This can help your doctor develop a follow-up schedule for you or your child.

Both adults and children may experience difficulties when they return to their daily routines after a long period of treatment. Getting support throughout this time, and for as long as needed, is important and will be helpful as you return to your normal life.



**Long-Term and Late Effects of Treatment.** Children and young adults who have been treated for ALL may be at increased risk for heart damage, other cancers and neurologic or cognitive problems. Patients should be seen by a primary care doctor for a general health examination at least once a year. They should also be examined regularly by an oncologist.

Treatment for individuals who have ALL sometimes causes effects that continue after treatment ends (long-term effects) or develop much later in life (late effects). It is important to know about the potential for long-term and late effects of treatment so any problems can be identified early and managed. Various factors can influence the risk of developing long-term or late effects, including

- Type and duration of treatment
- Age at the time of treatment
- Gender and overall health

Most ALL patients are treated with an anthracycline, such as daunorubicin (Cerubidine®). Anthracyclines have been associated with increased risk for heart muscle injury or chronic heart failure. Heart disease may not become apparent until many years after therapy ends.

Current prevention strategies for reducing heart damage include: limiting the cumulative dose of the anthracycline; altering drug schedules; using anthracycline structural analogs (the chemical structure of the anthracycline-analog drug is modified to be less toxic but equally effective as the original drug); using liposomal encapsulated anthracyclines (the therapeutic agent has a special coating to reduce side effects) and offering cardioprotective drugs and nutritional supplements.

Osteonecrosis, also called avascular necrosis (reduced blood flow to the bones) and bone pain are potential long-term side effects associated with steroid therapy. Osteonecrosis often affects weight-bearing joints, such as the hip bones or knees and seems to have a higher incidence among adolescents, (most likely due to skeletal growth) than in younger children or adults. To monitor patients who are at risk of developing this condition, routine measurements of calcium and vitamin D levels should be obtained and periodic imaging evaluation should be considered.

Sometimes cranial radiation is used for patients with obvious CNS disease involvement or those who experience a relapse. Doctors are limiting the use of this treatment (and using drug-therapy alternatives as much as possible) to avoid the risk of long-term or late effects such as neurocognitive impairment and the development of second cancers.

Children may experience side effects of treatment, both in the short and long term. These side effects can affect learning and impact growth, cognitive development and psychosocial development. When the child goes back to school, there will be new challenges facing families whose main focus, up to that point, has been getting

through treatment. By being aware of possible side effects, parents can work with school personnel who will be able to help their child cope and manage schoolwork.

For more information, see the free LLS booklets *Coping With Childhood Leukemia and Lymphoma* and *Learning & Living With Cancer: Advocating for your child's educational needs*. Both booklets provide information about the challenges children may face and what can be done, the laws that protect your child and ways in which schools can help.

**Fertility.** Certain childhood cancers and treatments can increase the risk for infertility and cause complications in pregnancy, such as preterm birth and low birth weight. Fertility issues should be addressed with all patients of reproductive age or with the parents of children receiving treatment. The risk of infertility in patients who have ALL (unless they have been treated with hematopoietic stem cell transplantation (HSCT) is very low as contemporary treatment protocols have either lowered doses of alkylating agents (which can cause fertility problems) or have avoided alkylating agents altogether. Treatment with tyrosine kinase inhibitors (TKIs) may not impair fertility in humans, but there is some data on how these medications can impact reproductive potential—tyrosine kinases are important for follicle growth and development. Fertility preservation recommendations include sperm banking and cryopreservation of ovarian tissue before stem cell transplantation.

Talk to your doctor for additional information about how long-term and late effects of treatment can be managed.

For more information see the free LLS booklets *Long-Term and Late Effects of Treatment for Childhood Leukemia or Lymphoma Facts*, *Long-Term and Late Effects of Treatment in Adults Facts*, *Fertility Facts* and *Understanding Side Effects of Drug Therapy*.

### **Talk to your doctor about**

- Possible long-term and late effects and follow-up care

**Treatment Outcomes.** A few decades ago there were very low cure rates in both children and adults diagnosed with ALL. Today, nearly 90 percent of children and 40 percent of adults can expect long-term remission with leukemia-free survival—and probable cure. Emphasis is placed not only on improving the cure rate but also on improving quality of life by preventing acute and late treatment-related complications, such as second cancers, cardiotoxicity (heart damage) and endocrinopathy (endocrine gland problems such as hyperthyroidism or hypothyroidism).

“Relative survival” compares the survival rate of a person diagnosed with a disease to that of a person without the disease. In children younger than age 15, the five-year relative survival rate has increased from 3 percent in 1964 to 91 percent in 2005-2011 as a result of successful treatments that are researched and developed, then tested in clinical trials.

In adults, the probability of remission has increased dramatically over the last 10 years, and extended remissions are also more frequent. Several areas of research are likely to lead to further progress.

# Research and Clinical Trials

New approaches under study in clinical trials for ALL treatment, many of which are being supported by LLS research programs, hold the promise of increasing the rate of remission and finding a cure for ALL.

**Clinical Trials.** Every new drug or treatment regimen goes through a series of clinical trials before it becomes part of standard therapy. Clinical trials are carefully designed and rigorously reviewed by expert clinicians and researchers to ensure as much safety and scientific accuracy as possible. Participation in a carefully conducted clinical trial may be the best available therapy. Patient participation in past clinical trials has resulted in the therapies we have today.

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized clinical-trial searches for patients, family members and healthcare professionals. Please visit [www.LLS.org/clinicaltrials](http://www.LLS.org/clinicaltrials).

**Research Approaches.** There are clinical trials for newly diagnosed patients and for patients whose disease is relapsed or refractory. A number of approaches are under study in clinical trials for the treatment of ALL patients. Some of the objectives are

- To achieve a greater understanding of ALL cytogenetic abnormalities and how they affect prognosis
- To refine techniques to assess the high risk of relapse in individual patients to ensure that intensive treatment is given primarily to high-risk cases
- To find the most effective combinations of chemotherapy drugs while reducing undesired side effects
- To develop treatment strategies to prevent or reverse chemotherapy resistance
- To refine stem cell transplants to increase effectiveness, reduce complications and determine which patients are most likely to benefit from this treatment
- To develop new and/or refine existing immunotherapy agents so that they can be used in frontline treatment
- To refine techniques for faster detection of minimal residual disease after induction therapy so that the patient's treatment plan can be more individualized

**Agents Under Study.** Here are examples (and some descriptions) of specific agents under study in clinical trials for ALL.

