NCCN GUIDELINES FOR PATIENTS®

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Acute Lymphoblastic Leukemia

Presented with support from:

NCCN NATIONAL COMPREHENSIVE CANCER NETWORK FOUNDATION®

Guiding Treatment, Changing Lives.

Available online at NCCN.org/patients

LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best cancer treatment. It explains which cancer tests and treatments are recommended by experts in acute lymphoblastic leukemia. The treatments in this book are also used for lymphoblastic lymphoma.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat acute lymphoblastic leukemia. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of acute lymphoblastic leukemia. Key points of the book are summarized in the related NCCN Quick Guide™. NCCN also offers patient resources on chronic lymphocytic leukemia, chronic myelogenous leukemia, multiple myeloma, and other cancer types. Visit NCCN.org/patients for the full library of patient books as well as other patient and caregiver resources.

About

These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNfoundation.org.

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LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients. www.LLS.org/informationspecialists

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How to use this book

Who should read this book?

Leukemia is a type of cancer that starts in blood-forming cells in the bone marrow. Acute lymphoblastic leukemia is a fast-growing type of leukemia that causes too many immature blood cells called lymphoblasts to be made in the bone marrow. Lymphoblastic lymphoma is similar, but it causes too many lymphoblasts to build up in lymph nodes or other parts of the lymphatic system. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with your doctors what care is best.

Does this book include all options?

This book includes information for many people. Your treatment team can point out what applies to you. They can also give you more information. While reading, make a list of questions to ask your doctors.

The treatment options are based on science and the experience of NCCN experts. However, their recommendations may not be right for you. Your doctors may suggest other options based on your health and other factors. If other options are given, ask your treatment team questions.

Are the book chapters in a certain order?

Early chapters explain concepts that are repeated in later chapters. Starting with **Part 1** may be helpful for many people. It explains what acute lymphoblastic leukemia is. Knowing more about this cancer may help you better understand its treatment.

Part 2 covers health tests and other care needed before starting treatment. Factors that help doctors plan treatment are described in **Part 3**.

Part 4 briefly describes all the types of treatment. Knowing what a treatment is will help you understand your options. Treatment options are presented in **Part 5**. Lastly, **Part 6** shares questions for your doctors and directs you to online resources.

Help! What do the words mean?

In this book, many medical words are included. These are words that your treatment team may say to you. Most of these words may be new to you. It may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the *Dictionary*. Acronyms are also defined when first used and in the *Glossary*. Acronyms are short words formed from the first letters of several words. One example is ALL for **a**cute **l**ymphoblastic **l**eukemia.

1
Acute lymphoblastic leukemia

You've learned that you have or may have ALL. Part 1 explains some basics about this cancer that may help you talk with your doctor. These basics may also help you start planning for treatment.

Lymphoblasts

Blood is made of many types of cells. The three main types are platelets, red blood cells, and white blood cells. Each type of blood cell has a different job.

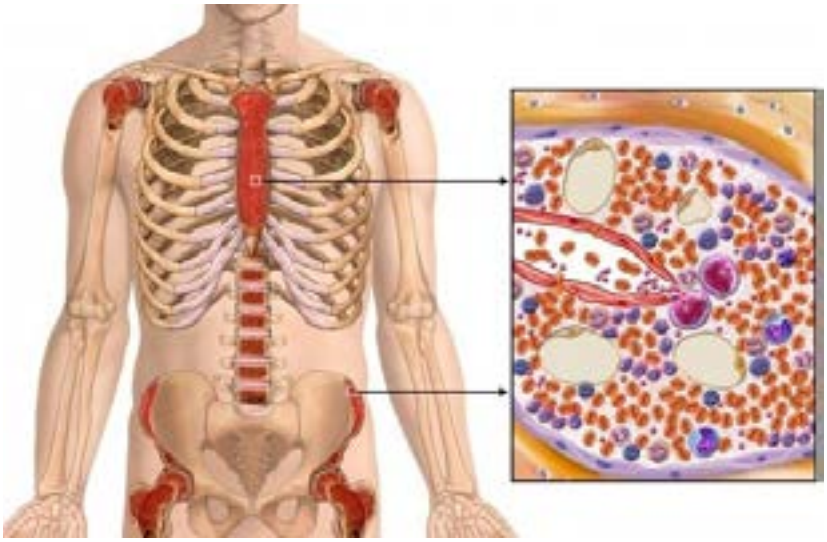
Platelets help control bleeding. Red blood cells carry oxygen throughout the body. White blood cells help fight germs and infections in the body. They are part of your body's disease-fighting system—called the immune system.

Lymphoblasts are a type of very young white blood cells. Over time, they become mature white blood cells called lymphocytes. Lymphocytes are mostly found in the blood and lymphatic system.

The two main types of lymphocytes are B-lymphocytes (B-cells) and T-lymphocytes (T-cells). B-cells make antibodies that mark germs for killing. T-cells alert your body that germs are present, kill diseased cells, and help B-cells work.

Figure 1
Blood cells in bone marrow

Bone marrow is the soft, sponge-like tissue in the center of most bones. Blood stem cells in the bone marrow make all types of blood cells.



Most blood cells are made in the bone marrow. Bone marrow is the soft, sponge-like tissue in the center of most bones. **See Figure 1**. Blood cells are made from special blood-forming cells called blood stem cells. Blood stem cells can become any type of mature blood cell.

Blood stem cells go through a series of changes as they grow and develop to make new blood cells. **See Figure 2.** Blast cells are new, very young (immature) blood cells that grow into adult (mature) blood cells over time. Different types of blast cells become different types of mature blood cells. Once they are mature, the blood cells leave the bone marrow and enter the bloodstream.

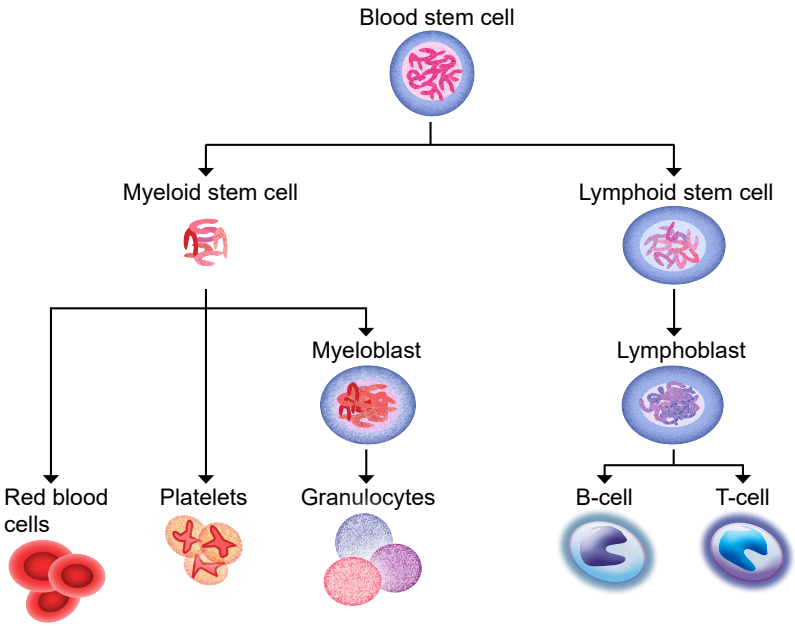
About ALL

Leukemias are cancers that start in blood-forming cells in the bone marrow. There is more than one type of leukemia. Each type of leukemia is named based on how fast it grows and the type of blood cell in which it begins.

This book focuses on ALL (**a**cute **l**ymphoblastic **l**eukemia). "Acute" means the leukemia grows and progresses very fast. "Lymphoblastic" means it starts in young white blood cells called lymphoblasts. Lymphoblastic lymphoma is similar to ALL. The main difference is that it starts in lymphoblasts within the lymphatic system.

Figure 2
Blood stem cells make all types of blood cells

A blood stem cell goes through many steps to become a red blood cell, white blood cell, or platelet. Blast cells are very young blood cells that grow into mature blood cells over time. Lymphoblasts grow into mature white blood cells called lymphocytes. White blood cells help protect the body from infection and disease.

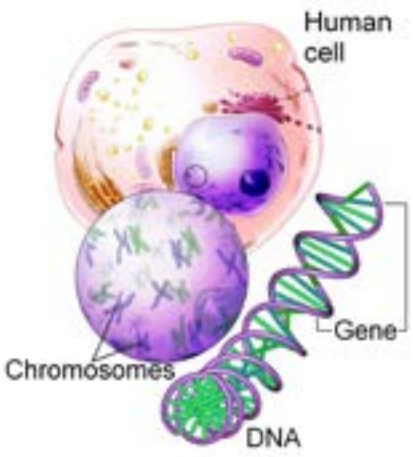


Normal blood cells grow and then divide to make new red blood cells, white blood cells, and platelets as the body needs them. When normal blood cells grow old or get damaged, they die. New blood cells are then made to replace the old ones. In a person with ALL, too many lymphoblasts are made.

Inside of all cells are coded instructions for building new cells and controlling how cells behave. These instructions are called genes. Genes are a part of DNA (**d**eoxyribo**n**ucleic **a**cid). DNA is grouped together into long strands called chromosomes. **See Figure 3.** Changes (mutations) in genes cause normal lymphoblasts to become cancer cells. Researchers are still trying to learn what causes genes to change and cause cancer.

Figure 3
Chromosomes and genes in cells

Genes are coded instructions in cells for making new cells and controlling how cells behave. Genes are a part of DNA, which is bundled into long strands called chromosomes. Every normal cell has 23 pairs of chromosomes.



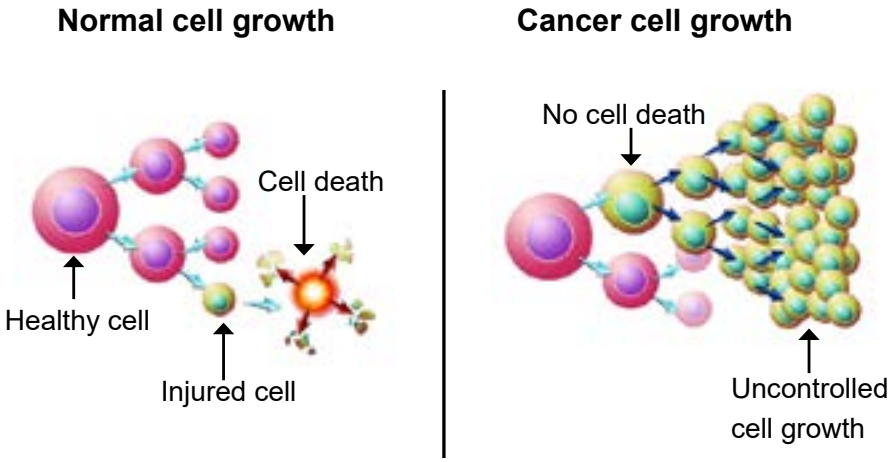
The abnormal lymphoblasts are called leukemia cells. Leukemia cells differ from normal cells in a few key ways. First, leukemia cells grow more quickly and live longer than normal cells. They divide and copy themselves to make more and more leukemia cells. **See Figure 4.** The leukemia cells quickly fill up the bone marrow and crowd out healthy blood cells that the body needs.

Second, leukemia cells don't grow into mature lymphocytes the way they should. They stay as young blast cells that don't work well. They don't help fight infections in the body.

Third, leukemia cells can spill out of the bone marrow into the bloodstream. They can then spread to other parts of the body. They may collect in the spleen, thymus, lymph nodes, liver, testicles, and the area around the brain and spinal cord.

Figure 4
Normal versus cancer cell growth

Normal cells divide to make new cells as the body needs them. Normal cells die once they get old or damaged. Cancer cells make new cells that aren't needed and don't die quickly when old or damaged.



Symptoms of ALL

A symptom is a health problem a person experiences that may indicate a disease. ALL can cause a number of different symptoms. But, some people with ALL may have few or no symptoms. Symptoms may result from a shortage of healthy blood cells or from leukemia cells collecting in certain parts of the body. See Guide 1 for a list of common symptoms that may be caused by ALL.

However, these symptoms may be caused by other health conditions. It is helpful to tell your doctor about symptoms and let him or her know how you are feeling each step of the way.

Guide 1. Common symptoms of ALL

Symptoms may include:
• Severe tiredness (fatigue)
• Weakness
• Dizziness
• Shortness of breath
• Frequent infections
• Fever
• Bruising or bleeding easily
• Pain in arms, legs, or joints
• Unusual sweating at night
• Unexplained weight loss
• Feeling of fullness in the belly area beneath the ribs

Review

- White blood cells are part of your body's disease-fighting system called the immune system.
- Most blood cells are made in the bone marrow—the soft tissue in the center of most bones.
- All types of blood cells are made from special blood-forming cells called blood stem cells.
- Blast cells are very young (immature) cells that become mature blood cells over time.
- Leukemia is a cancer that starts in blood-forming cells in the bone marrow.
- ALL is a fast-growing type of leukemia in which too many young white blood cells called lymphoblasts are made. The lymphoblasts build up in the bone marrow and crowd out healthy blood cells.
- Lymphoblastic lymphoma is similar to ALL. The key way it differs is that it starts in lymphoblasts within the lymphatic system.

2
Testing for ALL

Treatment planning starts with testing. This section describes the tests that are used to confirm (diagnose) ALL and plan treatment. This information can help you use the Treatment guide in Part 5. Not every person with acute lymphoblastic leukemia will receive every test listed.

Medical history

Your medical history includes any health events in your life and any medicines you've taken. You will be asked about any illnesses, injuries, and health problems you've had. Some health problems run in families. Thus, your doctor may also ask about the health of your blood relatives.

ALL may cause symptoms. It's important that your doctor knows if you have them. Symptoms may result from a shortage of blood cells. Or, they may result from leukemia cells collecting in certain parts of the body. But, some patients may have few or no symptoms of ALL.

A medical history is needed for treatment planning. See Guide 2 and Guide 3 for a full list of the tests that may be recommended before treatment for ALL. It may also help to make a list of old and current medicines while at home to bring to your doctor's office.

Physical exam

Doctors usually perform a physical exam along with taking a medical history. A physical exam is a review of your body for signs of disease such as infection and areas of unusual bleeding or bruising.

Your doctor may listen to your lungs, heart, and intestines. Your doctor may also feel different parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. For example, your doctor may feel your belly area (abdomen) to check for signs of an enlarged liver or spleen. In males, the testicles will also be examined.

Checking for signs of infection is a key part of the physical exam. This is often referred to as an infection evaluation. Enlarged lymph nodes are an example of a common sign of infection. Your doctor may feel certain areas such as your armpits and behind your jaw to check for enlarged lymph nodes.

Fertility

Fertility is important to think about after a cancer diagnosis. If you or your partner are able to have children, now is the time to think about this possibility before treatment gets started. Your doctor may order a pregnancy test before treatment as a precaution. This test measures the level of a hormone in the body called HCG (**h**uman **c**horionic **g**onadotropin). This hormone is made during pregnancy. Your doctor can check if you are pregnant by taking a urine sample or doing a blood test.

If you are not pregnant but interested in having children at a later time, your doctor may recommend fertility counseling. Here you can learn about fertility preservation, ways to try to protect your reproductive organs, and the ability to have children.

Once you know what you want to do, let your doctor know what your plans are for having children. Your doctor will take time to look into your case—including the risks of delaying treatment—to make a decision about the timing of fertility preservation.

Guide 2. Initial tests for diagnosis

Tests of blood or bone marrow needed for all patients
• Cell assessment (morphologic assessment)
• Cytogenetic testing
• Flow cytometry
• FISH (**f**luorescence **i**n **s**itu **h**ybridization)
• PCR (**p**olymerase **c**hain **r**eaction)

Guide 3. Tests for treatment planning

Tests needed for all patients	Tests that may be needed in some cases
• Medical history, physical exam, and check for infections	• HLA (**h**uman **l**eukocyte **a**ntigen) typing
• Pregnancy testing, fertility counseling and preservation	• MRI (**m**agnetic **r**esonance **i**maging) or CT (**c**omputed **t**omography) of the head, if symptoms
• CBC (**c**omplete **b**lood **c**ount) with differential	• If concern for cancer in lymph nodes: • CT of neck/chest/abdomen/pelvis and PET/CT (**p**ositron **e**mission **t**omography/**c**omputed **t**omography)
• Blood chemistry profile and liver function tests	• Testicular exam, including ultrasound of the scrotum as needed
• Hepatitis B/C, HIV (**h**uman **i**mmunodeficiency **v**irus), CMV (**c**yto**m**egalo**v**irus) Ab testing	• Echocardiogram or cardiac nuclear medicine scan
• Blood clotting tests	
• TLS (**t**umor **l**ysis **s**yndrome) panel	
• Lumbar puncture with IT (**i**ntra**t**hecal) chemotherapy	
• Urinalysis	

Blood tests and urinalysis

Doctors test blood to look for signs of disease and to check your general health. Blood tests are done along with other initial tests to help confirm ALL. Blood tests may be repeated to check how well treatment is working and to check for side effects. For a blood test, your doctor will insert a needle into a vein to remove a sample of blood. The blood sample will then be sent to a lab for testing. At the lab, a pathologist will examine the blood with a microscope and perform other tests.

