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ALL basics

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Acute lymphoblastic leukemia (ALL) is a fast-growing cancer that starts in lymphocytes, a type of white blood cell. In ALL, bone marrow makes too many immature lymphocytes called lymphoblasts. Lymphoblasts can crowd out other blood cells causing blood to not work as it should. Treatment depends on the type of ALL, age at diagnosis, and other factors. This book is for those being treated at an adult cancer center.

a group of cells that work together to perform a function. Blood's function is to move oxygen and nutrients throughout the body and carry away waste. Blood also plays an important role for the immune system and in preventing bleeding.

Blood cells

Your blood contains different types of cells that float in plasma. Plasma is a clear, yellowish fluid made up of mostly water. More than half of your blood is plasma.

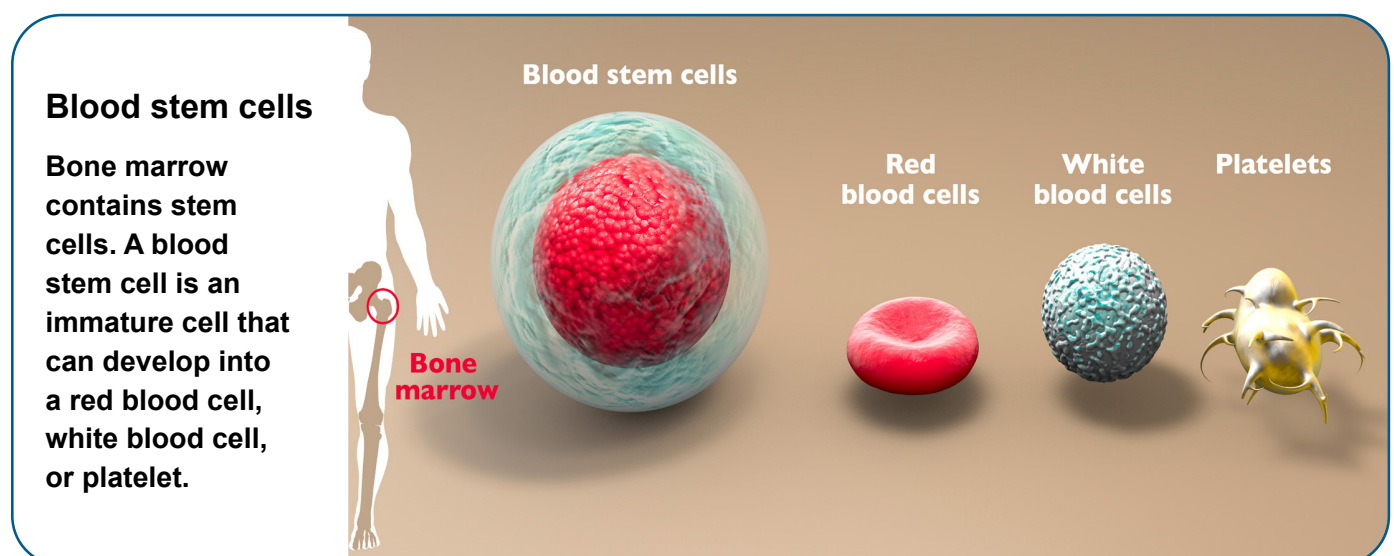
There are 3 types of blood cells:

- Red blood cells (erythrocytes)
- White blood cells (leukocytes), which include granulocytes, monocytes, lymphocytes, and others
- Platelets (thrombocytes)

Blood cells have important jobs. Red blood cells (RBCs) carry oxygen throughout the body. White blood cells (WBCs) fight infections. Platelets (PLTs) help control bleeding.

Blood

Acute lymphoblastic leukemia (ALL) is a type of blood cancer. Blood is a tissue. A tissue is



Blood cells are being replaced in your body all the time. Many have a short lifespan. Some white blood cells live less than one day. Your body makes one million red blood cells every second!

How blood cells are formed

Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are early blood-forming cells called blood (hematopoietic) stem cells. All types of blood cells are created from blood stem cells. At any given time, bone marrow will have cells in various stages of development, from very immature to almost fully mature. This process is called differentiation. After a blood stem cell develops into a red blood cell, white blood cell, or platelet, it is released in your bloodstream as needed.

Blood stem cells can copy themselves or “self-renew.” These cells are rare. The role of blood stem cells is to make cells that will become red blood cells, white blood cells, and platelets. These are called progenitor cells or precursor cells.