## Proteasome Inhibitor

- **Bortezomib (Velcade®)**—This drug, approved to treat myeloma and some types of lymphoma, is now being studied in combination with other drugs such as belinostat for the treatment of relapsed or refractory ALL. It is also being studied for treating newly diagnosed pediatric patients with T-cell ALL.

## Antimetabolite

- **Clofarabine (Clolar®)**—Already approved to treat pediatric ALL, clofarabine is now showing promising results in studies of adults with ALL. It is also being studied in combination with other drugs such as mitoxantrone in clinical trials for the treatment of children whose ALL is relapsed or refractory.
- **Nelarabine (Arranon®)**—This drug, a type of antimetabolite drug, is approved for patients who have relapsed T-cell ALL. It is now being studied in clinical trials in combination with other agents for the treatment of relapsed or refractory T-cell ALL. It is also being evaluated in combination with other drugs as part of an induction regimen for untreated T-cell ALL.

## Janus kinase (JAK) Inhibitor

- **Ruxolitinib (Jakafi®)**—Already approved to treat myelofibrosis and polycythemia vera patients, it is being studied in clinical trials in the treatment of pediatric refractory and relapsed ALL. It is also being studied in combination with several chemotherapy drugs in the treatment of children with Ph-like ALL and *CRLF2* and JAK mutations.

## Special Chemotherapy Combination

- **Augmented Hyper-CVAD**—The hyper-CVAD combination (cyclophosphamide, vincristine, doxorubicin and dexamethasone) is a well-established regimen for ALL. The augmented hyper-CVAD formulation was designed in 2011 and it includes intensified doses of vincristine, dexamethasone and asparaginase. Researchers are studying the efficacy of this combination for ALL treatment.

## Immunotherapies

- **Monoclonal antibodies rituximab (Rituxan®), alemtuzumab (Campath®), ofatumumab (Arzerra®)**—These drugs are already approved in the treatment of other blood cancers. They are currently being studied for their use in combination with chemotherapy in clinical trials for untreated and relapsed/refractory ALL.
- **Blinatumomab (Blinicyto®)**—This drug is a bispecific, anti-CD19, CD3 T-cell engager, approved for the treatment of relapsed or refractory Ph-negative B-cell precursor ALL. It is being studied in current trials for the treatment of refractory and relapsed ALL and also as therapy for older patients with newly diagnosed disease.
- **Inotuzumab ozogamicin**—This drug is an anti-CD22 monoclonal antibody that is bound to a toxic drug called calicheamicin. It is being studied, as part of a regimen with combination chemotherapy, in the treatment of relapsed and refractory ALL.

- **CAR T-cell Therapy**—This is a type of immunotherapy that consists of engineering patients’ own immune cells first to recognize and then to attack cancerous tumors. This approach has shown very promising results in patients with blood cancers. The T cells are genetically engineered to produce receptors on their surface called “chimeric antigen receptors” (CARs). These receptors recognize and bind to a specific target found on the cancerous cells. Clinical trials are studying the use of CAR T-cell therapy in the treatment of chemotherapy-resistant or refractory ALL in both adults and children.

For more information on this type of therapy, please see the LLS fact sheet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts*.

To learn more about clinical trials, see the free LLS booklet *Understanding Clinical Trials for Blood Cancers*. We also encourage you to contact an Information Specialist and visit [www.LLS.org](http://www.LLS.org) for more information about specific treatments for ALL that are under study in clinical trials.

## Normal Blood and Marrow

**Blood and Marrow.** Blood is composed of plasma and cells suspended in plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals include

- Proteins
  - Albumin, the most common protein in blood
  - Blood-clotting proteins, made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red cell production
  - Immunoglobulins, antibodies made by plasma cells in response to infections including those we develop from our vaccinations (such as poliovirus antibodies, which are made by normal plasma cells in the bone marrow)
- Hormones (such as thyroid hormone and cortisol)
- Minerals (such as iron and magnesium)
- Vitamins (such as folate and vitamin B12)
- Electrolytes (such as calcium, potassium and sodium)
- Antibodies, which are made by plasma cells

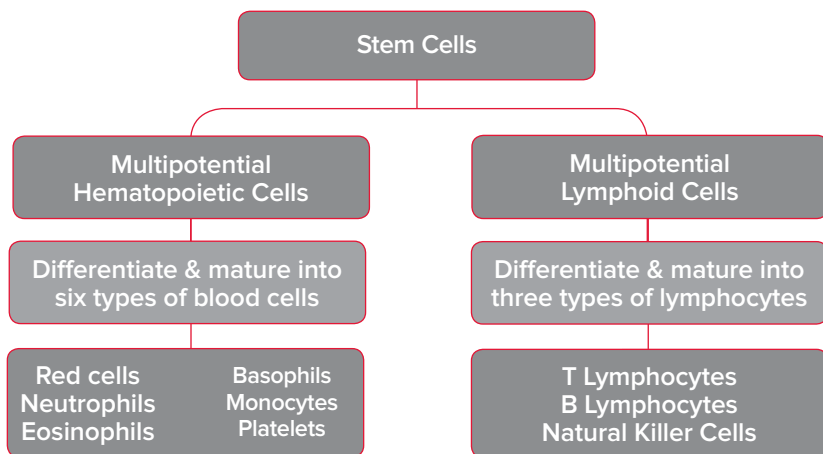
The cells suspended in plasma include red blood cells, platelets and white blood cells (neutrophils, monocytes, eosinophils, basophils, and lymphocytes).

- The red blood cells make up a little less than half the volume of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers it to the cells all around the body; hemoglobin then picks up carbon dioxide from the body’s cells and delivers it back to the lungs, where it is removed when we exhale.