CBC with differential

A CBC (**c**omplete **b**lood **c**ount) is a test that measures the number of blood cells in a blood sample. It includes the number of white blood cells, red blood cells, and platelets. The CBC includes a differential count. The differential measures the different types of white blood cells in the sample.

A high number of white blood cells and a low number of red blood cells and platelets may be signs of ALL. This is because ALL causes too many young white blood cells to be made. These white blood cells may crowd the bone marrow so that too few normal blood cells are made.

A CBC with differential is given with other initial tests when ALL is first suspected. It is not used alone to diagnose ALL, but it can tell your doctor about your overall health. This test is also repeated to check treatment results.

Blood chemistry profile

A blood chemistry profile measures the levels of different chemicals in your blood. Chemicals in your blood come from your liver, bone, and other organs and tissues. Abnormal levels of certain chemicals in the blood may be a sign that an organ isn't working well. Abnormal levels can be caused by cancer or other health problems.

A blood chemistry profile is given along with other initial tests for ALL. Doctors use this test to assess the general health of your body and organs. It can help check for organ damage caused by the leukemia cells or ALL treatments.

Liver function tests

The liver is an organ that removes waste from the blood and helps to digest food. Liver function tests may be done along with a blood chemistry profile. This is to check the health of your liver.

Liver function tests measure chemicals that are made or processed by the liver. Abnormal levels—too low or too high—may be a sign that your liver isn't working well. Abnormal levels may be caused by cancer, cancer treatments, or other health problems.

Testing for viruses

Certain chronic viral infections may have few symptoms, but require treatment in order to safely administer chemotherapy or SCT (**s**tem **c**ell **t**ransplant) for ALL.

For this reason, your doctor is likely to perform blood tests to look for these viruses, which include hepatitis B, hepatitis C, HIV, and in some cases CMV. See Guide 3 on page 15.

Hepatitis B and C are viruses that cause the liver to become inflamed. The HIV virus damages your immune system and causes AIDs (**a**cquired **i**mmuno**d**eficiency **s**yndrome). CMV is a common virus and causes harm to those with a weak immune system. These viruses can be transmitted through bodily fluids.

Blood clotting tests

Blood clotting tests are used to assess if blood is able to clot (coagulate) the way it should. Platelets and proteins called clotting factors help control bleeding in the body.

When a person is cut or injured, platelets and clotting factors clump together to form a clot to stop bleeding. Abnormal levels of platelets or clotting factors can cause bleeding problems.

TLS panel

TLS is a condition that occurs when many cancer cells die very quickly due to treatment. As cancer cells die, they release their contents into the blood. This can cause very high levels of certain chemicals in the blood.

A TLS panel measures the levels of these chemicals in the blood. Uric acid is one of the chemicals released by dying cancer cells. Very high levels of uric acid and other chemicals in the blood can be very dangerous. It can cause serious damage to organs such as the kidneys and heart.

HLA typing

HLAs are special proteins found on the surface of most cells in the body. The unique set of HLA proteins on a person's cells is called the HLA type or tissue type. All cells in a single person have the same HLA type. This helps the body to tell its own cells apart from foreign cells. It also affects how the body responds to foreign substances.

HLA typing is a blood test that finds a person's HLA type. This test is used to find the right donor for a stem cell transplant—a treatment that may be considered for some patients with ALL. (See Part 4 on page 38 for details about this treatment) Your tissue type and the donor's tissue type must be a near-perfect match for this treatment to work.

Type and screen

Blood types differ among people just like tissue types differ among people. Type and screen is a test that finds a person's blood type. It also looks for signs that certain blood types may not be a good match or may not be safe to give to a patient.

This test is needed if you will receive a transfusion of blood from another person (donor). The donor's blood type must be a good match that works well with your blood type.

Urinalysis

Urinalysis is a test that checks the content of urine using a microscope and chemical tests. Doctors use this test to look for small amounts of blood or other abnormal substances in urine that can't be seen with the naked eye. Blood in urine may be caused by kidney or other health problems.

Bone marrow tests

Bone marrow biopsy and aspiration

To confirm if you have ALL, a sample of tissue must be removed from your body for testing. This tissue might be a blood sample, a biopsy of an enlarged lymph node or organ, or a sample of bone marrow.

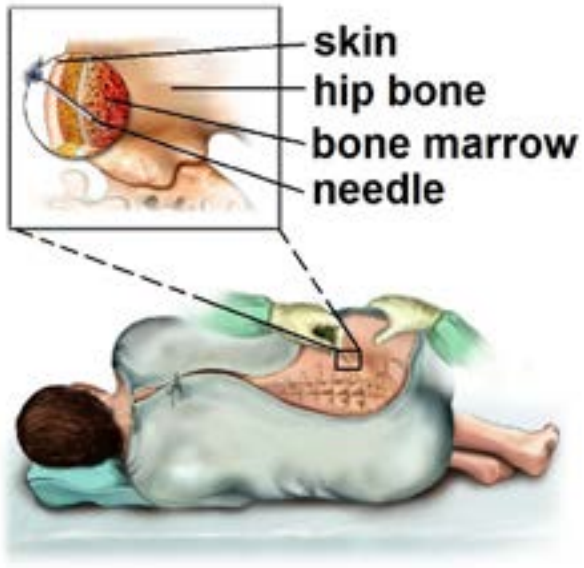
A bone marrow biopsy removes a small piece of solid bone along with a small amount of soft bone marrow inside the bone. A bone marrow aspiration removes a small amount of liquid bone marrow from inside the bone. Often, both tests are done at the same time on the back of the hip bone. You will likely lie on your side during this test. **See Figure 5.**

You may be given a light sedative before the test. Your doctor will then clean the area of skin where the biopsy will be done. Next, you will receive local anesthesia to numb the area of skin and bone beneath. Once numb, a hollow needle will be inserted into your skin and then pushed into the bone to remove the liquid bone marrow with a syringe. Then, a wider needle will be inserted into the bone to remove the solid bone and marrow sample.

You may feel some pain while the samples are being removed. Your skin may be bruised for a few days. The samples will be sent to a lab for testing.

Figure 5
Bone marrow biopsy

Doctors use a bone marrow biopsy and aspiration to remove a sample of bone marrow for testing. These tests are often done at the same time on the hip bone.



Cell assessment

At the lab, a pathologist will look at the cells in a blood or bone marrow sample with a microscope. This test is simply called cell assessment. Doctors may also refer to this test as a morphologic assessment. Special dyes may be used to stain the sample. This helps to show the differences between parts of a single cell and between many cells.

The pathologist will look at the size, shape, type, and other features of the cells in the blood or bone marrow sample. This is to see if the cells look more like normal, mature cells or more like abnormal, immature cells. The number of very immature cells—blast cells—in the sample is important.

Normally, there are no blast cells in the blood. And, in a healthy person, blast cells make up no more than 5% of cells in the bone marrow. This means that no more than 5 out of every 100 cells in the bone marrow are blast cells. In a person with ALL, blast cells make up 25% or more of cells in the bone marrow. This means that at least 25 out of every 100 cells are blast cells.

Flow cytometry

Flow cytometry is used to identify and count types of cells in a sample. It can show if cells are normal or abnormal. It can also tell the difference between types of leukemia cells. This test is used to help confirm ALL and find out the type of lymphocytes in which it started. Flow cytometry is also used to check treatment results.

ALL cells have a common pattern or “signature” of proteins. The type and pattern of proteins differs based on the type of maturity of the cell. The pattern of surface proteins is called the immunophenotype. Flow cytometry can identify the type of leukemia cells present based on the pattern of surface proteins. This is called immunophenotyping. A sample of bone marrow is often used for immunophenotyping, but a blood sample may also be used.

Flow cytometry involves first adding a marker—a light-sensitive dye—to cells. The marker reacts with surface proteins found only on certain types of cells. The cells are then passed through a flow cytometry machine. The machine identifies leukemia cells based on the pattern of surface proteins. It can also count the number of leukemia cells present. This is helpful for checking treatment results.

Flow cytometry is sometimes used to measure the amount of DNA in the leukemia cells. In such cases, a marker that reacts with DNA is used. The amount of DNA reflects the number of chromosomes in the cells. This can help to show if the cells have too many or too few chromosomes.

Genetic tests

Cytogenetic testing

Cytogenetic testing uses a microscope to examine the chromosomes inside cells. This type of test is used to look for abnormal changes in the chromosomes of the leukemia cells. It is often done on a sample of bone marrow. It can also be done on a sample of blood.

Certain chromosome changes in the leukemia cells can affect treatment options and outlook. Thus, this is a key test that is used to help plan treatment for ALL. This test is given along with other initial tests when ALL is first diagnosed. It may also be repeated to check treatment results.

For this test, a pathologist will look at a “map” of the chromosomes under a microscope. This map is called a karyotype. It will show if there are any abnormal changes in the size, shape, structure, or number of chromosomes. This test can also be used to count the number of leukemia cells.

Many types of chromosome changes can happen in ALL. The leukemia cells may have an abnormal number of chromosomes—too many or too few. The leukemia cells may also have more than one type of chromosome change.

Sometimes parts of chromosomes break off and switch with each other. This is called a translocation. The Philadelphia chromosome is a key example of a translocation that happens in some people with ALL. The Philadelphia chromosome is caused by a translocation between parts of chromosomes 9 and 22. **See Figure 6.**

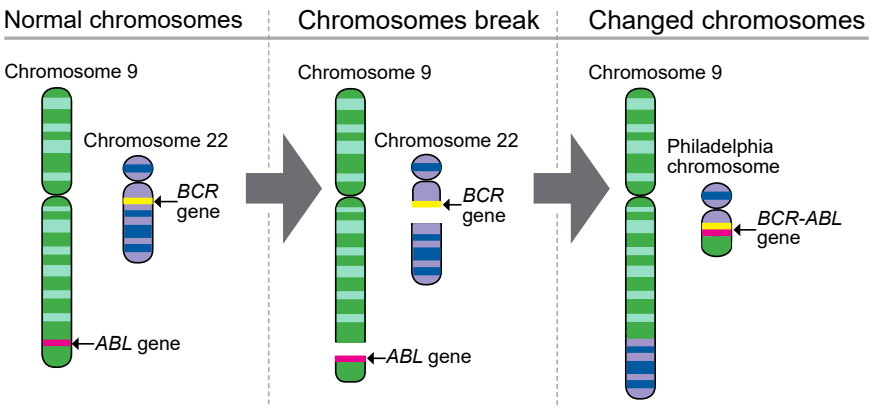
This translocation also forms the abnormal *BCR-ABL* fusion gene on the Philadelphia chromosome. A fusion gene is a new gene that is formed when parts of two separate genes are joined (fused) together.

FISH

FISH (**f**luorescence **i**n **s**itu **h**ybridization) is a very sensitive lab test that can detect certain abnormal changes in a cell's genes or chromosomes. It can detect most abnormal changes that can be seen with a microscope. It can also detect some changes that are too small to be seen with basic cytogenetic testing (karyotyping).

Figure 6 Philadelphia chromosome

The Philadelphia chromosome is formed by a translocation between parts of chromosomes 9 and 22. It contains the abnormal *BCR-ABL* fusion gene. This is a key chromosome change that affects which treatments are best for you.



Doctors use FISH to detect certain abnormal gene and chromosome changes in leukemia cells. This test uses special color dyes, called probes, that attach only to certain genes or parts of certain chromosomes.

For example, the Philadelphia chromosome is a common abnormal change found in adults with ALL. This chromosome contains the *BCR-ABL* fusion gene. To detect this, FISH uses color probes that attach to the *BCR* gene and the *ABL* gene. The *BCR-ABL* fusion gene is shown by the overlapping colors of the two probes.

Like cytogenetic testing, FISH is used to help plan and monitor treatment for ALL. This test can be performed on a sample of blood or bone marrow.

PCR/MRD

PCR (**p**olymerase **c**hain **r**eaction) is a very sensitive test. Like FISH, it detects abnormal gene and chromosome changes (mutations) in cells. However, it can find mutations that are too small to be seen with a microscope.

Doctors use this test to detect certain gene and chromosome changes that are commonly found in ALL. An example of this is the *BCR-ABL* fusion gene. This gene is found on the Philadelphia chromosome. PCR can detect gene mutations and measure the number of cells that have them.

PCR is very helpful for checking how well treatment is working. When the cells have certain genetic changes, PCR can find and measure the amount of leukemia cells left. This test can find one leukemia cell among more than 10,000 normal cells. PCR is the method used to find the amount of disease present after treatment. Doctors use this to assess for MRD (**m**inimal **r**esidual **d**isease). The presence of MRD is a key factor used to decide if more treatment is needed. (See page 37 for more details about checking treatment results.)

PCR can be done on a sample of bone marrow or blood. But, bone marrow is often preferred, especially when checking treatment results.

Spinal fluid test

ALL can spread to the fluid around your brain and spinal cord. This is called cerebrospinal fluid or spinal fluid. To determine whether or not cancer is in spinal fluid, a sample must be removed and tested.

A lumbar puncture is a procedure that is used to remove spinal fluid. It is also called a spinal tap. A lumbar puncture is often done when ALL is first diagnosed. But, it may be done at a later time that fits with your treatment plan. A lumbar puncture can also be used to inject cancer drugs into the spinal fluid.

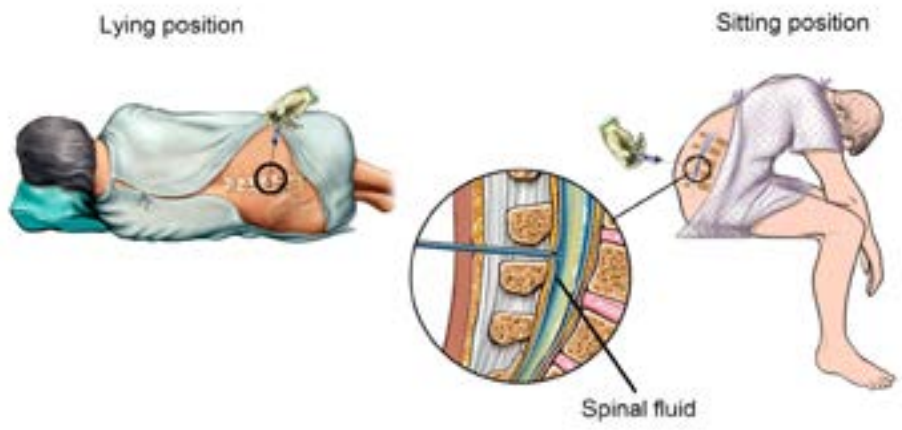
During this test, you will be lying down or sitting on an exam table as shown in **Figure 7**.

If lying down, your knees will be tucked up near your chest. If sitting, you will lean slightly forward and down over your knees.

Local anesthesia will be used to numb the lower part of your back over your spine. Next, a thin needle will be inserted between the bones of your spine and into the space around your spinal cord. The needle will be used to take a sample of spinal fluid. You may feel some pressure during the procedure. The fluid sample will then be sent to a lab for testing for the presence of leukemia cells.

Figure 7
Lumbar puncture

Doctors perform a lumbar puncture to remove a sample of spinal fluid to test for leukemia cells. A lumbar puncture may also be used to give liquids such as drug treatments. When drugs are injected into the spinal fluid, it is called IT (intrathecal) therapy.



Imaging tests

Imaging tests take pictures of the inside of your body. Imaging tests are not often used for ALL. However, they may be useful to look for infections or to check for signs that ALL has spread to the brain and spinal cord.

Imaging tests are often easy to undergo. Before the test, you may be asked to stop eating or drinking for several hours. You also should remove any metal objects that are on your body. For some imaging tests, a contrast dye may be injected into your vein to make the pictures clearer.