There are different types of progenitor cells:

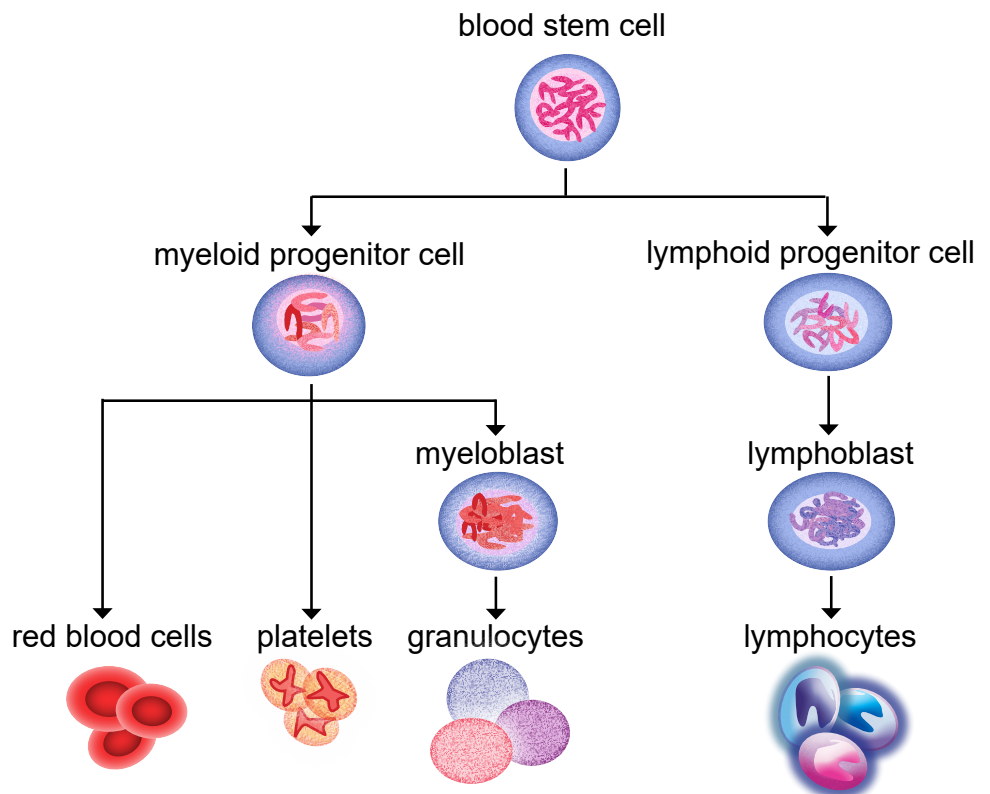
- **Lymphoid progenitor cells** form into lymphoblasts that mature into lymphocytes
- **Myeloid progenitor cells** form into myeloblasts and other non-lymphoid blood cells

ALL is thought to arise in lymphoid progenitor cells.

Blood cell formation

All blood cells start as blood stem cells. A blood stem cell has to mature or go through many stages to become a red blood cell, white blood cell, or platelet. ALL affects the lymphoid progenitor cells, which develop into lymphocytes.

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Lymphocytes

A lymphocyte is a type of white blood cell found in blood and lymph tissue, as well as all organs in the body. Lymph tissue includes lymph vessels and lymph nodes. Lymphocytes help fight and prevent infection.

There are 3 main types of lymphocytes:

- **B lymphocytes or B cells** make antibodies. An antibody is a protein.
- **T lymphocytes or T cells** help fight infections, kill tumor cells, and control immune responses.
- **Natural killer (NK) cells** can kill tumor cells or virus-infected cells.

ALL most often affects B cells or T cells.

Acute lymphoblastic leukemia

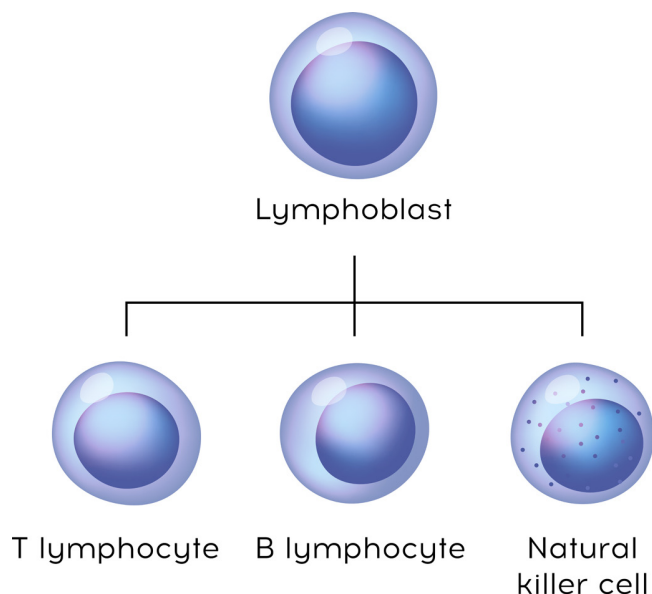
Acute lymphoblastic leukemia (ALL) is a fast-growing blood cancer that starts in disease-fighting lymphocytes of your immune system. In ALL, bone marrow makes too many immature lymphocytes called lymphoblasts. Lymphoblasts can crowd out other blood cells causing blood to not work as it should. Acute leukemias grow faster than chronic leukemias.