- The platelets are small cells (one-tenth the size of red blood cells) that help stop bleeding at the site of an injury in the body. For example, when a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together, and plug up the bleeding site with the help of blood-clotting proteins such as fibrin and electrolytes such as calcium. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils and monocytes are white blood cells. They are called “phagocytes” (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red blood cells and platelets, the monocytes can leave the blood and enter the tissue, where they can attack the invading organisms and help combat infection. Eosinophils and basophils are types of white blood cells that respond to allergens or parasites.
- Most lymphocytes, another type of white blood cell, are found in the lymph nodes, the spleen and the lymphatic channels, but some enter the bloodstream. There are three major types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells) and natural killer (NK) cells. These cells are a key part of the immune system.

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. The spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull contain the marrow that makes blood cells in adults. The process of blood cell formation is called “hematopoiesis.” A small group of cells, the stem cells, develop into all the blood cells in the marrow by the process of differentiation (see Figure 4).

### Blood Cell & Lymphocyte Development



**Figure 4.** | Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

In healthy individuals, there are enough stem cells to keep producing new blood cells continuously. Blood passes through the marrow and picks up the fully developed and functional red and white blood cells and platelets for circulation in the blood stream.

Some stem cells enter the bloodstream and circulate. They are present in such small numbers that they cannot be counted or identified by tests for standard blood counts. The presence of stem cells in the bloodstream is important because these cells can be collected by a special technique. There are also methods to induce more stem cells to leave their home in the marrow and circulate in the bloodstream, allowing for a greater stem cell collection. If enough stem cells are harvested from a compatible donor, they can be transplanted into a recipient.

Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth, placental and umbilical cord blood can be collected, stored and used as a source of donor stem cells for transplantation.

**The Lymphatic System.** The marrow is really two organs in one. The first is the blood cell-forming organ. The second is the lymphocyte-forming organ and is a part of the immune system.

The marrow produces three main types of lymphocytes. They are

- B lymphocytes (B cells), which make antibodies in response to foreign substances (antigens), especially microbes
- T lymphocytes (T cells), which mature in the thymus. The T lymphocytes have several functions, including assisting B lymphocytes to make antibodies against invading bacteria, viruses or other microbes. The antibody attaches to the microbe, making it possible for other white blood cells to recognize the antibody and pull it into the cell along with its attached microbe (ingesting it). The white cell then kills and digests the microbe
- Natural killer (NK) cells, which attack virus-infected cells without requiring antibody or other mediation. T cells and NK cells have other functions as well and are important elements in research efforts to design immunotherapies to treat lymphoma and other cancers

The lymphocytes circulate through channels called “lymphatics,” which connect the lymph nodes to each other throughout the body. The lymphatic channels collect into large ducts that empty into blood vessels. Lymphocytes enter the blood via these ducts. Most lymphocytes are found in the lymph nodes and other parts of the lymphatic system such as the skin; spleen; tonsils and adenoids (special lymph nodes), intestinal lining, and in young people, the thymus.

# Medical Terms

**Allogeneic Stem Cell Transplantation.** A treatment that uses donor stem cells to restore a patient's marrow and blood cells. The patient is given conditioning therapy (high-dose chemotherapy either with or without total body radiation) to treat the blood cancer and “turn off” the immune system so that the donor cells are not rejected. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

**Anemia.** A decrease in the number of red blood cells and, therefore, in the hemoglobin concentration of the blood. If severe, anemia can cause a pale complexion, weakness, fatigue and shortness of breath on exertion. Some types of anemia may present lifelong health problems.

**Anthracyclines (Antitumor Antibiotics).** Chemotherapy agents that interact directly with the DNA in the nucleus of cells, thus interfering with cell survival.

**Antibodies.** Proteins released by plasma cells that recognize and bind to foreign substances called “antigens.” Antibodies coat, mark for destruction or inactivate foreign particles such as bacteria, viruses or harmful toxins. They can be used to identify and classify types of blood cancers or altered to make them useful in antibody-mediated immunotherapy.

**Antigen.** A foreign substance, usually a protein, that stimulates an immune response when it is ingested, inhaled or comes into contact with the skin or mucous membranes. Examples of antigens are bacteria, viruses or allergens.

**Autologous Stem Cell Transplantation.** A treatment that uses a patient's own stem cells to delay the progression of certain blood cancers. The autologous transplantation process takes place after the patient achieves a complete response (remission), or a good partial response, to induction drug therapy. The stem cells are collected, then frozen for later use. After the patient receives conditioning therapy (intensive chemotherapy and/or radiation), the cells are thawed and infused back into the patient. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

**Basophil.** A type of white blood cell that participates in certain allergic reactions.

**Biopsy.** A procedure to obtain tissue for diagnosis. In many cases, a special needle can be used to obtain the tissue. In some cases, a larger piece of tissue may be surgically removed.

**Blast Cells.** The immature marrow cells identified by the light microscope. Blasts represent about one percent of normally developing marrow cells. In acute leukemias, abnormal blast cells (similar in appearance to normal blast cells)



accumulate in large numbers, and may constitute up to 80 percent of all marrow cells. Abnormal blast cells interfere with the production of normal red blood cells, white blood cells and platelets in the marrow.

**Blood Cell Count.** A laboratory test that requires a small blood sample to provide information about the types and numbers of cells in the bloodstream. The term “complete blood count” or CBC is often used to refer to this test.

**Blood Cells.** There are three main types of cells in the blood: red blood cells, which carry oxygen; white blood cells, which principally prevent or combat infections; and platelets, which help prevent bleeding.

**Bone Marrow.** A spongy tissue in the hollow central cavity of the bones that is the site of blood cell formation. See *Normal Blood and Marrow* on pages 34 through 36.

**Bone Marrow Aspiration.** A test to examine marrow cells to detect cell abnormalities. A marrow sample is usually taken from the patient’s hip bone. After medication is given to numb the area, the liquid sample is removed using a special needle inserted through the bone and into the bone marrow. Bone marrow aspiration and bone marrow biopsy are usually done at the same time.

**Bone Marrow Biopsy.** A test to examine marrow cells to detect cell abnormalities. This test differs from a bone marrow aspiration in that a small amount of bone filled with marrow is removed, usually from the hip (pelvic) bone. After medication is given to numb the skin, a special hollow biopsy needle is used to remove a core of bone containing marrow. Bone marrow aspiration and bone marrow biopsy may be done in the doctor’s office or in a hospital. The two tests are almost always done at the same time.