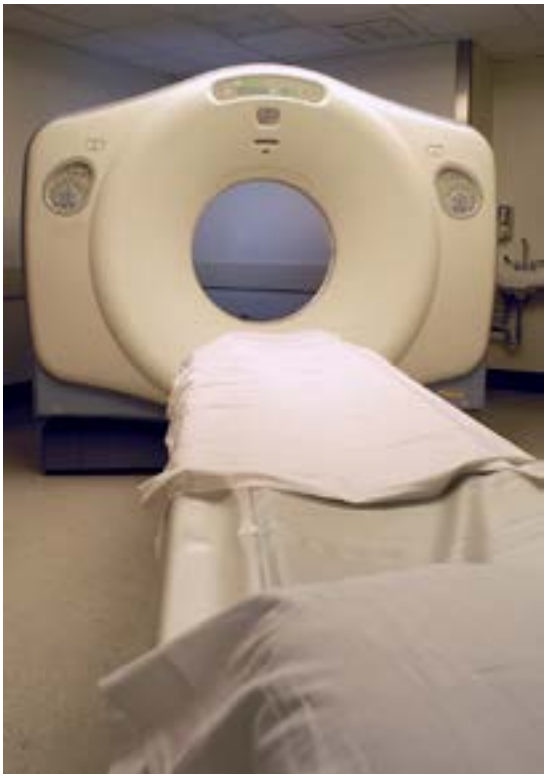
CT scan

CT (**c**omputed **t**omography) takes many pictures of a body part from different angles using x-rays. **See Figure 8**. A computer combines all the pictures to make one clear picture. A CT scan of your head may be needed if you have symptoms that suggest ALL might have spread to your brain and spinal cord.

Occasionally leukemia may grow outside of the bone marrow - most commonly in lymph nodes. A CT scan of the head, neck, chest, abdomen, and/or pelvis can be used to look for leukemia in these places. In some cases, your doctor may also perform a CT to look for infection.

Figure 8
CT scan machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.



MRI scan

MRI (**m**agnetic **r**esonance **i**maging) uses radio waves and magnets to take pictures of the inside the body. MRI scans create clear pictures of soft tissues and bones. MRI scans are also very helpful for looking at the brain and spinal cord. An MRI scan of your head and/or spinal cord should be done if you have symptoms that suggest ALL might have spread to your brain and spinal cord.

PET scan

PET (**p**ositron **e**mission **t**omography) shows how your cells are using a simple form of sugar. For a PET scan, a sugar radiotracer will first be injected into your body. The radiotracer is detected by a special camera during the scan. Any cells that use sugar more quickly, including normal cells (such as those within the brain) and abnormal cells (such as leukemia), can be detected by this scan. PET scans are often combined with a CT scan to help your doctors better understand which areas of the body may be impacted by leukemia. Like standard CT imaging, PET/CT imaging is most helpful when your doctor suspects there may be leukemia growing in places other than the bone marrow.

Ultrasound

An ultrasound is a test that uses sound waves to take pictures of the inside of the body. For males, this test may be ordered after a testicular exam to examine the area further. An ultrasound of the scrotum (sac that contains the testicles) may be needed. It can show if there is a mass in the testicles. If a mass is present, it will help doctors see if it is solid or fluid-filled (cyst). Cysts are usually not cancer (benign).

Echocardiogram or cardiac nuclear medicine scan

An echocardiogram is an imaging test of your heart. It uses sound waves to make pictures. This test is used to check how well your heart is working. It shows your doctor how your heart is beating and pumping blood.

A cardiac nuclear medicine scan also assesses how your heart is working. This test uses a radiotracer, just like a PET scan, to get detailed pictures. It can help doctors see how well your heart is able to pump blood.

Some treatments for ALL can damage your heart. Thus, your doctor may want to test how well your heart works in order to plan the best treatment. This is especially true for an MRI scan.

Review

- Cancer tests are used to plan treatment and check how well treatment is working.
- Your medical history and physical exam can reveal signs of disease.
- Blood tests are used to look for signs of cancer and check how well your organs are working.
- To confirm if you have ALL, a sample of tissue—blood or bone marrow—must be removed from your body for testing. A bone marrow biopsy and aspiration are used to remove a sample of bone marrow.
- Flow cytometry is used to identify the type of cells present in a sample based on the set on proteins on the cell surface. This is called immunophenotyping.
- Cytogenetic testing, PCR, and FISH help doctors detect abnormal chromosome changes in leukemia cells.

3
Treatment planning

Doctors look at a number of factors to plan the best treatment for you. This includes your age, general health, and certain features of the leukemia cells. Some of these factors can also affect and help predict the likely treatment outcome (prognosis). Part 3 describes each of these factors and how they are used to plan treatment.

Subtypes of ALL

ALL is divided (classified) into smaller groups based on certain features of the leukemia cells. These smaller groups are called subtypes. The ALL subtype is an important factor that doctors use to plan treatment.

Cell subtypes

Doctors classify ALL into two broad subtypes based on the type of lymphocyte the leukemia cells come from. These are called cell subtypes. Each type of lymphocyte can be identified by the unique set of proteins on the surface of the cells. The unique set and pattern of proteins is called the immunophenotype.

There are many ALL cell subtypes based on immunophenotype. Some are more common or more important for treatment planning than others.

The two main cell subtypes based on immunophenotype are described below.

- **B-cell ALL** – This subtype of ALL starts in young cells that normally become mature B-cells (B-lymphocytes). This is the most common ALL subtype overall. Among adults with ALL, about 75 out of 100 have B-cell ALL. Among children with ALL, about 88 out of 100 have this subtype.

- **T-cell ALL** – This subtype of ALL starts in young cells that normally become mature T-cells (T-lymphocytes). This subtype is less common overall, but occurs more often in adults than in children. Among adults with ALL, about 25 out of 100 have T-cell ALL. Among children with ALL, about 12 out of 100 have this subtype.

Cytogenetic subtypes

Doctors also group ALL into subtypes based on the type of abnormal changes found in the chromosomes of the leukemia cells. Cytogenetics is the study of chromosomes. Thus, ALL subtypes that are based on chromosome changes are called cytogenetic subtypes.

Many types of chromosome changes may happen in ALL. The Philadelphia chromosome is an abnormal chromosome found in the leukemia cells of some people with ALL. It is formed when parts of chromosomes 9 and 22 break off and switch with each other. ALL can be grouped into many subtypes based on chromosome changes. Some are more common or more important for treatment planning than others.

The two main cytogenetic subtypes that doctors use for treatment planning are described next.

- **Ph-positive ALL** – In this subtype of ALL, the leukemia cells have the Philadelphia chromosome. This is the most common cytogenetic subtype in adults with ALL. It is rare in children. The chance of having this cytogenetic subtype increases with age. Among adults with ALL, about 25 out of 100 have Ph-positive ALL. Among children with ALL, about 3 out of 100 have this subtype.

- **Ph-negative ALL** – In this subtype of ALL, the leukemia cells do not have the Philadelphia chromosome. This cytogenetic subtype is more common in children than in adults. Among adults with ALL, about 75 out of 100 have Ph-negative ALL. Among children with ALL, more than 95 out of 100 have this subtype.

Age issues in ALL

A person's age at the time ALL is diagnosed is one of the most important factors that doctors use to plan treatment. As a result, recommendations in the Treatment guide are divided into two age groups:

- AYA (**a**dolescent and **y**oung **a**dult) patients who are 15 to 39 years of age

- Older adult patients who are 40 years of age or older

AYAs and older adults differ in many ways. These differences carry over into personal, social, emotional, and medical needs. There are also key differences between AYAs and older adults with ALL that doctors must consider when making treatment decisions. In particular, AYAs have much better outcomes when given more intensive ALL treatments like those designed for children.

Intense treatments can cause serious side effects that get harder to tolerate with age. Because AYAs are usually able to tolerate the intensive treatments, they benefit greatly and have much better treatment results. The side effects of intensive treatments tend to be more severe and harder to recover from for older patients.

Generally, doctors use the age of 65 as the cut-off for intensive treatments. This is because older patients may not be able to tolerate them. But, age alone is not a good gauge for deciding if a person can tolerate these treatments.

A person older than 65 may be still in good health overall and not have other serious health problems. In this case, he or she may still benefit from more intensive treatments. Likewise, a person younger than 65 may be in poorer health overall and have other serious health problems. In this case, he or she may not be able to tolerate intensive treatments.

Thus, doctors must also consider your overall health as well as your age. Assessing your overall health, fitness, and other current health problems is very important. This includes checking how well organs such as your heart, lungs, liver, and kidneys are working.

About AYAs

AYAs have a unique set of needs and challenges that differ greatly from those of young children and older adults.

Discussing all of these important aspects is beyond the scope of this book. More details and information focused on AYAs with cancer can be found in the *NCCN Guidelines for Patients®: Adolescents and Young Adults with Cancer*. These guidelines are available for free at www.nccn.org/patients.

Prognostic factors

Several important factors affect treatment options and the likely outcome (prognosis) of ALL. Something that affects and helps predict prognosis is called a prognostic factor.

Doctors use certain prognostic factors to help predict how ALL will likely progress and respond to treatment. This helps doctors plan how intensive treatment needs to be for each patient to kill all the leukemia cells and keep them from coming back. These factors can also help doctors decide which type of treatment will likely work best.

Some prognostic factors are linked with a lower chance (risk) that ALL will come back after treatment. These are called “good risk” features. Other factors are linked with a higher risk that ALL will come back after treatment. These are called “poor risk” features.

Doctors give more intensive treatments for ALL that has poor risk features. But, the presence of poor risk features does not mean ALL can’t be cured.

A number of factors can affect prognosis in ALL. Some are more important for treatment planning than others. The two main factors doctors use to plan treatment are your age and the cytogenetic subtype. But, other prognostic factors for ALL that may also be helpful include:

- **Age:** The leukemia cells in older patients tend to be more resistant to treatment. Stronger treatments may be needed to kill all the leukemia cells and keep them from coming back.
- **Philadelphia chromosome:** Leukemia cells that have the Philadelphia chromosome can be harder to treat. But, new treatments have improved outcomes in the past few years.
- **Chromosome changes:** Certain changes in chromosomes can make leukemia cells harder to treat. This includes having fewer than the normal number of chromosomes and having five or more chromosome changes in the leukemia cells.
- **White blood cell count:** The number of white blood cells in the blood at the time ALL is diagnosed can also affect prognosis. Having a very high white blood cell count at diagnosis is a poor risk feature in children and adolescents with ALL. This factor has a much smaller effect on treatment planning for adults with ALL.

Review

- A number of factors help guide treatment options and the likely outcome (prognosis).
- Something that affects and helps predict the likely outcome is called a prognostic factor.
- Age is one of the most important factors that affect treatment options.
- To help plan treatment, ALL is classified into smaller groups called subtypes based on certain features of the leukemia cells.
- ALL is classified into groups based on the type of cell—called the cell subtype. It is also classified into smaller groups based on the type of chromosome changes in the leukemia cells. These are called cytogenetic subtypes.

4
Overview of cancer treatments

Part 4 describes the main treatments that are used for ALL. Knowing what a treatment is will help you understand your treatment options listed in the Treatment guide in Part 5. There is more than one treatment for ALL.

Clinical trials

Clinical trials are a very important treatment option for ALL. New tests and treatments aren't offered to the public as soon as they're made. They first need to be studied. A clinical trial is a type of research that studies a test or treatment.

Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow's standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with ALL. Future tests and treatments that may have better results than today's treatments will depend on clinical trials.

Clinical trials are an important treatment option for people with ALL. Doctors are still studying what treatments work best for ALL. NCCN experts recommend that all patients with ALL receive treatment on a clinical trial if possible. Receiving treatment on a clinical trial has been shown to improve outcomes.

New tests and treatments go through a series of clinical trials to make sure they're safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials are done in four steps, called phases.

Some examples of the four phases of clinical trials for treatment are:

- **Phase I** trials aim to find the best dose and way to give a new drug with the fewest side effects.
- **Phase II** trials assess if a drug works to treat a specific type of cancer.
- **Phase III** trials compare a new drug to the standard treatment.
- **Phase IV** trials test new drugs approved by the FDA (U.S. **F**ood and **D**rug **A**dministration) in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you'll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any other test or treatment, there may be side effects. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often have a similar cancer type and general health. This is to know that any progress is because of the treatment and not because of differences between patients.

To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study's risks and benefits should be described and may include others than those described above.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you are getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 6.

Chemotherapy

The main treatment for ALL involves the long-term use of chemotherapy. Chemotherapy is the use of drugs to kill cancer. Many people refer to this treatment as “chemo.” Chemotherapy drugs kill fast-growing cells throughout the body, including normal cells and cancer cells.

Different types of chemotherapy drugs work different ways to kill leukemia cells or stop new ones from being made. Thus, more than one drug is often used. When only one drug is used, it’s called a single agent. A combination regimen is the use of two or more cancer drugs. This is also called multiagent chemotherapy.

Chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next treatment cycle. Cycles vary in length depending on which drugs are used. The number of treatment days per cycle and the total number of cycles given also varies based on the regimen used. A regimen is a treatment plan that specifies the drug(s), dose, and schedule for a course of treatment. A chemotherapy regimen consists of a set number of cycles given over a set amount of time. You may be given one drug at a time or combinations of drugs at the same time.

Treatment for ALL often uses 4- or 5-drug combination regimens. Some of the most common chemotherapy drugs used for ALL are listed in Guide 4.

Guide 4. Common chemotherapy drugs for ALL

Generic name	Brand name (sold as)
Asparaginase erwinia chrysanthemi	Erwinaze®
Clofarabine	Clolar®
Cyclophosphamide	--
Cytarabine	Cytosar-U®
Daunorubicin	Cerubidine®
Doxorubicin	--
Idarubicin	Idamycin PFS
Ifosfamide	--
Mercaptopurine or 6-MP (6-**m**ercapto**p**urine)	Purinethol®, Purixan™
Methotrexate	--
Nelarabine	Arranon®
Pegaspargase	Oncaspar®
Vincristine	--
VSLI (**v**incristine **s**ulfate **l**iposome **i**njection)	Marqibo

Corticosteroids, also simply called steroids, are often given along with chemotherapy drugs to treat ALL. Steroids are drugs that are used to relieve swelling and inflammation. But, some steroids also have anti-cancer effects. The two main steroids used in ALL regimens are prednisone and dexamethasone.

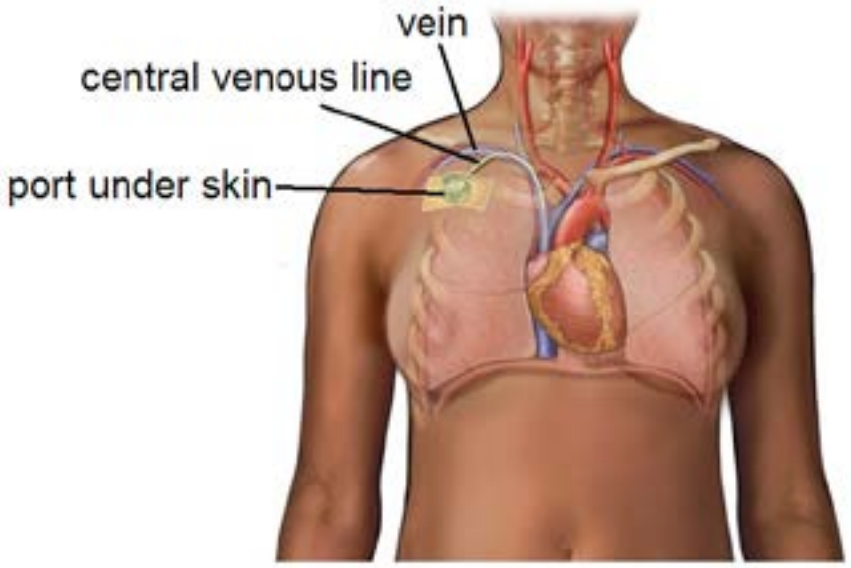
How chemotherapy drugs are given

Chemotherapy drugs may be given as a pill that you swallow or as a liquid that is injected into your body with a needle. When given this way, the drugs travel in your bloodstream to kill leukemia cells in all parts of your body. This is called systemic chemotherapy.