In general, to be diagnosed with ALL, 20 percent (20%) or more lymphoblasts must be present in the bone marrow. This means that at least 1 out of every 5 marrow cells are lymphoblasts. In certain cases, a diagnosis of ALL is possible with less than 20% lymphoblasts.

ALL can be found in bone marrow, blood, and organs such as the testicles or the central nervous system.

Lymphocytes

A lymphocyte is a type of white blood cell. In ALL, bone marrow makes too many immature lymphocytes called lymphoblasts.



There are 2 types of ALL:

- B cell or B-ALL
- T cell or T-ALL

Within each type there are several subtypes, which are based mainly on:

- The type of lymphocyte (most often B cell or T cell) within the leukemia cells and how mature the cells are. This is known as the immunophenotype of the leukemia.
- If the leukemia cells have specific gene or chromosome changes.

B-ALL

B-cell ALL or B-ALL starts in B-cell lymphocytes. B-ALL is more common than T-ALL. Mature B-cell ALL (also called Burkitt leukemia), a rare subtype, is essentially the same as Burkitt lymphoma (a type of non-Hodgkin lymphoma), but is treated differently from B-ALL. In some cases, the B-cell lymphoblasts grow mostly in the lymph nodes instead of in the bone marrow. When this happens, it is called B-cell lymphoblastic lymphoma, B-LL, or B-LBL.

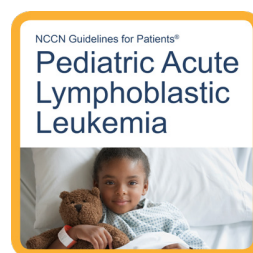
T-ALL

T-cell ALL or T-ALL starts in T-cell lymphocytes. T-ALL can cause an enlarged thymus (a small organ in front of the windpipe), which can sometimes lead to breathing problems. In some cases, the T-cell lymphoblasts grow mostly in the thymus instead of in the bone marrow. When this happens, it is called T-cell lymphoblastic lymphoma, T-LL, or T-LBL.

About this book

This book applies to AYAs and adults who are being treated for ALL at an adult cancer center. An adolescent and young adult (AYA) is someone 15 to 39 years of age at the time of initial cancer diagnosis. AYAs are a unique group that can be treated by pediatric or adult oncologists in pediatric or adult centers depending on the type of cancer. This book applies to those being treated at an adult cancer center.

More information for AYAs seeking ALL treatment at a pediatric cancer center can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Key points

- Acute lymphoblastic leukemia (ALL) is a fast-growing blood cancer. In ALL, bone marrow makes too many immature lymphocytes called lymphoblasts. This makes it hard for bone marrow or blood to do its work.
- To be diagnosed with ALL, 20 percent (20%) or more lymphoblasts must be present in the bone marrow. This means that at least 1 out of every 5 marrow cells are lymphoblasts.
- An adolescent and young adult (AYA) is someone 15 to 39 years of age at the time of initial cancer diagnosis. This book is for AYAs and adults being treated at an adult cancer center.
- There is more than one type of ALL. It is based on the type of lymphocyte, genetic mutations, and other features.
- Those with ALL should be treated at experienced cancer centers.

Those with ALL
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Testing for ALL

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Accurate testing is needed to diagnose and treat. This chapter presents an overview of possible tests and what to expect.

Be prepared to have many blood tests.

Test results

Results from blood and bone marrow tests and imaging studies will be used to determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access test results.

Keep these things in mind:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment.
- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your

refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list.

- Include in your contact list information on the exact type of cancer, as well as any treatment and the date it started.

For possible tests and procedures, **see Guide 1.**

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched.
- Feel for enlarged lymph nodes in your neck, underarm, and groin.