**CBC.** Complete blood count. See Blood Cell Count.

**Central Line (Indwelling Catheter).** A special tube inserted into a large vein in the upper chest. The central line, sometimes referred to as an “indwelling catheter,” is tunneled under the skin of the chest to keep it firmly in place. The external end of the catheter can be used to administer medications, fluids or blood products or to withdraw blood samples. With meticulous care, central lines can remain in place for long periods of time (many months), if necessary. They can be capped and remain in place in patients after they leave the hospital, and be used for outpatient chemotherapy or blood product administration. See Port.

**Central Nervous System (CNS) Prophylaxis.** In certain types of leukemia, particularly acute lymphoblastic leukemia and acute monocytic leukemia with high blood cell counts, leukemic cells may enter the covering of the spinal cord and brain (the meninges). This process is often not apparent until months or years after remission—when the leukemia returns, first in the coverings of the CNS, then in the marrow and blood. To prevent this type of relapse (meningeal leukemia), virtually all children and adults with acute lymphoblastic leukemia who enter

remission are treated by placing appropriate chemotherapy in the fluid that bathes the spinal cord and brain. In some cases, x-ray therapy is administered to the head as well.

**Chemotherapy.** The use of chemicals (drugs or medications) to kill cancerous cells. Numerous chemicals have been developed for this purpose, and most act to injure the DNA of the cancer cells. When the DNA is injured, the cells cannot grow or survive.

**Chromosome.** Any of the 46 structures in the nucleus of all cells in the human body (except the red blood cells) that contain a strand of DNA. This strand is made up principally of genes, which are specific stretches of the DNA. Each chromosome has a long arm (called “q”) and a short arm (called “p”). The number or size of chromosomes may be altered in blood cancer cells due to chromosome breakage and rearrangement. See Translocation.

**Clinical Trials.** Carefully planned and monitored research studies conducted by doctors. The goal of clinical trials for blood cancers is to improve treatment and quality of life and to increase survival.

**Clonal.** The designation for a population of cells derived from a single transformed parent cell. Virtually all cancers are derived from a single cell with an injury (mutation) to its DNA and thus are monoclonal (mono- means “one”). Leukemia, lymphoma and myeloma are examples of clonal cancers; that is, cancers derived from a single abnormal cell.

**Colony-Stimulating Factor.** See Growth Factor.

**Complete Blood Count (CBC).** See Blood Cell Count.

**Computed Tomography (CT) Scan.** A technique for imaging body tissues and organs. X-ray transmissions are converted to detailed images using a computer to synthesize x-ray data. The images are displayed as a cross-section of the body at any level, from the head to the feet.

**Conditioning Treatment.** Intensive therapy given to a patient in preparation for stem cell transplant. It typically includes cytotoxic drugs either with or without total body radiation.

**Cord Blood Stem Cells.** Stem cells that are present in the blood drained from the placenta and umbilical cord after a baby is born. These stem cells have the capability to repopulate the marrow of a compatible recipient and produce blood cells. Frozen cord blood is a source of donor stem cells for transplantation to HLA-matched recipients. Most cord blood transplants are made possible by matched or nearly matched unrelated donors.

**Cytogenetic Analysis.** The process of analyzing the number and size of the chromosomes of cells. In addition to detecting chromosome alterations, in some cases it is possible to identify the actual genes that have been affected.

**Cytopenia.** A reduction in the number of cells in the bloodstream.

**Cytotoxic Drugs.** Anticancer drugs that act by killing cells or preventing them from dividing. See Chemotherapy.

**Differentiation.** The process by which stem cells give rise to functional cells of a single blood cell line. Differentiation of stem cells forms red blood cells, platelets and white blood cells (neutrophils, monocytes, eosinophils, basophils and lymphocytes). See Hematopoiesis.

**DNA.** The genetic material in the cell.

**DNA Repair Enzyme Inhibitors.** Chemotherapy drugs that prevent certain cell proteins from working and make the DNA of cancer cells and tumors more susceptible to injury.

**DNA Synthesis Inhibitors.** Chemotherapy drugs that react with DNA to alter it chemically and keep it from permitting cell growth.

**Eosinophil.** A type of white blood cell that participates in allergic reactions and helps fight certain parasitic infections.

**Erythrocytes.** See Red Blood Cells.

**Erythropoietin (EPO).** A hormone required for the normal production of red blood cells. It is produced mainly by the kidneys and is released into the blood in response to decreased levels of oxygen in the blood. Epoetin alfa (Procrit® or Epogen®) and darbepoetin alfa (Aranesp®) are laboratory-made forms of the human hormone erythropoietin that can be used to treat anemia.

**FDA.** The short name for the United States Food and Drug Administration. Part of the FDA's job is to assure the safety and security of drugs, medical devices and the US food supply.

**FISH.** See Fluorescence In Situ Hybridization (FISH).

**Flow Cytometry.** A test that permits the identification of specific cell types within a sample of cells. The test may be used to examine blood, marrow or tissue cells obtained from a biopsy. One use of flow cytometry is to determine whether a sample of cells is composed of T cells or B cells. This permits the doctor to determine if the leukemia or lymphoma is of the B-cell or T-cell type. Flow cytometry is also used to select stem cells from a mixed-cell population so they can be used later in a stem cell transplant.

**Fluorescence In Situ Hybridization (FISH).** A technique for studying chromosomes in tissue using DNA probes tagged with fluorescent molecules that emit light of different wavelengths (and different colors). The probes match to the chromosomes within the cells, and the chromosomes fluoresce in color.

**G-CSF (Granulocyte Colony-Stimulating Factor).** See Growth Factor.

**GM-CSF (Granulocyte-Macrophage Colony-Stimulating Factor).** See Growth Factor.

**Graft-Versus-Host Disease (GVHD).** The immune attack by lymphocytes in the donor's marrow or blood cell suspension (the graft) against the tissues of the recipient (the host). The principal sites affected by GVHD are the skin, the liver and the gastrointestinal tract.

**Granulocyte.** A type of white blood cell that has a large number of granules in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.