Drugs may be injected into a vein, muscle, or under your skin. An IV (**i**ntra**v**enous) infusion is a slow injection into a vein. The IV infusion may take a few hours. Or, it may be given over several days—called a continuous infusion. An intramuscular injection is when drugs are given into a muscle. A subcutaneous injection is when drugs are given under the skin.

Figure 9
Central venous line and port

Chemotherapy is often given as a slow injection into a vein through a long, thin tube. This tube is called a central venous line or catheter. The central line may be attached to a port that is placed just under your skin.



Regimens for AYAs and older adults

A protocol is a detailed outline or plan of a medical treatment, study, or procedure. A treatment protocol covers all phases of ALL treatment. It states which drugs and regimens will be used during each phase of treatment. A protocol often includes many chemotherapy regimens that are given at different times over the course of ALL treatment.

Treatments designed for children with ALL are called pediatric protocols. The chemotherapy regimens used for children are often called pediatric regimens. Treatments designed for older adults with ALL are called adult protocols and adult regimens.

Many of the same drugs are used for children and older adults with ALL. But, the doses and schedules are different. AYAs are patients aged 15 to 39 years. Importantly, studies show that AYAs have much better outcomes when treated more like children.

Experts recommend that treatment for AYAs should be based on pediatric protocols. This is referred to as a pediatric-inspired protocol. The main differences between pediatric and adult treatments are described below.

Differences between pediatric and adult treatment regimens

Drug dosage

Pediatric regimens are more intense and complex than those given to older adults. They use high (intensified) doses of certain chemotherapy drugs that can be hard for older adults to tolerate.

Drugs used

Pediatric regimens tend to use more pegaspargase, vincristine, and steroids such as dexamethasone and prednisone. Overall, the doses of these drugs are higher than what is given to adults. Some patients may develop an allergy to pegaspargase. If this happens, asparaginase erwinia chrysanthemi may be given instead.

In contrast, adult regimens tend to use more cyclophosphamide and anthracyclines such as doxorubicin and daunorubicin. These drugs lower (suppress) the bone marrow's ability to make new blood cells. Thus, they are also called myelosuppressive drugs. Adult regimens also use allogeneic SCT (**s**tem **c**ell **t**ransplant) more often.

Dose intensification

Intensified doses of drugs are given at certain points during treatment for children and adults. But, pediatric protocols give intensified doses more often throughout the course of treatment. In contrast, adult regimens tend to be less intense. The types and doses of drugs used in adult regimens are meant to be tolerable for people across a wide age range. AYAs treated with these regimens may be under-dosed.

Length of treatment

In pediatric protocols, treatment is given for a longer period of time overall. CNS (**c**entral **n**ervous **s**ystem) preventive treatment is started earlier and given longer. Children often receive maintenance therapy for about 3 years. Adult regimens tend to give maintenance for about 2 years.

Side effects of chemotherapy

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each treatment for ALL can cause side effects. The reactions to chemotherapy differ between people. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious.

Often, doctors give IV chemotherapy through a thin, soft tube called a central venous line or catheter. One end of the central line will be inserted into a large vein in your chest or upper arm. The other end of the central line may stay outside of your body. Or, it may be attached to a port that is placed just under your skin. **See Figure 9** on page 33.

With a central line, doctors can give IV chemo treatments without "sticking" your vein with a needle every time. Doctors can also use the central line to give other medicines and take blood samples. A central line can be left in place for weeks or months.

Leukemia cells can also spread to the brain and spinal cord. This is called CNS disease. Chemotherapy that is injected into a vein cannot always reach this area. Instead, drugs must be injected directly into the spinal fluid. When drugs are given this way, it is called IT (**i**ntra**t**hecal) therapy or IT chemotherapy. IT chemotherapy is often given during a lumbar puncture. (**See Figure 7** on page 22.) IT chemotherapy is used to prevent and treat CNS disease.

Chemotherapy treatment phases

The treatment of ALL is a long-term process that lasts two to three years. ALL treatment is given in three main steps, called phases. The length of each phase may vary based on the intensity of the treatments and other factors.

1 Induction

The first phase of ALL treatment is called induction. This phase may also be called by other names such as remission induction or induction therapy. The goal of induction therapy is to kill as many leukemia cells as possible. It is meant to cause (induce) a remission. A remission is when no leukemia cells can be seen in blood or bone marrow viewed with a microscope and blood cell counts are back to normal.

The induction phase often lasts about four weeks (one month). You may need to stay in the hospital for some or most of this time.

CNS prevention and treatment is started during induction. It is given throughout all phases of ALL treatment. This part of treatment is also referred to as CNS prophylaxis. CNS treatment is given to keep ALL from spreading to the area around the brain and spinal cord. When leukemia cells are found in this area, it is called CNS disease.

2 Consolidation

The second phase of ALL treatment is called consolidation. This phase may also be called by other names such as intensification or postremission consolidation. Consolidation therapy is given once ALL is in remission. The goal of consolidation therapy is to kill any leukemia cells that may still be in your body. During this phase, treatments are intensified. This means that drugs are given in higher doses than during induction. The consolidation phase often lasts for a few months.

3 Maintenance

The third phase of ALL treatment is called maintenance. The goal of maintenance therapy is to keep ALL from coming back. Most maintenance drugs are given orally, and patients are usually treated in an outpatient setting. The lower doses tend to have less severe side effects. The maintenance phase lasts about two to three years. Consolidation and maintenance are often jointly called postremission therapy. Postremission therapy refers to any treatments given after ALL is in complete remission.

Targeted therapy

Targeted therapy is treatment with drugs that target a specific or unique feature of cancer cells. Because these drugs specifically target cancer cells, they may be less likely to harm normal cells throughout your body. The targeted therapy drugs that are used for ALL are listed in Guide 5 and are described next.

Guide 5. Targeted therapy drugs for ALL

Generic name	Brand name (sold as)	Type of drug
Blinatumomab	Blincyto™	Monoclonal antibody
Bosutinib	Bosulif®	TKI
Dasatinib	Sprycel®	TKI
Imatinib mesylate	Gleevec®	TKI
Nilotinib	Tasigna®	TKI
Ponatinib	Iclusig®	TKI
Rituximab	Rituxan®	Monoclonal antibody

Tyrosine kinase inhibitors

TKI (**t**yrosine **k**inase **i**nhibitor) therapy is a type of targeted therapy. TKIs are used for a subtype of ALL in which the leukemia cells have the Philadelphia chromosome. This subtype is called Ph-positive ALL. The Philadelphia chromosome contains the abnormal *BCR-ABL* fusion gene.

TKIs target the abnormal BCR-ABL protein that helps leukemia cells grow. This protein is made by the *BCR-ABL* gene. It is a type of protein called a tyrosine kinase. TKIs block (inhibit) the BCR-ABL protein from sending the signals that cause too many leukemia cells to form.

TKIs are made in the form of a pill that is swallowed. TKIs are typically not used alone to treat ALL. Instead, a TKI is added to a combination chemotherapy regimen. The use of TKIs has greatly improved treatment outcomes for this type of ALL.

TKI drug resistance

A treatment response is an improvement in disease that is caused by treatment. Drug resistance is when ALL doesn't respond to a drug. There is more than one type of drug resistance.

Primary resistance is when ALL doesn't respond at all to a drug taken for the first time. This type of resistance is rare in ALL. Secondary resistance is more common. It is when ALL responds to a drug at first and then stops responding over time.

A number of factors may cause or lead to secondary resistance. Most often, it is caused by mutations in the part of the *BCR-ABL* gene that makes the BCR-ABL protein. These mutations change the shape of the BCR-ABL protein. This can affect how well certain TKIs work. New mutations can happen over time during TKI therapy. This can cause the TKI to stop working.

But, each TKI drug works in a slightly different way. One TKI drug may be able to work against a mutation that another TKI can't. Therefore, switching to a different TKI may result in a treatment response after a prior TKI stops working.

Treatment response

A *treatment response* is an outcome or improvement caused by treatment. Doctors first check for a treatment response at the end of induction therapy. To check how well treatment worked, your doctor will test a sample of blood and bone marrow with a microscope.

The goal of ALL treatment is to result in a complete remission. Even with a complete remission, there may still be a small number of leukemia cells left in the body that can't be seen with a microscope. This is called *MRD* (**m**inimal **r**esidual **d**isease).

Once ALL is in complete remission, very sensitive tests are used to check for MRD. After a complete remission, more treatment is needed to kill every last leukemia cell and keep them from coming back. This is called *postremission therapy*.

A *relapse* is when ALL comes back after a complete remission. Sometimes the leukemia cells don't respond to induction therapy. ALL that is not in complete remission after induction is called *refractory ALL*.

A complete remission is when:

- ✓ No leukemia cells are seen in your bone marrow with a microscope.
- ✓ No more than 5 out of 100 cells in your bone marrow are blast cells.
- ✓ No blast cells are in your bloodstream.
- ✓ All blood cell counts are back to normal.
- ✓ All signs and symptoms of ALL are gone.

Side effects of TKIs

Some side effects listed below are caused by only one TKI. Others are caused by all or most TKIs but differ in how likely they are to occur. Some common side effects of TKIs are low blood cell counts, abnormal bleeding, fatigue, nausea and vomiting, diarrhea, and stomach or belly pain.

These drugs may cause swelling due to fluid buildup around the eyes or in the hands and feet. Fluid may also collect around the lungs. Other common side effects include skin rashes, headaches, and muscle, bone, and joint pain. A rare but serious side effect that may happen with TKIs is a change in the rhythm of your heartbeat.

Other rare but serious side effects may be caused by certain TKIs. For example, dasatinib may cause fluid buildup around the lungs. Nilotinib may cause the amount of sugar (glucose) in the blood to be higher than normal. Serious side effects of ponatinib include heart problems, blood clots, narrowing of blood vessels, heart attack, and stroke. Liver problems or inflammation of the pancreas may also happen.

Monoclonal antibodies

Monoclonal antibodies are another type of targeted therapy used for ALL. A monoclonal antibody is a type of immune system protein that is made in a lab. Monoclonal antibodies attach (bind) to proteins on cancer cells. Most monoclonal antibodies can bind to only one protein.

Blinatumomab

Blinatumomab is one of the newer treatments for ALL. It is a monoclonal antibody that may be used for certain patients with B-cell ALL after other treatments didn't work well.

Blinatumomab is a special kind of antibody that can bind to two proteins at the same time. It binds to a protein called CD19 that is found on immature B-cells and some leukemia cells. It also binds to a protein called CD3 that is found on normal T-cells. T-cells are part of the body's immune system. By binding to these two proteins, blinatumomab links the T-cells to the leukemia cells. This helps the immune system find and kill the leukemia cells.

Blinatumomab is a liquid that is slowly injected into a vein over 28 days. This is called a continuous infusion. Blinatumomab should only be given in a cancer center that has experience with this drug. You may need to stay in the hospital for the first few days of treatment.

Side effects of this drug are fever, skin rash, nausea, diarrhea, constipation, swelling of the hands and feet, headache, and shaking (tremor). It can also cause low white blood cell counts, which increases the risk of infection.

Though uncommon, a severe reaction during the infusion may happen. This can cause trouble breathing, headache, feeling dizzy or lightheaded, low blood pressure, fever, chills, and face swelling. Other less common but serious side effects are seizures, trouble speaking or slurred speech, passing out, confusion, and loss of balance.

Rituximab

Rituximab is a monoclonal antibody that may be used to treat certain patients with B-cell ALL. It binds to a protein called CD20. This protein is found on the surface of normal and abnormal B-cells. And, it is found on the leukemia cells of about half of adults with B-cell ALL.

When rituximab binds to CD20, it sends a signal to the cell to die. It also marks the cells for destruction by the immune system. Rituximab is not used alone to treat ALL. Instead, it is added to a chemotherapy combination regimen. It is given as a liquid that is slowly injected into a vein.

You may have an allergic reaction while receiving rituximab. Other common side effects are chills, infections, body aches, tiredness, and low blood cell counts. Rituximab rarely increases the chance of developing TLS, heart problems, and blockage and holes in your intestines.

Stem cell transplant

An SCT is a treatment that destroys cells in the bone marrow then replaces them with new, healthy blood-forming cells. These blood-forming cells are called blood stem cells or hematopoietic stem cells. This treatment is also called a hematopoietic cell transplant.

The goal of an SCT is to cure cancer by replacing unhealthy blood stem cells with healthy ones that will attack cancer cells. This is done by suppressing the bone marrow and cancer with chemotherapy then transplanting healthy blood stem cells. The healthy blood stem cells will grow, form new bone marrow and blood cells, and attack remaining cancer cells.

For the treatment of ALL, blood stem cells from a donor are used for the transplant. This is called an allogeneic SCT. Before the transplant, special testing must be done to make sure the donor is a good match for you. HLA typing is used to find a person's tissue type, called an HLA type. (See page 17 for more details on HLA typing.)

An allogeneic SCT creates a new immune system for your body. Another benefit of this transplant is the GVL (**g**raft-**v**ersus-**l**eukemia) effect. The GVL effect is an attack on the leukemia cells by the transplanted blood stem cells. The steps of treatment with an allogeneic SCT are described next.

Conditioning treatment

Before the transplant, you will receive high-dose chemotherapy and maybe high-dose radiation therapy. This is called conditioning treatment since it prepares (conditions) your body to receive the donated blood stem cells.

The chemotherapy is given to destroy any remaining leukemia cells in your bone marrow. But, it also destroys normal blood cells in your bone marrow. This greatly weakens your immune system so that your body doesn't kill the transplanted blood stem cells.

For some patients, lower doses of chemotherapy or radiation may be used before the transplant. This is called non-myeloablative or reduced-intensity conditioning. This type of conditioning may be a good option for certain patients who are older or in poorer health. It can often work just as well as high-dose conditioning.

Transplanting the stem cells

After the chemotherapy, the blood stem cells will be put into your body with a transfusion. A transfusion is a slow injection of blood products into a large vein. This process can take several hours to complete.

The transplanted stem cells then travel to your bone marrow and grow. They will make new, healthy blood cells. This is called engraftment. It usually takes about 2 to 4 weeks.

Until then you will have little or no immune defense. This puts you at high risk for infection and bleeding. You will likely need to stay in a hospital in a very clean room for some time. It may take a few weeks or months for blood cells to fully recover so that your immune system is back to normal.

Considering allogeneic SCT

An allogeneic SCT is a complex treatment and can cause very serious side effects. Thus, it may not be a good treatment choice for every patient with ALL. Many treatment centers will only consider this treatment option for patients younger than 65 years of age.

Your doctor will look at many factors to help decide if an allogeneic SCT is a good choice for you. These factors include your age and general health, certain prognostic factors, how well other treatments worked, and if a well-matched donor has been found.

An allogeneic SCT is not used as the first or main treatment for ALL. It may be used as part of consolidation therapy for certain patients with Ph-positive ALL or in patients with other poor risk features. Doctors may also consider an allogeneic SCT if prior treatments fail to kill all of the leukemia cells or keep them away.

Side effects of allogeneic SCT

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Common side effects of chemotherapy, which is given before the transplant, are described on page 34. You will likely feel tired and weak shortly after the transplant while waiting for the new blood stem cells to grow in the bone marrow.

Allogeneic transplants have a high risk of GVHD (**g**raft-**v**ersus-**h**ost **d**isease). GVHD is when the donated cells see the cells in your body as foreign and attack them. The parts of the body most commonly damaged by GVHD are the skin, intestines, and liver.

GVHD is a serious side effect that can cause the transplant to fail by stopping the donated blood stem cells from growing in your bone marrow. GVHD can happen within a few weeks after the transplant or much later. Your doctor may give you medicine that suppresses your immune system to try to prevent this side effect.

Radiation therapy

Radiation therapy uses high-energy rays to treat cancer. The rays damage the genes in cells. This either kills the cancer cells or stops new cancer cells from being made. Radiation therapy may be given in different ways. For ALL, radiation therapy is given from a machine outside the body. This method is called EBRT (**e**xternal **b**eam **r**adiation **t**herapy).

Radiation therapy is not usually part of the main treatment for ALL. But, it may be used to treat leukemia cells that have spread to fluid around the brain and spinal cord. This is called CNS disease. To treat CNS disease, radiation therapy is aimed at the brain and/or spine. Doctors may refer to this as cranial irradiation or cranial-spinal irradiation. Radiation therapy may also be used to treat leukemia cells that have spread to the testicles. Lastly, radiation therapy can be used as part of the treatment given prior to an SCT.

During radiation treatment

You will lie down on a treatment table and stay very still. You will be alone while a technician operates the EBRT machine from a nearby room. The technician will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. A session can take between 15 and 30 minutes. Radiation therapy is often given 5 days a week for 2 to 3 weeks.

Side effects of radiation therapy

Side effects of radiation therapy depend on the dose and the area of your body being treated. Most of the side effects go away soon after treatment ends. Some of the most common side effects of radiation therapy include:

- Skin changes
- Hair loss
- Fatigue
- Upset stomach
- Diarrhea

Supportive care

Supportive care is treatment given to relieve the health problems caused by cancer and side effects of cancer treatment. Managing symptoms and side effects with supportive care is important for your quality of life and treatment outcome. Supportive care options for common health problems that affect patients with ALL are described next.

Nausea and vomiting

Many chemotherapy drugs can cause nausea and vomiting. Medicine can be given to lessen or prevent this side effect. Drugs that prevent nausea and vomiting are called antiemetics. Antiemetics should be given before starting chemotherapy treatment. See *NCCN Guidelines for Patients®: Nausea and Vomiting*. These guidelines are available for free at www.nccn.org/patients.

Low blood cell counts

ALL and its treatment can cause low blood cell counts. Very low blood cell counts can cause a number of health problems. But, there are many ways to manage this side effect.

A low number of red blood cells can cause fatigue and shortness of breath. If your red blood cell count is low, you may be given a transfusion of red blood cells. A low number of platelets can cause you to bleed or bruise easily. A transfusion of platelets may be given if your platelet count is very low.

Having a low number of white blood cells is also very common during treatment for ALL. Transfusions are not used to treat low white blood cell counts. Instead, you may be given a type of drug called a growth factor.

Growth factors help the bone marrow to make new healthy white blood cells. This helps to increase the white blood cell count quickly. Growth factors are recommended during parts of ALL treatment that lower (suppress) the bone marrow's ability to make new blood cells.

Infection risks

ALL and its treatment can cause very low white blood cell counts. White blood cells are part of the immune system and help fight off infection and disease. Having a very low white blood cell count puts you at risk for infections.

Medicines may be given to prevent or treat infections. Antibiotics can prevent or treat infections caused by bacteria. An antifungal is medicine for infection caused by fungus. An antiviral is medicine for infection caused by a virus. Your doctor may also suggest that you get vaccines for pneumonia and the flu.

Tumor lysis syndrome

TLS (**t**umor **l**ysis **s**yndrome) is a rare condition that occurs when many cancer cells die very quickly due to cancer or its treatment. Chemotherapy may destroy large numbers of leukemia cells quickly. As the cells die, they break down and release their contents into the blood. This changes the normal balance of chemicals in the blood. It can cause very high levels of certain chemicals.

Uric acid is one of the chemicals released by dying cancer cells. Very high levels of uric acid and other chemicals can be very bad for the body. It can cause severe damage to organs such as the kidneys and heart. Drugs such as allopurinol and rasburicase may be given to prevent or lessen the effects of TLS.

Complementary and alternative medicine

CAM (**c**omplementary and **a**lternative **m**edicine) is a group of treatments sometimes used by people with cancer. Many CAMs are being studied to see if they are truly helpful.

- Complementary medicines are meant to be used alongside standard therapies, most often for relaxation, improving your health, or to prevent or reduce side effects.

- Alternative medicine is treatment or techniques that are used instead of standard treatments such as chemotherapy or radiation. Some are sold as cures even though they haven't been proven to work in clinical trials.

Many cancer centers or local hospitals have complementary therapy programs that offer acupuncture, yoga, and other types of therapy.

It's important to tell your treatment team if you are using any complementary medicine, especially supplements, vitamins, or herbs. Some of these things can interfere with your cancer treatment. For more information about CAM, ask your doctor and visit the websites in Part 6.

Review

- Treatment for ALL is given in steps, called phases: induction, consolidation, and maintenance.
- CNS preventive treatment is given during all phases of treatment.
- The main treatment of ALL involves long-term use of chemotherapy.
- Chemotherapy is treatment with drugs that kill fast-growing cells, including leukemia cells and normal cells.
- Targeted therapy drugs specifically target cancer cells.
- A stem cell transplant replaces damaged or diseased bone marrow with healthy donor blood stem cells.
- A clinical trial studies a test or treatment to see how safe it is and how well it works. Clinical trials are how we learn which treatments are best.
- Treatment for AYA patients should be based on regimens which have been highly effective for children with ALL.
- Supportive care is treatment given to relieve the symptoms of cancer or side effects of cancer treatment.

No family facing a cancer diagnosis should have to search the internet to get facts. We need something we can trust. Because of the endorsement of The Leukemia and Lymphoma Society, we know we can trust the updated NCCN Guidelines. Knowledge is power and understanding ALL helped me be a better advocate for our son.

- Jill, for her son Aaron

5
Treatment guide

Part 5 is a guide through the treatment options for patients with ALL. However, these treatments may also be used for patients with lymphoblastic lymphoma.

This information is taken from the treatment guidelines written by NCCN experts of ALL. These treatment guidelines list options for people with ALL in general. Your doctors may suggest other treatment for you based on your health and personal needs. Discuss and decide on your treatment options with your doctor.

NCCN experts recommend that all patients receive treatment in a specialized cancer center with expertise and experience in ALL. The treatment of ALL is very complex. It's important to be cared for by a multidisciplinary team of experts with experience in treating patients your age. Access to clinical trials is also a chief priority. Specialized cancer centers, such as large academic centers, have the experts, experience, and research to provide the best care for patients with ALL.

Treatment options

There are multiple treatment options for ALL. Treatment options that are best for you depend on a number of factors. This includes the features of the cancer, such as the cytogenetic subtype, as well as your age and health status.

The treatment options in Part 5 are grouped by patient age and presence of the Philadelphia chromosome. The type and intensity of treatment differs based on your age and health. To plan treatment, doctors put patients into two main age groups.

The AYA group includes patients who are 15 to 39 years of age. The older adult group includes patients who are 40 years of age or older. The other main factors that affect treatment planning and options are described in Part 3 on page 26.

AYAs with Ph-positive ALL

Guide 6. Remission induction for AYAs with Ph-positive ALL

Induction therapy options	Response	Next options
Clinical trial or Multiagent chemotherapy regimen + TKI or TKI + corticosteriods	Complete remission	Monitor for MRD
	Less than complete remission	Treatment for relapsed/refractory ALL

Guide 6 shows the induction therapy options for AYAs with Ph-positive ALL. Induction therapy is the first phase of treatment for ALL. It is also called remission induction. The goal is to kill all of the leukemia cells in your bone marrow and put ALL into complete remission.

Induction therapy usually consists of high doses of chemotherapy drugs. It is very intensive and lasts about four weeks (one month). You may need to stay in the hospital for some or all of the time during this treatment.

Induction therapy options

In general, there are a few options to choose from for induction therapy. Treatment within a clinical trial is preferred if one is open and is the right fit for you. Other options include a multiagent chemotherapy regimen or a corticosteroid (prednisone or dexamethasone), both combined with a TKI.

TKIs are a type of targeted therapy. TKIs block the cancer-causing action of the *BCR-ABL* fusion gene. This gene is found on the Philadelphia chromosome. The use of TKIs has greatly improved treatment outcomes for Ph-positive ALL. Importantly, adding a TKI to the multiagent chemotherapy regimen increases the chance of a complete remission. Imatinib, dasatinib, ponatinib, or nilotinib are the TKIs used for induction therapy.

Induction regimens for AYAs generally include a combination of vincristine, pegaspargase, a steroid (prednisone or dexamethasone), and an anthracycline (doxorubicin or daunorubicin). Some regimens may also include cyclophosphamide.

CNS preventive treatment is given to all patients during the induction phase. For CNS treatment, drugs are often injected into the spinal fluid during a lumbar puncture. When drugs are given this way, it is called IT therapy or IT chemotherapy.

CNS treatment may include IT methotrexate alone or with other drugs such as IT cytarabine and an IT steroid (prednisone or dexamethasone). When all three drugs are given, it is called triple IT therapy. Methotrexate, cytarabine, and 6-MP may also be given as IV injections for CNS treatment. Rarely, CNS disease may be found when ALL is first diagnosed. In this case, your doctor may consider giving cranial irradiation as well.

Response and next options

At the end of induction, your doctor will assess how well treatment worked. A treatment response is an outcome or improvement caused by treatment. To check the response, your doctor will test a sample of blood and bone marrow with a microscope. A complete remission is when no leukemia cells are seen in the blood or bone marrow and all signs and symptoms of ALL are gone. (See page 37 for more details about treatment responses.)

If tests show a complete remission, then your doctor will test for MRD. MRD is when a very small amount of leukemia cells remains in your body after a course of treatment. With MRD, the amount of leukemia cells left is too small to be seen with a microscope.

PCR and flow cytometry are very sensitive tests that doctors use to check for MRD. These tests can detect a single leukemia cell among more than 10,000 normal cells. They can be done on a sample of blood or bone marrow. But, bone marrow is preferred. Testing for MRD can help your doctor decide if more intensive treatments are needed for consolidation. (See page 21 for more details on PCR/MRD.)

If tests show less than a complete remission, this means treatment wasn't able to kill enough leukemia cells in your body. ALL that is not in complete remission after induction is called refractory ALL. In this case, treatment with other drugs or regimens will be tried. See *Next steps* at the end of this section.

Next steps

If induction therapy resulted in a complete remission, see Guide 7 on page 48 for the next options. If induction therapy resulted in less than a complete remission, see Guide 16 on page 65 for the next options.

Guide 7. Postremission consolidation and maintenance

Consolidation therapy options		Maintenance therapy options
Allogeneic SCT if a donor is available	→	• Consider post-SCT TKI

or
If an allogeneic SCT donor is not available, continue multiagent chemotherapy regimen + TKI
	→	• TKI, and
		• Maintenance therapy with:
		  • Monthly vincristine/prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

Guide 7 shows the treatment options for AYAs with Ph-positive ALL in complete remission after induction therapy. Consolidation therapy is the second phase of treatment for ALL. The goal of this phase is to kill any leukemia cells that may still be in your body. It is followed by maintenance therapy. These phases are jointly referred to as postremission therapy since they are given after ALL is in remission.

Your doctor will look at many factors to help plan consolidation therapy. This includes the ALL cell subtype, chromosome changes, results of MRD testing, and other prognostic factors. Your general health, current symptoms, and side effects will also be noted. This can help to decide if you need and can tolerate more intensive treatment for consolidation.

Consolidation therapy options

There are two main options for consolidation therapy. The first option is to have an allogeneic SCT. This option is recommended if a well-matched donor has been found. Consolidation with an allogeneic SCT may help keep ALL from coming back after a complete remission.

But, it is a very intensive treatment and may not be a good choice for everyone.

Your doctor will look at a number of factors to decide if an allogeneic SCT is a good choice for you. This includes your age, prognostic factors, and how well prior treatments worked. For some AYA patients, an allogeneic SCT may offer the best chance of a long-lasting remission. For other patients, an allogeneic SCT might not be better than chemotherapy and a TKI.

The second option is to stay on multiagent chemotherapy combined with a TKI. This option is suggested if a well-matched donor for the SCT has not been found. This may also be a good option if your doctor thinks an allogeneic SCT is too intense for you.

Consolidation therapy may include combinations of drugs similar to those used for induction. A TKI should be added to the consolidation therapy regimen for all patients with Ph-positive ALL. Imatinib, dasatinib, nilotinib, and ponatinib are TKIs used for this phase. Staying on treatment with a TKI can help keep ALL from coming back after a complete remission.

Chemotherapy drugs are given in higher (intensified) doses during consolidation. CNS preventive treatment is also usually given throughout this phase of treatment. Consolidation therapy may last several months. How long it lasts and the total number of cycles varies based on the regimen used. The full treatment regimen should be followed all the way through consolidation and to the end of maintenance.

Maintenance therapy options

The third phase of ALL treatment is called maintenance. This phase is started after you finish consolidation therapy. Maintenance therapy is given to keep up (maintain) the good results of prior treatments. The goal is to prevent a relapse after induction and consolidation therapy. A relapse is when leukemia cells come back after a complete remission.

Staying on treatment with a TKI is a key part of maintenance therapy. Most maintenance regimens include weekly methotrexate and daily 6-MP. Often, monthly pulses of vincristine and a steroid (prednisone or dexamethasone) are also given for 2 to 3 years. A TKI such as imatinib, dasatinib, nilotinib, or ponatinib should be added to the maintenance regimen your doctor plans for you.

Staying on treatment with a TKI is a key part of maintenance therapy. If you are not treated with an allogeneic SCT, you will likely receive a TKI together with a maintenance chemotherapy regimen for 2 to 3 years.

Maintenance therapy drugs are often given in lower doses and cause fewer side effects. CNS preventive treatment can also be given throughout this treatment phase. This regimen may include weekly methotrexate, daily 6-MP, monthly vincristine, and a steroid (prednisone or dexamethasone). Methotrexate and 6-MP can affect the liver or lead to low blood counts, and may require dose reduction or discontinuation when treating together with a TKI.

Your doctor will typically continue the same TKI used during your earlier phases of therapy, as long as you are tolerating and responding well to it.

If you are treated with an allogeneic SCT, maintenance therapy with a TKI may be recommended. In this situation, the TKI is most commonly given without other chemotherapy medicines. It is usually given for at least one year but doctors are not completely sure how long it should continue.

At this point of care, your doctor will consider MRD testing on a regular basis if you have a complete remission. This testing may happen at least every 3 months. Testing may occur more often if MRD is detected.

Next steps

After completing consolidation and maintenance therapy, see Guide 15 on page 63 for follow-up testing.

Older adults with Ph-positive ALL

Guide 8. Remission induction for older adults with Ph-positive ALL

Health status	Induction therapy options	Response
Patients <65 years of age without serious health problems	• Clinical trial • Multiagent chemotherapy regimen + TKI	• Complete remission, monitor for MRD • Less than complete remission, start treatment for relapsed/refractory ALL
Patients ≥65 years of age or with other serious health problems	• Clinical trial • TKI + corticosteroids • TKI + chemotherapy	• Complete remission, monitor for MRD • Less than complete remission, start treatment for relapsed/refractory ALL

Guide 8 shows the induction therapy options for older adults with Ph-positive ALL. Induction therapy is the first phase of treatment for ALL. It is also called remission induction. The goal is to kill all of the leukemia cells in your bone marrow and put ALL into complete remission.

Induction therapy may consist of high doses of chemotherapy drugs. It is very intensive and lasts about four weeks. You may need to stay in the hospital some or all of the time during this treatment.

CNS preventive treatment is given to all patients during the induction phase. For CNS treatment, drugs are often injected into the spinal fluid during a lumbar puncture. When drugs are given this way, it is called IT therapy or IT chemotherapy.

CNS treatment may include IT methotrexate alone or with other drugs such as IT cytarabine and an IT steroid (dexamethasone or prednisone). When all three drugs are given, it is called triple IT therapy. Methotrexate, cytarabine, and 6-MP may also be given as IV injections for CNS treatment. Rarely, CNS disease may be found when ALL is first diagnosed. In this case, your doctor may consider giving cranial irradiation as well.

Induction therapy options

Often, age 65 is the cut-off for intensive treatment. But, age alone is not a good gauge of a person's overall health or fitness for intensive treatment. When choosing an induction regimen, your doctors will look at your age, general health, organ function, and other current health conditions. This will help your doctor to know if you are able to receive very strong treatments.

If you are younger than age 65, or you don't have other serious health problems, there are two main options to choose from. Treatment within a clinical trial is preferred if one is open and is the right fit for you. The other option is to have a multiagent chemotherapy regimen combined with a TKI. The TKIs used for induction therapy include imatinib, dasatinib, nilotinib, and ponatinib.

TKIs are a type of targeted therapy. TKIs block the cancer-causing action of the *BCR-ABL* fusion gene. This gene is found on the Philadelphia chromosome. The use of TKIs has greatly improved treatment outcomes for Ph-positive ALL. Importantly, adding a TKI to the multiagent chemotherapy regimen increases the chance of a complete remission.

If you are age 65 or older, or you have other serious health problems, there are three main options to choose from. Treatment within a clinical trial is preferred if one is open and is the right fit for you. The second option is to have treatment with a TKI (imatinib or dasatinib) and a steroid. Prednisone and dexamethasone are the main steroids that may be used. The third option is to receive a TKI along with a multiagent chemotherapy regimen.