**Growth Factor.** A chemical used to stimulate the production of neutrophils and shorten the period of low neutrophil counts in the blood after chemotherapy. Granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) are examples of growth factors that are made commercially. GM-CSF can also stimulate monocytes.

**Hematocrit.** The percentage of the blood that comprises red blood cells. Normal values are 40 to 54 percent in men and 35 to 47 percent in women. If the hematocrit is below normal, the condition is called "anemia." If the hematocrit value is above normal, the condition is called "erythrocytosis."

**Hematologist.** A doctor who has special training in the treatment of blood cell diseases. This person is either an internist who treats adults or a pediatrician who treats children.

**Hematopathologist.** A pathologist who studies diseases of the blood by looking at peripheral blood smears, bone marrow aspirates and biopsies, and lymph nodes and other tissues. The hematopathologist uses his or her expertise to identify diseases such as blood cancers.

**Hematopoiesis.** The process of blood cell development in the marrow. The most undeveloped cells in the marrow are stem cells. They start the process of blood cell development. The stem cells begin to develop into young or immature blood cells such as red blood cells or white blood cells of various types. This is called "differentiation." The young or immature blood cells then further develop into fully functional blood cells. This is called "maturation." The mature cells leave the marrow, enter the bloodstream and circulate throughout the body. Hematopoiesis is a process that is active throughout life since most blood cells live for short periods and must be replaced continuously.

**Hemoglobin.** The iron-containing pigment in red blood cells that carries oxygen to the tissue cells. A reduction in the number of red blood cells decreases the amount of hemoglobin in the blood. A condition in which blood hemoglobin concentration is low can be serious and is called “anemia.”

**HLA.** The abbreviation for human leukocyte antigen(s). These antigens are proteins on the surface of most tissue cells, and they give an individual his or her unique tissue type. HLA factors are inherited from mother and father, and the greatest chance of having the same HLA type is between siblings. On average, one in four siblings is expected to share the same HLA type. The testing for HLA factors is referred to as “tissue typing.” Before transplantation takes place, tissue typing is performed in order to determine if the donor and recipient are compatible.

**Immune System.** Cells and proteins that defend the body against infection. Lymphocytes, lymph nodes and the spleen are parts of the body’s immune system.

**Immunophenotyping.** A method that uses the reaction of antibodies with cell antigens to determine a specific type of cell in a sample of blood cells, marrow cells or lymph node cells. The antibodies react with specific antigens on the cell. In immunophenotyping, a tag is attached to an antibody so that it can be detected. The tag can be identified by the laboratory detector used for the test. Cells carrying their array of antigens are tagged with specific antibodies, so they can be identified; for example, myeloid leukemic cells can be distinguished from lymphoblastic leukemic cells.

**Immunosuppression.** A state in which the immune system does not function properly and its protective functions are inadequate. The patient is more susceptible to infections, including those from microbes that are usually not highly infectious. This can occur as a result of intensive chemotherapy and radiation therapy, especially when used in high doses to condition a patient for transplantation. See Graft-Versus-Host Disease (GVHD).

**Indwelling Catheter.** See Central Line (Indwelling Catheter).

**Intrathecal.** The designation for the space between layers of tissue that cover or line the central nervous system (CNS) and the brain or spinal cord. The tissue layers are called the “meninges.” In some situations, drugs have to be administered directly into the spinal canal when cancer cells are present in the meninges. This procedure is called “intrathecal therapy.”

**Karyotype.** The systematic arrangement, using images, of the 46 chromosomes in the human cell in 22 matched pairs (maternal and paternal member of each pair) by length (from longest to shortest) and other features, with the sex chromosomes shown as a separate pair (either XX or XY). The 22 pairs are referred to as “autosomes.”

**Leukocytes.** See White Blood Cells.

**Leukocytosis.** An above-normal concentration of leukocytes (white blood cells) in the bloodstream.

**Leukopenia.** A below-normal concentration of leukocytes (white blood cells) in the bloodstream.

**Lumbar Puncture.** A procedure that can be used to remove spinal fluid from the space surrounding the spinal cord. It can also be used to administer anticancer drugs to prevent or treat leukemia or lymphoma of the central nervous system (CNS). Another term for lumbar puncture is “spinal tap.”

**Lymphatic System.** The system comprising the lymph nodes, the thymus (in the first several decades of life), the lymphatic channels, the lymphatic tissue of the marrow, the gastrointestinal tract, the skin, the spleen, and the T cells, B cells, (and etc) and natural killer cells contained in those sites.

**Lymph Nodes.** Small structures about the size of beans that contain large numbers of lymphocytes and are connected with each other by small channels called “lymphatics.” These nodes are distributed throughout the body.

**Lymphoblast.** A leukemic cell that should have become a normal lymphocyte cell. Uncontrolled and exaggerated growth and accumulation of these leukemic cells means that they fail to function as normal blood cells.

**Lymphocyte.** A type of white blood cell that is the essential cell type in the body’s immune system. There are three major types of lymphocytes: B lymphocytes, which produce antibodies to help combat infectious agents like bacteria, viruses and fungi; T lymphocytes, which have several functions, including assisting B lymphocytes to make antibodies; and natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

**Macrophage.** See Monocyte/Macrophage.

**Magnetic Resonance Imaging (MRI).** A technology that provides detailed images of body structures. It differs from the CT scan in that the patient is not exposed to x-rays. The signals generate from the tissues in response to a magnetic field produced by the instrument and are converted by computer into images of body structures. Thus, the size or a change in size of organs (eg, lymph nodes, liver, spleen) or tumor masses can be measured.

**Marrow.** See Bone Marrow.

**Minimal Residual Disease (MRD).** The small amounts of cancer cells that may remain after treatment, even when blood and marrow may appear to be normal. These residual cells can only be identified by sensitive molecular or flow cytometry-based techniques.

**Monoclonal.** See Clonal.

**Monoclonal Antibodies.** Antibodies made by cells belonging to a single clone.

These highly specific antibodies can be produced in the laboratory. In cancer therapy, they can be used for the targeted delivery of drugs or radioactive substances to cancer cells.