Steroids may be easier to take than chemotherapy. Chemotherapy regimens can cause severe side effects that may be very hard for some patients to tolerate. If needed, chemotherapy drugs may be given in lower doses to lessen the side effects.

Response

At the end of induction, your doctor will assess how well treatment worked. A treatment response is an outcome or improvement caused by treatment. To check the response, your doctor will test a sample of blood and bone marrow with a microscope. A complete remission is when no leukemia cells are seen in the blood or bone marrow and all signs and symptoms of ALL are gone. (See page 37 for more details about treatment responses.)

If tests show a complete remission, then your doctor will test for MRD. MRD is when a very small amount of leukemia cells remains in your body after a course of treatment. With MRD, the amount of leukemia cells left is too small to be seen with a microscope.

PCR and flow cytometry are very sensitive tests that doctors use to check for MRD. These tests can detect a single leukemia cell among more than 10,000 normal cells. They can be done on a sample of blood or bone marrow. But, bone marrow is preferred. Testing for MRD can help your doctor decide if more intensive treatments are needed for consolidation therapy.

If tests show less than a complete remission, this means treatment wasn't able to kill enough leukemia cells in your body. ALL that is not in complete remission after induction is called refractory ALL. In this case, treatment with other drugs or regimens will be tried.

Next steps

If induction therapy resulted in a complete remission, see Guide 9 on page 52 for the next options. If induction therapy resulted in less than a complete remission, see Guide 16 on page 65 for the next options.

Guide 9. Postremission consolidation and maintenance

Health status	Consolidation therapy options	Maintenance therapy options

Patients <65 years of age without serious health problems	• Allogeneic SCT if a donor is available
	
	or
	
	• If allogeneic SCT donor is not available, continue multiagent chemotherapy regimen + TKI
		• Consider post-SCT TKI
		
		• TKI, and
		• Maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

Patients ≥65 years of age or with other serious health problems	• Continue TKI ± corticosteroids
	• Continue TKI ± chemotherapy
		• TKI, and
		• Maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

Guide 9 shows the treatment options for older adults with Ph-positive ALL after induction therapy resulted in a complete remission. Consolidation—also called intensification—is the second phase of treatment for ALL. This may also be referred to as postremission therapy since it is given after ALL is in complete remission. The goal of consolidation is to kill any leukemia cells that may still be in your body.

Consolidation therapy

Your doctor will look at many factors to help plan consolidation therapy. This includes the ALL cell subtype, chromosome changes, results of MRD testing, and other prognostic factors. Your general health, current symptoms, and side effects will also be noted. This can help to decide if you need and can tolerate more intensive treatment for consolidation.

If you are younger than age 65, or you don't have other serious health problems, there are two main options to choose from. The first option is to have an allogeneic SCT. This option is recommended if a well-matched donor has been found. Consolidation with an allogeneic SCT may help keep ALL from coming back after a complete remission. But, it is a very intensive treatment that may not be a good choice for everyone.

Your doctor will look at a number of factors to decide if an allogeneic SCT is a good choice for you. This includes your age, general health, and ability to tolerate intensive treatments.

For some patients, an allogeneic SCT may offer the best chance of a long-lasting remission.

The second option is to stay on the multiagent chemotherapy regimen and TKI. This option is suggested if a well-matched donor for the SCT has not been found. This may also be a good option if your doctor thinks an allogeneic SCT is too intense for you.

Consolidation therapy may include combinations of drugs similar to those used for induction. A TKI should be added to the consolidation therapy regimen for all patients with Ph-positive ALL. Imatinib, dasatinib, nilotinib, and ponatinib are the TKIs used for this phase. Staying on treatment with a TKI can help keep ALL from coming back after a complete remission.

Often, chemotherapy drugs are given in higher (intensified) doses during consolidation. CNS preventive treatment can also be given throughout this phase of treatment. Consolidation therapy may last several months. How long it lasts and the total number of cycles varies based on the regimen used. The full treatment regimen should be followed all the way through consolidation and to the end of maintenance.

If you are age 65 or older, or you have other serious health problems, there are two main options to choose from. A key part of both options is to continue treatment with a TKI. Imatinib, dasatinib, nilotinib, and ponatinib are the TKIs that may be used. The first option is to keep taking the TKI with or without steroids such as prednisone or dexamethasone. The second option is to keep taking the TKI with or without chemotherapy.

Maintenance therapy options

The third phase of ALL treatment is called maintenance. This phase is started after you finish consolidation therapy. Maintenance therapy is given to keep up (maintain) the good results of prior treatments. The goal is to prevent a relapse after induction and consolidation therapy. A relapse is when leukemia cells come back after a complete remission.

Staying on treatment with a TKI is a key part of maintenance therapy. Most maintenance regimens include weekly methotrexate and daily 6-MP. Often, monthly pulses of vincristine and a steroid (prednisone or dexamethasone) are also given. A TKI such as imatinib, dasatinib, nilotinib, or ponatinib should be added to the maintenance regimen your doctor plans for you.

After consolidation with an allogeneic SCT, maintenance therapy with a TKI is often recommended. The TKI may be given alone. Or, other drugs may also be given if side effects aren't too severe.

Methotrexate and 6-MP can affect the liver and lower the bone marrow's ability to make new blood cells. These side effects can be severe and hard to tolerate. If needed, lower doses of these drugs may be given to lessen the side effects.

Maintenance therapy drugs are often given in lower doses and cause fewer side effects. CNS preventive treatment can also be given throughout this treatment phase. Maintenance therapy is given for about two to three years. But, the total length varies based on the regimen used. Adult regimens tend to give maintenance therapy for a shorter amount of time than pediatric-inspired regimens.

Your doctor will consider MRD testing on a regular basis for if you have a complete remission. This testing may happen at least every 3 months. Testing may occur more often if MRD is detected.

AYAs with Ph-negative ALL

Guide 10. Remission induction for AYAs with Ph-negative ALL

Induction therapy options	Response	Next options
Clinical trial or Pediatric-inspired chemotherapy regimen or Multiagent chemotherapy regimen	• Complete remission	• Monitor for MRD
	• Less than complete	• Treatment for relapsed/refractory ALL

Guide 10 shows the induction therapy options for AYAs with Ph-negative ALL. Induction therapy is the first phase of treatment for ALL. It is also called remission induction. The goal is to kill all of the leukemia cells in your bone marrow and put ALL into complete remission.

Induction therapy usually consists of high doses of chemotherapy drugs. It is very intensive and lasts about four weeks (one month). You may need to stay in the hospital for some or all of the time during this treatment.

Induction therapy options

In general, there are three main options to choose from for induction therapy. Treatment within a clinical trial is preferred if one is open and is the right fit for you. The other options are to receive multiagent chemotherapy outside of a clinical trial.

A regimen based on treatment designed for children with ALL may be selected. This is called a pediatric-inspired regimen or a pediatric-inspired protocol. But, other multiagent chemotherapy regimens that have been studied in AYAs may also be used.

Induction regimens tend to use a combination of vincristine, pegaspargase, a steroid (prednisone or dexamethasone), and an anthracycline (doxorubicin or daunorubicin). Some regimens may also include cyclophosphamide, etoposide, or (for CD20-positive disease) rituximab.

Pediatric-inspired regimens often start CNS preventive treatment very early at the start of the induction phase. For CNS treatment, drugs are often injected into the spinal fluid during a lumbar puncture. When drugs are given this way, it is called IT therapy or IT chemotherapy.

CNS treatment may include IT methotrexate alone or with other drugs such as IT cytarabine and an IT steroid (dexamethasone or prednisone). When all three drugs are given, it is called triple IT therapy. Methotrexate, cytarabine, and 6-MP may also be given as IV injections for CNS treatment. Rarely, CNS disease may be found when ALL is first diagnosed. In this case, your doctor may consider giving cranial irradiation as well.

Response and next options

At the end of induction, your doctor will assess how well treatment worked. A treatment response is an outcome or improvement caused by treatment. To check the response, your doctor will test a sample of blood and bone marrow with a microscope. A complete remission is when no leukemia cells are seen in the blood or bone marrow and all signs and symptoms of ALL are gone.

If tests show a complete remission, then your doctor may test for MRD. MRD is when a very small amount of leukemia cells remains in your body after a course of treatment. With MRD, the amount of leukemia cells left is too small to be seen with a microscope.

PCR and flow cytometry are very sensitive tests that doctors use to check for MRD. These tests can detect a single leukemia cell among more than 10,000 normal cells. They can be done on a sample of blood or bone marrow. Bone marrow is usually preferred. Testing for MRD can help your doctor decide if more intensive treatments are needed during consolidation therapy.

If tests show less than a complete remission, this means treatment wasn't able to kill enough leukemia cells in your body. ALL that is not in complete remission after induction is called refractory ALL. In this case, treatment with other drugs or regimens will be tried.

Next steps

If induction therapy resulted in a complete remission, see Guide 11 on page 56 for the next options. If induction therapy resulted in less than a complete remission, see Guide 17 on page 67 for the next options.

Guide 11. Postremission consolidation and maintenance

MRD results	Consolidation therapy options	Next options
Persistent or late MRD	• Blinatumomab • Consider allogeneic SCT	• Start follow-up testing

MRD not found	• Continue multiagent chemotherapy regimen	• Maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

	• Consider allogeneic SCT	• Start follow-up testing

MRD unknown	• Allogeneic SCT
	• Consider continuing multiagent chemotherapy regimen
		• After chemotherapy, maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP
		• After SCT, start follow-up testing

Guide 11 shows the treatment options for AYAs with Ph-negative ALL in complete remission after induction therapy. Consolidation therapy is the second phase of treatment for ALL. The goal of this phase is to kill any leukemia cells that may still be in your body. It is followed by maintenance therapy. These phases are jointly referred to as postremission therapy since they are given after ALL is in remission.

Your doctor will look at many factors to help plan consolidation therapy. This includes the ALL cell subtype, chromosome changes, results of MRD testing, and other prognostic factors. Your general health, current symptoms, and side effects will also be considered. This can help to decide if you need and can tolerate more intensive treatment for consolidation.

Consolidation therapy options

There are some main options to choose from for consolidation therapy. The options depend on whether or not MRD is found.

If MRD is found, that means the disease is persistent, so your doctor may consider blinatumomab. This medication has been shown to be helpful in treating disease that continues despite other treatment. It is known as a bispecific T-cell engager for how it works with the immune system to find and attack leukemia cells. It can cause serious side effects, so your doctor will assess your health and monitor you closely if you take this drug. An allogeneic SCT may also be considered.

Your doctor will look at a number of factors to decide if an allogeneic SCT is a good choice for you. This depends on your age, general health, and ability to tolerate intensive treatments.

Consolidation therapy when MRD is not found or is unknown may include combinations of drugs similar to those used for induction. In pediatric-inspired regimens, it tends to include high-dose methotrexate, cytarabine, 6-MP, and pegaspargase. Chemotherapy drugs are often given in higher (intensified) doses during consolidation. CNS preventive treatment is also usually given throughout this phase of treatment.

Another option to consider when MRD is not found or is unknown is allogeneic SCT. This is a very intensive treatment performed in specialized centers, and may not be a good choice for everyone. Your doctor may consider this option if tests found MRD after induction, even if MRD is not found later in treatment. This may also be a good choice if the leukemia cells have certain poor risk features. A poor risk feature is something that increases the chance that ALL might come back after treatment. Examples of poor risk features include having less than the normal number of chromosomes or having five or more abnormal chromosome changes.

Consolidation therapy may last several months. How long it lasts and the total number of cycles varies based on the regimen used. The full treatment regimen should be followed all the way through consolidation and to the end of maintenance.

Next options and maintenance therapy

After consolidation with an allogeneic SCT, you will begin follow-up testing. After consolidation with multiagent chemotherapy, you will receive maintenance therapy. Maintenance therapy is the third phase of ALL treatment.

Maintenance therapy is given to keep (maintain) the good results of prior treatments. The goal is to prevent a relapse after induction and consolidation therapy. A relapse is when leukemia cells come back after a complete remission.

If you are not treated with an allogeneic SCT, you will likely be treated with a maintenance chemotherapy regimen for 2 to 3 years. Maintenance therapy drugs are often given in lower doses and cause fewer side effects. CNS preventive treatment can also be given throughout this treatment phase. This regimen may include weekly methotrexate, daily 6-MP, monthly vincristine, and a steroid (prednisone or dexamethasone). Methotrexate and 6-MP can affect the liver or lead to low blood counts, and may require dose reduction or discontinuation.

Next steps

After the allogeneic SCT or after completing consolidation and maintenance therapy, see Guide 15 on page 63 for follow-up testing.

Older adults with Ph-negative ALL

Guide 12. Remission induction for older adults with Ph-negative ALL

Health status	Induction therapy options	Response
Patients <65 years of age without serious health problems	• Clinical trial • Multiagent chemotherapy regimen	Complete remission, monitor for MRD Less than complete remission, start treatment for relapsed/refractory ALL
Patients ≥65 years of age or with other serious health problems	• Clinical trial • Multiagent chemotherapy regimen • Corticosteroids	Complete remission, monitor for MRD Less than complete remission, start treatment for relapsed/refractory ALL

Guide 12 shows the induction therapy options for older adults with Ph-negative ALL. Induction therapy is the first phase of treatment for ALL. It is also called remission induction. The goal is to kill all of the leukemia cells in your bone marrow and put ALL into complete remission.

Induction therapy consists of high doses of chemotherapy drugs. It is very intensive and lasts about four weeks (one month). You may need to stay in the hospital for some or all of the time during this treatment.

There are many treatment regimens used for adults with ALL. These regimens are typically designed to include steroids, vincristine, doxorubicin, cytarabine, and/or methotrexate. Rituximab may also be included if the leukemia expresses the CD20 protein.

There are many treatment regimens used for adults with ALL. These regimens usually include a steroid and chemotherapy agents such as vincristine, doxorubicin, cytarabine, cyclophosphamide, and/or methotrexate. Rituximab may also be included if the leukemia expresses the CD20 protein. Your doctor may also consider other drugs as part of the treatment regimen.

CNS preventive treatment is given to all patients during the induction phase. For CNS treatment, drugs are often injected into the spinal fluid during a lumbar puncture. When drugs are given this way, it is called IT therapy or IT chemotherapy.

CNS treatment may include IT methotrexate alone or with other drugs such as IT cytarabine and an IT steroid (dexamethasone or prednisone). When all three drugs are given, it is called triple IT therapy. Methotrexate, and cytarabine, may also be given as IV injections for CNS treatment. Rarely, CNS disease may be found when ALL is first diagnosed. In this case, your doctor may consider giving cranial irradiation as well.

Induction therapy options

Often, age 65 is the cut-off for intensive treatment. But, age alone is not a good gauge of a person's overall health or fitness for intensive treatment.

When choosing an induction regimen, your doctors will look at your age, general health, organ function, and other current health conditions. This will help your doctor to know if you are able to receive very strong treatments.

If you are younger than age 65, or without serious health problems, there are two main options to choose from. Treatment within a clinical trial is preferred if one is open and is the right fit for you. The other option is to receive multiagent chemotherapy based on a regimen designed for adults. Induction regimens for adults tend to use a combination of vincristine, a steroid (prednisone or dexamethasone), cyclophosphamide, and doxorubicin or daunorubicin.

If you are age 65 or older, or you have other serious health problems, there are three main options to choose from. Treatment within a clinical trial is preferred if one is open and is the right fit for you. The second option is to have multiagent chemotherapy based on a regimen for adults as described above. The third option is treatment with corticosteroids such as prednisone or dexamethasone with our without vincristine. This option is not designed to cure ALL, but rather to control the symptoms and improve the blood counts. These drugs may be easier to take than chemotherapy. Some patients may not be able to tolerate the side effects of intensive (high-dose) regimens. If needed, some chemotherapy drugs may be given in lower doses to lessen the side effects.

Response

At the end of induction, your doctor will assess how well treatment worked. A treatment response is an outcome or improvement caused by treatment. To check the response, your doctor will test a sample of blood and bone marrow with a microscope.

A complete remission is when no leukemia cells are seen in the blood or bone marrow and all signs and symptoms of ALL are gone. (See page 37 for more details about treatment responses.)

If tests show a complete remission, then your doctor may test for MRD. MRD is when a very small amount of leukemia cells remains in your body after a course of treatment. With MRD, the amount of leukemia cells left is too small to be seen with a microscope.