**Monoclonal Antibody Therapy.** Therapy using proteins made in the laboratory that either react with or attach to antigens on the cancer cells to which they are targeted. The antibodies are used therapeutically in three ways: as “naked” antibodies (monoclonal antibodies); as antibodies to which radioactive isotopes are attached (radioimmunotherapies); and as antibodies to which toxins are attached (immunotoxins).

**Monocyte/Macrophage.** A type of white blood cell that represents about 5 to 10 percent of the cells in normal human blood. The monocyte and the neutrophil are the two major microbe-eating and microbe-killing cells in the blood. When a monocyte leaves the bloodstream and enters the tissue, it becomes a macrophage.

**Multidrug Resistance (MDR).** A situation in which bacteria, viruses, or other disease-causing organisms are or become resistant to the effects of several different classes of drugs.

**Mutation.** An alteration in the structure of a gene that results from a change to the part of the DNA that represents the gene. See Oncogene.

**Myelocyte.** A cell in the marrow that should become a mature granulocyte in the blood. Myelocytes are not present in the blood of healthy individuals.

**Neutropenia.** A below-normal concentration of neutrophils in the bloodstream; a neutrophil is a type of white blood cell.

**Neutrophil.** The principal phagocyte (microbe-eating cell) in the blood. This blood cell is the main cell that combats infections. A severe deficiency of neutrophils increases the patient’s susceptibility to infection.

**Oncogene.** A mutated gene that can transform a cell into a cancer cell. Several subtypes of acute myeloid leukemia, acute lymphoblastic leukemia and lymphoma, and nearly all cases of chronic myeloid leukemia are associated with an oncogene.

**Oncologist.** A doctor who diagnoses and treats patients with cancer. Oncologists are usually cancer specialists who treat adults or cancer-specialist pediatricians who treat children. Radiation oncologists specialize in the use of radiation to treat cancer, and surgical oncologists specialize in the use of surgical procedures to diagnose and treat cancer. These doctors cooperate and collaborate to provide the best treatment plan (surgery, radiation therapy, chemotherapy, and immunotherapy) for the patient.

**Pancytopenia.** A decrease below normal in the concentration of all three major blood cell types: red blood cells, white blood cells and platelets.

**Pathologist.** A specialist doctor who identifies disease by studying tissues under a microscope. See Hematologist; Hematopathologist.

**Percutaneously Inserted Central Venous Catheter (PICC or PIC Line).** A long, thin, flexible tube that is inserted into the body and can be left in place for weeks or even months for administration of medications, fluids and nutrition. It can also be used to obtain blood samples. The PICC eliminates the need for standard intravenous (IV) administration.

**Peripheral Blood Smear.** A sample of blood placed on a slide and stained (dyed) so that the cells can be visualized and examined under a microscope.

**Petechiae.** Pinhead-sized sites of bleeding in the skin. This type of bleeding results from a very low platelet count and is typically seen on the legs, feet, trunk and arms.

**Phagocytes.** Cells that readily eat (ingest) microorganisms such as bacteria or fungi and kill them as a means of protecting the body against infection. The two principal phagocytes are neutrophils and monocytes. They leave the blood and enter the tissues where an infection has developed.

**Philadelphia Chromosome (Ph Chromosome).** An abnormality of chromosome 22 found in the marrow and blood cells of patients with chronic myeloid leukemia and of some patients with acute lymphoblastic leukemia. The abnormality, a shortening of the long arm of this chromosome, was first observed and reported by doctors at the University of Pennsylvania; hence the name “Philadelphia chromosome.” Since this discovery, the lost piece of chromosome 22 has been shown to stick (translocate) to chromosome 9 in most cases. Indeed, some of chromosome 9 also sticks (translocates) to chromosome 22. This is known as a “balanced translocation,” because virtually equal lengths of partial chromosome arms exchange position. Because chromosome 22 is a very short chromosome and chromosome 9 a very long one, the lengthening of chromosome 9 was less apparent than the shortening of 22 until more sensitive detection techniques became available. The abnormality of chromosome 22 is now usually abbreviated as “Ph chromosome.”

**PIC/PICC Line.** See Percutaneously Inserted Central Venous Catheter (PIC/PICC Line).

**Plasma.** The liquid portion of the blood, in which the blood cells, platelets, proteins and various other components are suspended. It is also referred to as “blood plasma.”

**Platelets.** Small blood cells (about one-tenth the volume of red blood cells) that stick to the site of blood vessel injury, aggregate in a process called clotting, and seal off the injured blood vessel to stop bleeding. “Thrombocyte” is a synonym for platelet and is often used as the prefix in terms describing platelet disorders, such as thrombocytopenia (too few platelets) or thrombocythemia (too many platelets).



**Platelet Transfusion.** Transfusion of donor platelets, which may be needed to support some patients treated for blood cancer. The platelets can be collected from several unrelated donors and given as pooled, random-donor platelets. Sometimes the platelets are collected from a single donor using a special machine that separates the platelets from the blood.

**Polymerase Chain Reaction (PCR).** A technique to expand trace amounts of DNA or RNA so the specific type of the DNA or RNA can be studied or determined. This technique has become useful in detecting a very low concentration of residual blood cancer cells, too few to be seen using a microscope. PCR can detect the presence of one blood cancer cell among 500,000 to 1 million blood cells. PCR requires a specific DNA (or RNA) abnormality or marker, like an oncogene, in the leukemia or lymphoma cells in order to be used for identifying residual abnormal cells.

**Port.** A small device used with a central line (catheter) that allows access to a vein. The port is placed under the skin of the chest. To give medicines or nutrition and to take blood samples, the doctor or nurse inserts a needle through the skin into the port. A numbing cream can be put on the skin before the port is used.

**Promyelocyte.** A cell of the marrow that is very early in development along the pathway to myeloid cells. It represents the next stage after the blast cell stage.

**Radiation Therapy.** The use of x-rays and other forms of radiation in treatment. Radiation therapy may be useful in the treatment of some localized blood cancers.

**Recurrence/Relapse.** The return of a disease after it has been in remission following treatment.

**Red Blood Cells.** Blood cells that carry hemoglobin, which binds oxygen and carries it to the tissues of the body. Red blood cells are also called “erythrocytes.”