PCR and flow cytometry are very sensitive tests that doctors use to check for MRD. These tests can detect a single leukemia cell among more than 10,000 normal cells. They can be done on a sample of blood or bone marrow. But, bone marrow is preferred. Testing for MRD can help your doctor decide if more intensive treatments are needed for consolidation.

If tests show less than a complete remission, this means treatment wasn't able to kill enough leukemia cells in your body. ALL that is not in complete remission after induction is called refractory ALL. In this case, treatment with other drugs or regimens will be tried. See *Next steps* at the end of this section.

Next steps

If induction therapy resulted in a complete remission, see Guide 13 and 14 on page 60 for the next options. If induction therapy resulted in less than a complete remission, see Guide 17 on page 67 for the next options.

Guide 13. Postremission consolidation and maintenance Patients ≥65 years of age or with other serious health problems

Health status	Consolidation therapy options	Maintenance therapy options

Patients ≥65 years of age or with other serious health problems →	• Chemotherapy →	• Maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

Guide 14. Postremission consolidation and maintenance for patients <65 years of age without serious health problems

MRD results	Consolidation therapy options	Next options
Persistent or late MRD →	• Blinatumomab • Consider allogeneic SCT →	• Start follow-up testing

MRD not found →	• Continue multiagent chemotherapy regimen →	• Maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP

	• Consider allogeneic SCT →	• Start follow-up testing

MRD unknown →	• Allogeneic SCT
	• Consider continuing multiagent chemotherapy regimen →
		• After chemotherapy, maintenance therapy with:
		  • Monthly vincristine/ prednisone pulses
		  • Weekly methotrexate
		  • Daily 6-MP
		• After SCT, start follow-up testing

Guides 13 and 14 show the treatment options for older adults with Ph-negative ALL in a complete remission after induction therapy. Consolidation therapy is the second phase of treatment for ALL. The goal of this phase is to kill any leukemia cells that may still be in your body. It is followed by maintenance therapy. These phases are jointly referred to as postremission therapy since they are given after ALL is in remission.

Consolidation therapy options

Your doctor will look at many factors to help plan consolidation therapy. This includes the ALL cell subtype, chromosome changes, results of MRD testing, and other factors described in Part 3. Your general health, current symptoms, and side effects will also be noted. This can help to decide if you need and can tolerate more intensive treatment for consolidation.

If you are younger than age 65, or you don't have other serious health problems, there are some main options to choose from for consolidation therapy. See Guide 12 on page 58. The options you have depend on whether or not MRD is found.

If MRD is found, that means the disease is persistent, so your doctor may consider blinatumomab. This medication has been shown to be helpful in treating disease that continues despite other treatment. It is known as a bispecific T-cell engager for how it works with the immune system to find and attack leukemia cells. It can cause serious side effects so your doctor will assess your health and monitor you closely if you take this drug. An allogeneic SCT may also be considered. Your doctor will look at a number of factors to decide if an allogeneic SCT is a good choice for you. This depends on your age, general health, and ability to tolerate intensive treatments.

Consolidation therapy for when MRD is not found or is unknown may include combinations of drugs similar to those used for induction. In regimens designed for adults, it tends to include drugs such as methotrexate, cytarabine, and 6-MP. Chemotherapy drugs are often given in higher (intensified) doses during consolidation. CNS preventive treatment is also usually given throughout this phase of treatment.

Consolidation therapy may last several months. How long it lasts and the total number of cycles varies based on the regimen used. The full treatment regimen should be followed all the way through consolidation and to the end of maintenance.

Another option to consider if MRD is not found or is unknown is allogeneic SCT. This is a very intensive treatment performed in specialized centers, and may not be a good choice for everyone. It can cause very severe side effects that may be too much for some patients to take. Your doctor will look at a number of factors to assess if an allogeneic SCT is a good choice for you. This includes your age, general health, and if you can tolerate intensive treatments.

If you are age 65 or older, or you have other serious health problems, there is one main option for consolidation. See Guide 13. The option is to stay on a chemotherapy regimen for consolidation as described above for adults younger than age 65. Allogeneic SCT is a very intense treatment and can cause very severe side effects. Thus, it is often not recommended if you are older than age 65 or you have other serious health problems.

Maintenance therapy options

After consolidation with an allogeneic SCT, you will begin follow-up testing. After consolidation with multiagent chemotherapy, you will receive maintenance therapy. Maintenance therapy is the third phase of ALL treatment.

Maintenance therapy is given to keep up (maintain) the good results of prior treatments. The goal is to prevent a relapse after induction and consolidation therapy. A relapse is when leukemia cells come back after a complete remission.

If you are not treated with an allogeneic SCT, you will likely be treated with a maintenance chemotherapy regimen for 2 to 3 years. Maintenance therapy drugs are often given in lower doses and cause fewer side effects. CNS preventive treatment can also be given throughout this treatment phase. This regimen may include weekly methotrexate, daily 6-MP, monthly vincristine, and a steroid (prednisone or dexamethasone). Methotrexate and 6-MP can affect the liver or lead to low blood counts, and may require dose reduction or discontinuation.

Next steps

After the allogeneic SCT or after completing consolidation and maintenance therapy, see Guide 15 for follow-up testing.

Follow-up after treatment for ALL

Guide 15. Follow-up testing after treatment

Year	Tests	Timing
Year 1	• Physical exam, including testicular exam (if needed)	Every 1–2 months
	• CBC with differential and liver function tests	Every 1–2 months (liver function tests continue until normal)
	• Lumbar puncture	As needed
	• Echocardiogram	As needed
	• Bone marrow aspiration	As needed
	• If bone marrow aspiration is done, other tests may include: Flow cytometry, cytogenetic testing, FISH, and PCR	As needed
	• Cytogenetic tests (*BCR-ABL*1) for PH-postive ALL	Routine testing
Year 2	• Physical exam, including testicular exam (if needed)	Every 3–6 months
	• CBC with differential	Every 3–6 months
Year 3+	• Physical exam, including testicular exam (if needed)	Every 6–12 months or as needed
	• CBC with differential	Every 6–12 months or as needed

Guide 15 shows the tests that are recommended after completing the entire treatment regimen, including induction, consolidation, and maintenance. Follow-up tests are given after treatment to check how well treatment worked.

It is important for treatment to kill all of the leukemia cells and keep them away. Doctors use follow-up tests to look for signs of cancer return (relapse) after treatment. These tests also check how well your organs and body systems are working. This is needed since ALL and its treatment can cause much damage.

Follow-up tests

The suggested schedule of follow-up tests is shown in Guide 15. Many of the tests used to diagnose ALL and plan treatment are repeated during follow-up.

During the first year of follow-up, a physical exam should be done every 1 to 2 months. The physical exam gives your doctor an idea about your general health. For males, it may include a testicular exam.

A CBC with differential should also be done every 1 to 2 months during the first year of follow-up. This test will show if there is a normal number of each type of blood cell.

Liver function tests will be done to check how well your liver is working. Some ALL treatments can damage the liver and cause abnormal liver function test results. But, this is usually temporary and should go away over time.

A lumbar puncture removes a sample of spinal fluid for testing. (See page 22 for more details.) This test may be used to check for a CNS relapse. A CNS relapse is when leukemia cells come back after treatment and are found in the spinal fluid.

An echocardiogram is an imaging test that shows how well your heart is working. Doctors use this test to check for signs of heart damage that may be caused by ALL treatments.

A bone marrow aspiration may also be done at certain times during the first year of follow-up. When this test is done, your doctor may want to perform other lab tests on the bone marrow sample. This may include flow cytometry, cytogenetic testing, FISH, and PCR. See Part 2 on page 13 to read more about each type of test for ALL.

Follow-up tests are given less often during the second and third years of follow-up. During the second year of follow-up, tests are recommended once every three months. And during the third year of follow-up, tests are only recommended once every six months or as needed.

Next steps

If follow-up tests show ALL has come back, more treatment is needed. For relapsed Ph-positive ALL, see Guide 16. For relapsed Ph-negative ALL, see Guide 17 on page 67.

Relapsed or refractory Ph-positive ALL

Guide 16. Treatment for relapsed or refractory Ph-positive ALL

Tests	Treatment options
Consider BCR-ABL gene mutation testing	• Clinical trial • TKI ± chemotherapy • TKI ± corticosteroids • Blinatumomab (If no response to 2 TKIs)
	TKIs and chemotherapy for relapsed or refractory Ph-positive ALL: • Dasatinib • Imatinib • Ponatinib • Nilotinib • Bosutinib • Blinatumomab (If no response to 2 TKIs) • Any TKI above + induction chemotherapy regimen not used before • MOpAD regimen includes methotrexate, vincristine, pegaspargase, and dexamethasone, with rituximab for CD20-positive disease and TKI • If no response to TKIs, consider chemotherapy regimens for relapsed or refractory Ph-negative ALL

Guide 16 shows the treatment options for relapsed or refractory Ph-positive ALL. Ph-positive means the leukemia cells have the Philadelphia chromosome.

A relapse is when leukemia cells come back after a complete remission. Refractory means that the leukemia cells didn't respond to treatment. ALL that isn't in complete remission after induction therapy is called refractory ALL. (See page 37 to read more about treatment responses.) Similar treatments are used for relapsed ALL and refractory ALL.

Tests

Before starting treatment, *BCR-ABL* gene mutation testing should be done. This test checks for changes (mutations) in the *BCR-ABL* fusion gene that affect how well certain TKIs work. Each TKI drug works in a slightly different way. One TKI drug may be able to work against a mutation that another TKI can't. Knowing which mutations the *BCR-ABL* gene has will help your doctor choose which TKI is best for you.

Along with the mutation testing results, your doctor will look at other factors to help plan treatment. Some factors include your age, general health, symptoms, and side effects. This helps your doctor to know if you are healthy enough to receive strong treatments.

Treatment options

There are several treatment options to choose from. But, any treatment given should include CNS preventive treatment. The options for treating relapsed and refractory ALL are described next.

Treatment within a clinical trial is preferred if one is open and is the right fit for you. A clinical trial is a type of research that studies how safe and helpful a treatment is. If you aren't able to join a clinical trial, there are a few other choices.

A second option is to receive a different TKI than you had during induction therapy. Many patients with Ph-positive ALL receive imatinib during induction therapy. TKI options for relapsed or refractory ALL are dasatinib, ponatinib, imatinib, nilotinib, and bosutinib. Blinatumomab may be an option if the cancer is not responding to 2 other TKI treatments.

The TKI may be given alone. Or, it may be combined with multiagent chemotherapy or with a corticosteroid. Prednisone and dexamethasone are the main steroids that may be used. If combined with chemotherapy, an induction regimen other than the one you had before can be used. The MOpAD regimen is another option and includes methotrexate, vincristine, pegaspargase, and dexamethasone, with rituximab for CD20-positive disease.

Some older adults may not be able to tolerate multiagent chemotherapy. Steroids can be easier to take than chemotherapy. Thus, treatment with a TKI and steroids may be the best choice for some patients.

If ALL doesn't respond to treatment with TKIs, then the regimens for relapsed or refractory Ph-negative ALL may be tried. See Guide 17.

An allogeneic SCT is also an option if you are healthy enough and a well-matched donor has been found. Some patients may not be able to tolerate this intensive treatment. This is especially true for older adults who may have other health problems.

If ALL relapses after the first allogeneic SCT, a second allogeneic SCT is an option. Or your doctor may consider a donor lymphocyte infusion. For this treatment, you are given white blood cells called lymphocytes from the same donor used for the SCT.

Relapsed or refractory Ph-negative ALL

Guide 17. Treatment for relapsed or refractory Ph-negative ALL

Status	Treatment options
Refractory ALL or Relapsed ALL	• Clinical trial • Chemotherapy regimen for relapsed or refractory ALL ± allogeneic SCT • Blinatumomab
	Chemotherapy regimens for relapsed or refractory Ph-negative ALL: • Blinatumomab for B-cell ALL • Regimens with cytarabine • Combination regimens with alkylating agents • Nelarabine for T-cell ALL • Augmented hyper-CVAD regimen • VSLI (**v**incristine **s**ulfate **l**iposome **i**njection) • Regimens with clofarabine for B-cell ALL • MOpAD regimen includes methotrexate, vincristine, pegaspargase, and dexamethasone, with rituximab for CD20-positive disease

Guide 17 shows the treatment options for relapsed or refractory Ph-negative ALL. Ph-negative means the leukemia cells do not have the Philadelphia chromosome.

A relapse is when leukemia cells come back after a complete remission. Refractory means that the leukemia cells didn't respond to treatment. ALL that isn't in complete remission after induction therapy is called refractory ALL. (See page 37 to read more about treatment responses.) Similar treatments are used for relapsed ALL and refractory ALL.

Treatment options

Your doctor will look at a number of factors unique to you to decide which treatment is the best choice. Some factors include your age, general health, symptoms, and side effects. This helps your doctor to know if you are healthy enough to receive strong treatments. How well prior treatment worked and how long the treatment response lasted may also affect which option is best.

There are several treatment options to choose from. But, any treatment given should include CNS preventive treatment. The options for treating relapsed and refractory ALL are described next.

Treatment within a clinical trial is preferred if one is open and is the right fit for you. A clinical trial is a type of research that studies how safe and helpful a treatment is. If you aren't able to join a clinical trial, there are a few other choices.

A second option is to have a different induction regimen than you had before. ALL that relapses more than three years after diagnosis is called a late relapse. For AYAs with a late relapse, treatment with the same induction regimen used before is an option to consider.

Another option is to have chemotherapy for relapsed or refractory ALL. There are many drugs and drug combinations to choose from. Blinatumomab is the preferred option for B-cell ALL. Blinatumomab is a type of targeted therapy called a bispecific T-cell engager. It uses the immune system to help kill leukemia cells.

Combination regimens that include cytarabine or an alkylating agent such as ifosfamide are also options. An alkylating agent is a type of chemotherapy drug that directly damages the DNA in leukemia cells. Nelarabine is an option for patients with T-cell ALL.

Augmented hyper-CVAD is an intense chemotherapy regimen that may be used for relapsed or refractory ALL. It uses many drugs and gives some in higher (intensified) doses. This regimen includes cyclophosphamide, vincristine, doxorubicin, dexamethasone, pegaspargase, methotrexate, and cytarabine.

VSLI is a form of the chemotherapy drug called vincristine. VSLI has a special coating around it called a liposome. The coating helps to limit the side effects of vincristine. This allows doctors to give higher doses of the drug without increasing side effects.

Another option for patients with B-cell ALL is to have a regimen that includes clofarabine. Clofarabine is approved for patients aged 21 years or younger. But, adults may also benefit from regimens with this chemotherapy drug. The MOpAD regimen is another option and includes methotrexate, vincristine, pegaspargase, and dexamethasone, with rituximab for CD20-positive disease.

If you did not previously receive an allogeneic SCT, this is an important option to consider if you are able to obtain a remission and a matched donor has been found. In this case, your doctor will assess if you are healthy enough to have an allogenic SCT. Some patients may not be able to tolerate this intensive treatment. This is especially true for older adults who may have other health problems.

If ALL relapses after an initial allogeneic SCT, a second allogeneic SCT is an option. Or, your doctor may consider a donor lymphocyte infusion. For this treatment, you will be given white blood cells called lymphocytes from the same donor used for the SCT.

6
Making treatment decisions

Cancer can be very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time you have to decide on a treatment plan may feel short. Parts 1 through 5 aimed to teach you about ALL, its treatment, and other challenges. Part 6 may help you talk with your doctor and make treatment decisions that are right for you.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. However, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, your treatment team may still ask that you sign a consent form

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works best for you when it comes to your personal and health needs.

Questions to ask your doctors

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn't clear. You can get copies of your medical records. It may be helpful to have a family member or friend with you at these visits to listen carefully and even take notes. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions below are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1. Where did the cancer start? In what type of cell?
2. Is this cancer common?
3. Is this a fast- or slow-growing leukemia?
4. What is the ALL cell subtype and cytogenetic subtype? What does this mean for me and my treatment options?
5. How often will I have bone marrow tests?
6. How often will I have spinal fluid tests?
7. What other test results are important to know?
8. How often are these tests wrong?
9. Would you give me a copy of the pathology report and other test results?
10. Can the cancer be cured? If not, how well can treatment stop the cancer from growing?

What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you use NCCN recommendations when considering options?
4. Do you suggest options other than what NCCN recommends? If yes, why?
5. Do your options include clinical trials? Please explain why. What kinds of treatments would the clinical trial involve? Is it for people my age?
6. How do my age, health, and other factors affect my options?
7. Which option is proven to work best?
8. What are the benefits and risks of each option?
9. What can be done to prevent or relieve the side effects of treatment?
10. Are there supportive services that I can get involved in? Support groups?

What does each option require of me?

Many patients consider how each option will affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that fits your needs may be important to you.

1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
3. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
4. Should I bring someone with me when I get treated?
5. Will the treatment hurt?
6. How much will the treatment cost me? What does my insurance cover?
7. Will I miss work or school? Will I be able to drive?
8. Is home care after treatment needed? If yes, what type?
9. How soon will I be able to manage my own health?
10. When will I be able to return to my normal activities?

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

1. Are you board certified? If yes, in what area?
2. How much experience do you have in treating ALL?
3. How many patients like me have you treated? How many of them were my age?
4. How many treatments or procedures like the one you're suggesting have you done?
5. Is this treatment a major part of your practice?
6. How many of your patients have had complications?
7. Are you involved in any clinical trials for the treatment of ALL? For people my age?
8. Does your hospital have a program specifically for people my age with cancer?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Getting a 2nd opinion

Even if you like and trust your doctor, it is helpful to get a 2nd opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- Check with your insurance company about its rules on 2nd opinions. You want to know about out-of-pocket costs for doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your 2nd opinion. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.

If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with ALL. If your hospital or community doesn't have support groups for people with ALL, check out the websites on the next page.

You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and to those with children, so they can connect and get support.

Keep in mind...

- ✓ Every treatment option has benefits and risks. Consider these when deciding which option is best for you.
- ✓ Talking to others may help identify benefits and risks you haven't thought of.

Websites

American Cancer Society
cancer.org/cancer/leukemia-acutelymphocyticallinadults/index

cancer.org/Treatment/FindingandPayingforTreatment/index

Leukemia and Lymphoma Society
LLS.org/informationspecialists

National Cancer Institute
cancer.gov/types/leukemia

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox

NCCN
nccn.org/patients/resources/life_with_cancer/default.aspx

Resources for AYAs

Cancer.Net
cancer.net/navigating-cancer-care/young-adults/resources-young-adults

National Cancer Institute
cancer.gov/types/aya/psychosocial-challenges-cancer

cancer.gov/types/aya

Stupid Cancer
stupidcancer.org

The Samfund
thesamfund.org

The Ulman Cancer Fund for Young Adults
ulmanfund.org

Critical Mass
criticalmass.org

The LIVESTRONG Foundation
livestrong.org/we-can-help/fertility-services/

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.

Glossary

Dictionary

acute lymphoblastic leukemia (ALL)
A fast-growing cancer that causes too many immature white blood cells called lymphoblasts to be made.

adolescents and young adults (AYAs)
Patients who are 15 to 39 years of age.

allogeneic stem cell transplant (SCT)
A treatment in which the patient receives immature blood-forming cells (blood stem cells) from another person to replace damaged or diseased cells in the bone marrow.

anesthesia
Loss of feeling with or without loss of wakefulness caused by drugs.

anthracycline
A cancer drug that damages and disrupts the making of DNA in cells.

B-cell
One of two main types of white blood cells called lymphocytes that help protect the body from infection and disease. Also called B-lymphocyte.

B-cell ALL
A fast-growing (acute) blood cancer (leukemia) that starts in a B-lymphoblast—an immature cell that normally becomes a mature white blood cell called a B-cell or B-lymphocyte.

***BCR-ABL* fusion gene**
An abnormal set of coded instructions for controlling cells that is formed when the *BCR* gene and *ABL* gene join (fuse) together on the Philadelphia chromosome.

BCR-ABL protein
An abnormal protein that is made by the *BCR-ABL* fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

biopsy
Removal of small amounts of tissue from the body to be tested for disease.

blast cell
An immature blood cell.

blood cell count
The number of blood cells in a sample of blood.

blood chemistry profile
A test that measures the amount of chemicals in the blood to look for signs of disease and check how well organs are working.

blood stem cell
An immature cell from which all other types of blood cells are made.

bloodstream
Blood that flows throughout the body in small tubes called blood vessels.

B-lymphocyte
One of two main types of white blood cells called lymphocytes that help protect the body from infection and disease.

bone marrow
The soft, sponge-like tissue in the center of most bones where blood cells are made.

bone marrow aspiration
The removal of a small amount of liquid bone marrow (soft tissue in the center of most bones where blood cells are made) to test for disease.

bone marrow biopsy
The removal of a small amount of solid bone and bone marrow (the soft tissue in the center of most bones where blood cells are made) to test for disease.

cell assessment
Use of a microscope and special dyes to examine the physical features of cells in a sample of blood or tissue removed from your body. Also called morphologic assessment.

cell subtype
Smaller groups that leukemia cells are classified into based on the specific type of lymphocyte affected.

central nervous system (CNS)
The brain and the spinal cord—the bundle of nerves that runs from the base of the skull down the back.

central nervous system (CNS) disease
Leukemia cells in the fluid around the brain and spinal cord, which make up the central nervous system.

central nervous system (CNS) preventive treatment
Treatment given to keep leukemia cells from spreading to the fluid around the brain and spinal cord. Also called CNS prophylaxis.

central venous line
A thin, flexible tube that is inserted into a vein to give medicine or take a sample of blood. Also called central line or catheter.

cerebrospinal fluid
The fluid that surrounds the brain and spinal cord. Also called spinal fluid.

chemotherapy
Drugs that kill fast-growing cells, including cancer cells and normal cells.

chromosomes
Long strands of coded instructions in cells for making and controlling cells.

clinical trial
Research on a test or treatment to assess its safety or how well it works.

combination regimen
The use of two or more drugs.

complete blood count (CBC)
A test of the number of blood cells in a sample.

complete remission
No leukemia cells are found in the blood or bone marrow and all signs and symptoms of the cancer are gone.

computed tomography (CT) scan
A test that uses x-rays from many angles to make a picture of the inside of the body.

consolidation
The second round (phase) of treatment that is given when leukemia cells are no longer seen in the blood or bone marrow. Also called intensification or consolidation therapy.

contrast
A dye put into your body to make clearer pictures during imaging tests.

corticosteroid
A drug used to reduce redness, swelling, and pain, but also to kill leukemia cells. Also called steroid.

cranial irradiation
Treatment with high-energy rays (radiation) directed at the brain.

cycle
Days of treatment followed by days of rest.

cytogenetic subtype
Smaller groups a type of cancer is classified into based on abnormal changes in the chromosomes (long strands of coded instructions) of the cancer cells.

cytogenetic testing
A test that uses a microscope to examine a cell's chromosomes.

deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions for making and controlling cells.

diagnose
To confirm or identify a disease or health condition.

differential
Measurement of the different types of white blood cells present in a blood sample.

donor
A person who gives their organs, tissues, or cells to another person.

echocardiogram
A test that uses sound waves to make pictures of the heart.

fatigue
Severe tiredness despite getting enough sleep that limits one's ability to function.

flow cytometry
A test that looks at certain substances on the surface of cells to identify the type of cells present.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal changes in a cell's genes (coded instructions for controlling cells) and chromosomes (long strands of genes).

follow-up test
Tests done after the start of treatment to check how well treatment is working.

fusion gene
A gene that is made by joining parts of two separate genes.

gene
A set of coded instructions in cells needed to make new cells and control how cells behave.

gene mutation
Abnormal change in the coded instructions in cells for making and controlling cells.

good risk feature
Something linked with a lower chance (risk) that cancer will come back after treatment.

graft-versus-host disease (GVHD)
A disease that occurs when transplanted stem cells attack a patient's normal cells.

graft-versus-leukemia (GVL) effect
An attack on cancer cells by transplanted blood stem cells.

growth factor
A substance that helps new blood cells to be made.

human leukocyte antigen (HLA)
Special proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

human leukocyte antigen (HLA) type
The unique set of proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

human leukocyte antigen (HLA) typing
A blood test that finds a person's HLA type—the unique set of proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

imaging test
A test that makes pictures (images) of the inside of the body.

immune system
The body's natural defense against infection and disease.

immunophenotype
The unique set and pattern of proteins on the surface of white blood cells that can be used to identify the type of cell.

immunophenotyping
The process of identifying the specific type of cells present based on the unique set of proteins on the surface of the cells.

induction
The first round (phase) of treatment given to rid the body of leukemia cells. Also called remission induction or induction therapy.

inflammation
Redness, heat, pain, and swelling caused by illness or injury.

intensification
The second round (phase) of treatment that is given when leukemia cells are no longer seen in the blood or bone marrow. Also called consolidation or intensification therapy.

intestine
The organ that food passes through after leaving the stomach.

intrathecal (IT) chemotherapy
Cancer drugs that are injected into the fluid that surrounds the brain and spinal cord—the bundle of nerves that runs from the base of the skull down the back.

intravenous (IV)
Given by a needle or tube inserted into a vein.

kidneys
A pair of organs that filter blood and remove waste from the body through urine.

leukemia
A type of cancer that starts in blood-forming cells in the bone marrow—the soft, sponge-like tissue in the center of most bones where blood cells are made.

leukemia cell
Abnormal, immature white blood cell that grows and divides all the time without control.

liver
Organ that removes waste from the blood and helps to digest food.

liver function test
Test that measures chemicals in the blood that are made or processed by the liver.

local anesthesia
A controlled loss of feeling in a small area of the body caused by drugs.

lumbar puncture
A procedure in which a thin needle is inserted between the bones of the spine to remove a sample of spinal fluid or give drugs into the spinal fluid.

lymph node
A small group of disease-fighting cells.

lymphatic system
A network of organs and tissues in the body that collects and transports a fluid (lymph) and fights germs. This system includes the bone marrow, lymph nodes, lymph vessels, thymus, and spleen.

lymphoblast
An immature cell that becomes a mature white blood cell called a lymphocyte.

lymphoblastic lymphoma
A fast-growing cancer that starts in the lymphatic system and causes too many lymphoblasts to build up in lymph nodes or other parts of the lymph system.

lymphocyte
A type of white blood cell that helps protect the body from infection and disease.

magnetic resonance imaging (MRI) scan
A test that uses radio waves and powerful magnets to make pictures of the inside of the body.

maintenance
The third round (phase) of treatment that is given to keep up (maintain) good treatment results.

microscope
A tool that uses lenses to see things the eyes can't.

minimal residual disease (MRD)
A very small amount of cancer cells left in the body after treatment that can't be seen with a microscope.

monoclonal antibody
A type of immune system protein that is made in a lab and can attach to a certain target, such as a substance on the surface of cancer cells.

multiagent chemotherapy
The use of two or more cancer drugs.

multidisciplinary
Includes many doctors and other health care professionals who are experts in different areas of cancer care.

mutation
An abnormal change.

pathologist
A doctor who's an expert in testing cells and tissue to find disease.

pediatric-inspired
Based on treatment designed for or given to children.

pediatric protocol
A detailed plan of a medical treatment for children.

pediatric regimen
A treatment plan that specifies the drug(s), dose, and schedule for a course of treatment designed for or given to children.

Philadelphia chromosome
An abnormal, short chromosome 22 that is formed when parts of chromosomes 9 and 22 switch with each other. Also called Ph chromosome.

Ph-negative ALL
The leukemia cells do not contain the abnormal Philadelphia chromosome.

Ph-positive ALL
The leukemia cells contain the abnormal Philadelphia chromosome.

physical exam
A review of the body by a health expert for signs of disease.

platelet
A type of blood cell that helps control bleeding.

polymerase chain reaction (PCR)
A sensitive lab test that is used to look for abnormal changes in a cell's genes (coded instructions for controlling cells) and chromosomes (long strands of genes).

poor risk feature
Something linked with a higher chance (risk) that cancer will come back after treatment.

positron emission tomography (PET) scan
A test that uses radioactive material to take pictures of the inside of the body.

postremission therapy
Treatment given after all signs and symptoms of cancer have disappeared (called a remission) following initial treatment.

prognosis
The likely or expected course, pattern, and outcome of a disease based on tests.

prognostic factor
Something that affects and helps predict the likely outcome of a disease.

protocol
A detailed plan of a medical study, treatment, or procedure.

radiation therapy
Use of high-energy rays to destroy cancer cells.

red blood cell
A type of blood cell that carries oxygen from the lungs to the rest of the body.

refractory
Disease that does not improve or go away in response to treatment.

regimen
A treatment plan that specifies the drug(s), dose, and schedule for a course of treatment.

relapse
The return of leukemia cells after a period of improvement.

remission
The signs and symptoms of cancer have disappeared as a result of treatment.

remission induction
The first round (phase) of treatment that is given to rid the body of leukemia cells and make all signs and symptoms of the cancer disappear. Also called induction or induction therapy.

sedative
A drug that helps a person to relax or go to sleep.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

spinal cord
The bundle of nerves that runs from the base of the skull down the back and carries messages between the brain and other parts of the body.

spinal fluid
The fluid that surrounds the brain and spinal cord. Also called cerebrospinal fluid.

spleen
An organ to the left of the stomach that helps protect the body from disease.

stem cell transplant (SCT)
Treatment that replaces damaged or diseased cells in the bone marrow—soft tissue in the center of bones where blood cells are made—with healthy blood-forming cells called blood stem cells.

steroid
A drug used to reduce redness, swelling, and pain, but also to kill leukemia cells. Also called corticosteroid.

subtype
Smaller groups that a type of cancer is divided into based on certain features of the cancer cells.

supportive care
Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

symptom
A new or changed health problem a person experiences that may indicate a disease.

targeted therapy
Treatment with drugs that target a specific or unique feature of cancer cells.

T-cell
One of two main types of white blood cells called lymphocytes that help protect the body from infection and disease. Also called T-lymphocyte.

T-cell ALL
A fast-growing (acute) blood cancer (leukemia) that starts in a T-lymphoblast—an immature cell that normally becomes a mature white blood cell called a T-cell or T-lymphocyte.

testicles
Two egg-shaped glands found inside the sac between the legs of a man.

thymus
A small organ in the upper, front part of the chest that is part of the body's disease-fighting system.

T-lymphocyte
One of two main types of white blood cells called lymphocytes that help protect the body from infection and disease. Also called T-cell.

transfusion
Replacing lost blood with new blood.

translocation
When pieces of two chromosomes (long strands of coded instructions for controlling cells) break off and switch with each other.

treatment response
An outcome or improvement related to treatment.

tumor lysis syndrome (TLS)
A condition that occurs when many cancer cells die very quickly and release their contents into the blood, which can damage the kidneys and other organs.

tumor lysis syndrome (TLS) panel
A test that measures certain chemicals that are released into the blood when cancer cells die.

tyrosine kinase inhibitor (TKI)
A type of drug that targets and blocks the protein made by the *BCR-ABL* gene so that it can't tell leukemia cells to grow.

U.S. Food and Drug Administration (FDA)
A federal government agency that regulates drugs and food.

uric acid
A chemical that is made and released into the blood when cells and other substances in the body break down.

vaccine
A biological agent inserted into the body to prevent a disease.

vein
A small tube that carries blood to the heart from anywhere in the body.

white blood cell
A type of blood cell that helps fight infections in the body.

Acronyms

6-MP
6-mercaptopurine

AIDS
acquired immunodeficiency syndrome

ALL
acute lymphoblastic leukemia

AYA
adolescent and young adult

CAM
complementary and alternative medicine

CBC
complete blood count

CMV
cytomegalovirus

CNS
central nervous system

CT
computed tomography

DNA
deoxyribonucleic acid

EBRT
external beam radiation therapy

FDA
U.S. Food and Drug Administration

FISH
fluorescence in situ hybridization

GVHD
graft-versus-host disease

GVL
graft-versus-leukemia

HCG
human chorionic gonadotropin

HIV
human immunodeficiency virus

HLA
human leukocyte antigen

IT
intrathecal

IV
intravenous

MRD
minimal residual disease

MRI
magnetic resonance imaging

PCR
polymerase chain reaction

PET
positron emission tomography

Ph-negative
Philadelphia chromosome negative

Ph-positive
Philadelphia chromosome positive

SCT
stem cell transplant

TKI
tyrosine kinase inhibitor

TLS
tumor lysis syndrome

VSLI
vincristine sulfate liposome injection

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Acute Lymphoblastic Leukemia

Version 1.2017

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