**Reduced-Intensity Stem Cell Transplantation.** A form of allogeneic transplantation, now in clinical trials. In reduced-intensity transplantation (also called “nonmyeloablative stem cell transplantation”) patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

**Refractory Disease.** Disease that does not go into remission or improve substantially after treatment with initial standard therapy for the disease. Newly diagnosed patients or relapsed patients may have refractory disease. In refractory leukemia, a proportion of malignant cells resist the effects of one or several drugs. See Resistance to Treatment.

**Relapsed Disease.** Disease that initially responded to therapy but has begun to progress.

**Remission.** The disappearance of evidence of a disease, usually as a result of treatment. The terms “complete” and “partial” are sometimes used to modify the term “remission.” Complete remission means that all evidence of the disease is gone. Partial remission means the disease is markedly improved by treatment, but residual evidence of the disease is present. Long-term benefit usually requires a complete remission, especially in acute leukemia or progressive lymphomas.

**Resistance to Treatment.** The ability of cancer cells to grow despite exposure to a drug that ordinarily kills cells or inhibits their growth. Cells develop drug resistance in several different ways. See Multidrug Resistance (MDR).

**Risk Factor.** A factor that is scientifically established to increase a person’s chance of getting a disease. Risk factors can be classified as either genetic (inherited), lifestyle-related, or environmental.

**RNA.** Abbreviation for ribonucleic acid, a molecule in cells that carries out the DNA’s instructions for making proteins.

**Sanctuary Sites.** Areas in which it is difficult to get a sufficient concentration of chemotherapy to destroy leukemia cells. For example, in acute lymphoblastic leukemia, the coverings (meninges) of the brain and spinal cord and the testes are noteworthy sanctuary sites.

**Spinal Tap.** See Lumbar Puncture.

**Spleen.** An organ located in the left upper portion of the abdomen just under the left side of the diaphragm. It contains clusters of lymphocytes and also filters old or worn-out cells from the blood. Enlargement of the spleen is called “splenomegaly.” Surgical removal of the spleen is known as “splenectomy.”

**Stem Cells.** Primitive cells in marrow that are essential to the formation of red blood cells, white blood cells and platelets. Stem cells are largely found in the marrow, but some leave the marrow and circulate in the blood. Using special techniques, the stem cells in blood can be collected, preserved by freezing and later thawed and then used for stem cell therapy. See Hematopoiesis.

**Stem Cell Transplantation.** See Allogeneic Stem Cell Transplantation and Autologous Stem Cell Transplantation.

**Thrombocythemia.** An above-normal concentration of platelets in the bloodstream.

**Thrombocytopenia.** A below-normal concentration of platelets in the bloodstream.

**Toxin.** A naturally derived substance that is poisonous to cells. A toxin can be attached to antibodies that then attach to cancer cells. The toxin may kill the cancer cells.

**Translocation.** An abnormality of chromosomes in marrow or lymph node cells that occurs when a piece of one chromosome breaks off and attaches to the end of another chromosome. See Mutation.

**Transplantation.** See Allogeneic Stem Cell Transplantation and Autologous Stem Cell Transplantation.

**White Blood Cells.** Any of the five major types of infection-fighting cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes. White blood cells are also called “leukocytes.”

## More Information

### Free LLS booklets include

*Blood Transfusion*

*Cancer-Related Fatigue Facts*

*Choosing a Blood Cancer Specialist or Treatment Center Facts*

*Coping With Childhood Leukemia and Lymphoma*

*Learning & Living With Cancer: Advocating for your child's educational needs*

*Long-Term and Late Effects of Treatment for Childhood Leukemia or*

*Lymphoma Facts*

*Long-Term and Late Effects of Treatment in Adults Facts*

*Pictures of My Journey: Activities for kids with cancer*

*The ALL Guide—Information for Patients and Caregivers*

*Understanding Clinical Trials for Blood Cancers*

*Understanding Side Effects of Drug Therapy*

*Understanding Lab and Imaging Tests*

Visit “Suggested Reading” at [www.LLS.org/SuggestedReading](http://www.LLS.org/SuggestedReading) to see helpful books on a wide range of topics.

# References

Acute Lymphoblastic Leukemia. National Comprehensive Cancer Network. Practice Guidelines in Oncology—v.2.2015. <http://www.nccn.org>. Accessed May 30, 2016.

Amgen announces positive Blincyto (blinatumomab) phase 2 study results in patients with relapsed/refractory Philadelphia chromosome-positive B-cell precursor acute lymphoblastic leukemia [news release]. Amgen; July 16, 2015. <http://www.amgen.com/media/news-releases/2015/07/amgen-announces-positive-blinicyto-blinatumomab-phase-2-study-results-in-patients-with-relapsedrefractory-philadelphia-chromosomepositive-bcell-precursor-acute-lymphoblastic-leukemia/>.

Amrolia P, Pule M. Chimeric antigen receptor T cells for ALL [comment]. *Lancet*. 2015;385:488-490.

Borowitz MJ, Wood BL, Devidas M, et al. Prognostic significance of minimal residual disease in high risk B-ALL: a report from Children's Oncology Group Study AALL0232. *Blood*. 2015;126(8):964-971.

Chiaretti S, Zini G, Bassan R. Diagnosis and subclassification of acute lymphoblastic leukemia [review]. *Mediterranean Journal of Hematology and Infectious Diseases*. 2014;6(1):e2014073. doi: 10.4084/MJHID.2014.073.

FDA approves Erwinaze to treat a form of leukemia [news release]. FDA; November 18, 2011. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm280525.htm>. Accessed May 30, 2016.

FDA approves Marqibo to treat rare type of leukemia [news release]. FDA; August 9, 2012. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm315027.htm>. Accessed May 30, 2016.

Howlander N, Noone AM, Krapcho M, et al, eds. SEER Cancer Statistics Review 1975-2013 [archived]. Bethesda, MD: National Cancer Institute; November 2015. [http://www.seer.cancer.gov/csr/1975\\_2013](http://www.seer.cancer.gov/csr/1975_2013). Posted April 2016. Accessed May 30, 2016.

Hunger SP, Mullighan CG. The genomic characterization of Philadelphia chromosome-like acute lymphoblastic leukemia reveals new opportunities for targeted therapy. National Cancer Institute, Office of Cancer Genomics; News & Publications, e-Newsletters (13); February 2015. <https://ocg.cancer.gov/news-publications/e-newsletter-issue/issue-13#586>. Accessed May 30, 2016.

Inaba H, Greaves M, Mullighan Mulligan CG. Acute lymphoblastic leukemia [seminar]. *Lancet*. 2013;381:(9881):1943-1955.

ISFP Practice Committee, Kim SS, Donnez J, et al. Recommendations for fertility preservation in patients with lymphoma, leukemia, and breast cancer. *Journal of Assisted Reproduction and Genetics*. 2012;29(6):465-468. doi:10.1007/s10815-012-9786-y.

Jabbour E, Kantarjian , Hagop M. How we treat patients with acute lymphoblastic leukemia? *Oncology Times*. 2016;38(1):19-21. [http://journals.lww.com/oncology-times/Fulltext/2016/01100/How\\_We\\_Treat\\_Patients\\_with\\_Acute\\_Lymphoblastic.8.aspx](http://journals.lww.com/oncology-times/Fulltext/2016/01100/How_We_Treat_Patients_with_Acute_Lymphoblastic.8.aspx). Accessed January 12, 2016.

The Leukemia & Lymphoma Society. *Facts 2015-2016*. Available at [www.LLS.org/booklets](http://www.LLS.org/booklets). Accessed May, 2016.

National Cancer Institute PDQ is not the name of an author, nor is NCI. Use the title first, since there is no author stated. Adult Acute lymphoblastic leukemia treatment (PDQ®)-Health professional version: general information about adult acute lymphoblastic leukemia (ALL). National Cancer Institute. . <http://www.cancer.gov/cancertopics/pdq/treatment/adultALL/HealthProfessional>. Updated May 27, 2016. Accessed May 30, 2016.

National Cancer Institute PDQ®. Childhood Acute Lymphoblastic Leukemia Treatment. Bethesda, MD: National Cancer Institute. <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional>. Updated May 20, 2016. Accessed May 30, 2016.

Pui CH, Mullighan CG, Evans W. Pediatric acute lymphoblastic leukemia: where are we going and how do we get there? *Blood*. 2012;120(6):1165-1174.

Qian LR, Fu W, Shen JL. Agents for refractory/relapsed acute lymphocytic leukemia in adults. *European Review for Medical and Pharmacological Sciences*. 2014;18:2465-2474.

Rheingold S., Simon C. Pediatric ALL: update on treatment and follow up care. Teleconference of The Leukemia & Lymphoma Society, Leukemia Education Series; October 23, 2013. [https://www.lls.org/sites/default/files/file\\_assets/transcript\\_all\\_102313.pdf](https://www.lls.org/sites/default/files/file_assets/transcript_all_102313.pdf). Accessed May 30, 2016.

Roberts KG, Pei D, Campana D, et al. Outcomes of children with bcr-abl 1-like acute lymphoblastic leukemia treated with risk-directed therapy based on the levels of minimal residual disease. *Journal of Clinical Oncology*. 2014;32(27):3012-3020.

Zerra P, Cochran TR, Franco VI. An expert opinion on pharmacological approaches to reducing the cardiotoxicity of childhood acute lymphoblastic leukemia therapies. *Expert Opinion on Pharmacotherapy*. 2013;14(11):1497-1513. doi: 10.1517/14656566.2013.804911.







**someday  
is today®**

fighting blood cancers

## REACH OUT TO OUR **INFORMATION SPECIALISTS**

**The Leukemia & Lymphoma Society's (LLS) Information Specialists provide patients, families and healthcare professionals with the latest information on leukemia, lymphoma and myeloma.**

Our team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 am to 9 pm (ET).

### **Co-Pay Assistance**

LLS's Co-Pay Assistance Program helps blood cancer patients cover the costs of private and public health insurance premiums, including Medicare and Medicaid, and co-pay obligations. Support for this program is based on the availability of funds by disease.

**For more information, call 877.557.2672 or visit [www.LLS.org/copay](http://www.LLS.org/copay).**



**For a complete directory of our patient services programs, contact us at**

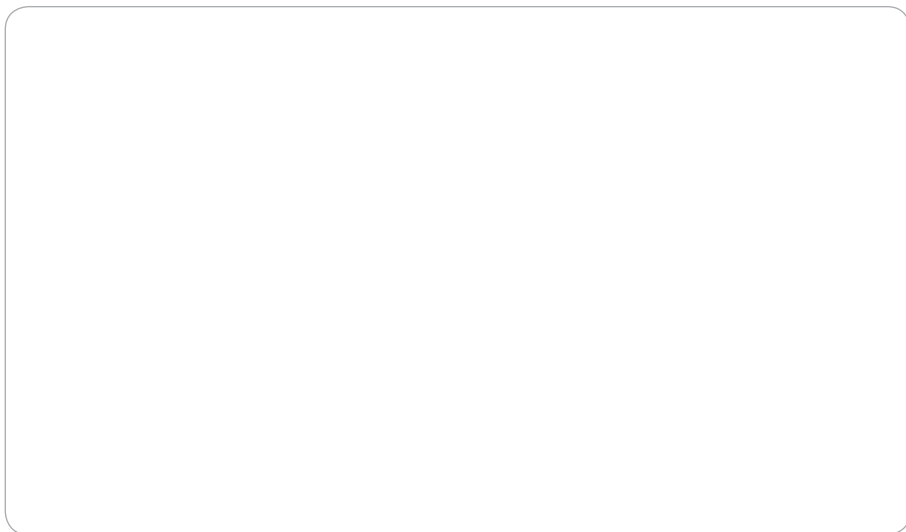
**800.955.4572 or [www.LLS.org](http://www.LLS.org)**

*(Callers may request a language interpreter.)*





For more information, please  
contact our Information Specialists  
800.955.4572 (Language interpreters  
available upon request)  
[www.LLS.org](http://www.LLS.org)



or:

**National Office**

3 International Drive, Suite 200  
Rye Brook, NY 10573

**Our Mission:**

Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

LLS is a nonprofit organization that relies on the generosity of individual, foundation and corporate contributions to advance its mission.