Guide 1

Possible tests and procedures

Medical history and physical exam (H&P)

Bone marrow aspirate and biopsy

Complete blood count (CBC), platelets, differential, chemistry profile, liver function tests (LFTs)

Disseminated intravascular coagulation (DIC) panel (blood clotting tests)

Tumor lysis syndrome (TLS) panel: Lactate dehydrogenase (LDH), uric acid, potassium (K), calcium (Ca), phosphorus (Phos)

Testing for hepatitis B and C, HIV, cytomegalovirus (CMV) antibodies (Ab)

Pregnancy testing, fertility counseling, and preservation as needed

CT and MRI of head with contrast, if neurologic symptoms

Lumbar puncture (LP) with intrathecal (IT) chemotherapy

CT of neck, chest, abdomen, pelvis with contrast. PET-CT is possible

Testicular exam, including scrotal ultrasound as needed

Screen for opportunistic infections as needed

Echocardiogram or cardiac nuclear medicine scan should be considered

Strongly consider early hematopoietic cell transplant evaluation and donor search

Consider possible cancer predisposition syndromes

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer, or where the cancer started, and if it is in multiple locations. Those with a family history of leukemia, blood cancer or abnormalities, or certain genetic mutations might be referred to genetic counseling.

Ask blood relatives on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.



What is your family health history?

Some cancers and other diseases run in families – those who are related to you through genes passed down from parent to child. This information is called a family health history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who have died, ask about the cause and age of death.

Start by asking your parents, siblings, and children. Next, talk to half-siblings, aunts and uncles, nieces and nephews, grandparents, and grandchildren.

Write down what you learn about your family history and share with your health care provider.

Some of the questions to ask include:

- Do you have any chronic diseases, such as heart disease or diabetes, or health conditions such as high blood pressure or high cholesterol?
- Have you had any other diseases, such as cancer or stroke?
- How old were you when each of these diseases and health conditions was diagnosed?
- What is our family's ancestry – from what countries did our ancestors originate?

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into a vein. Be prepared to have many blood tests during ALL treatment and recovery to check treatment results, blood counts, and the health of organs like your liver and kidneys.

B12 and folic acid

Vitamin B12 and folic acid (folate) work with vitamin C to help the body make new proteins. They are needed for normal red blood cell (RBC) and white blood cell (WBC) formation. B12 and folic acid levels will be monitored. You may be given vitamin supplements, if needed.

Blood clotting tests

Your body stops bleeding by turning blood into a gel-like form. The gel-like blood forms into a solid mass called a blood clot. Clotting is a process or series of events. Proteins, called coagulation factors, are needed for clotting. They are made by the liver. Blood clotting tests are known together as a coagulation panel or disseminated intravascular coagulation (DIC) panel.

It is standard to screen for clotting problems. An impaired clotting process is common in leukemia. This is called coagulopathy. You may have bleeding and bruises.

Blood urea nitrogen

Blood urea nitrogen (BUN) is a waste product filtered out of the blood by the kidneys. A high level of BUN can be a sign your kidneys aren't working well.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) is a test that measures 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

Complete blood count and differential

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. A CBC is a key test that gives a picture of your overall health. ALL often causes low counts of healthy blood cells.

There are several types of white blood cells. A differential counts the number of each type of white blood cell. It also checks if the counts are in balance with each other. This test may show a high number of blasts in the blood.

Creatinine

Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys aren't working as well as they were when someone had lower levels of creatinine.

Electrolytes

Electrolytes help move nutrients into cells and help move waste out of cells. Electrolytes are ions or particles with electrical charges that help the nerves, muscles, heart, and brain work as they should. Your body needs electrolytes to function properly. Phosphate

(PO₄) is important for strong bones and teeth. Too much phosphate in blood can be a sign your kidneys aren't working well.

Iron

Iron is important in maintaining body functions such as producing hemoglobin, the molecule in your blood that carries oxygen. You might be monitored for low levels of iron called iron deficiency. You may be given intravenous (IV) iron supplement, if needed. It is possible to have too much iron in the body called overload. Therefore, only take what is prescribed by your doctor.

Lactate dehydrogenase

Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is a protein found in most cells. Dying cells release LDH into blood. Fast-growing cells also release LDH. High levels of LDH can be a sign of ALL.

Liver function tests

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well.

Phosphate

Cells have a lot of phosphate in them. Therefore, when many cells are breaking down at the same time, the levels of phosphate in the blood can go up. Your kidneys help get rid of extra phosphate, but too much phosphate in the blood can also damage the kidneys, making it harder to get the levels back down to normal.

Uric acid

Uric acid is released by cells when DNA (deoxyribonucleic acid) breaks down. It is a normal waste product that dissolves in your blood and is filtered by the kidneys where it leaves the body as urine. Too much uric acid in the body is called hyperuricemia. With ALL, it can be caused by a fast turnover of white blood cells. High uric acid might be a side effect of chemotherapy or radiation therapy. Very high levels of uric acid in the blood can damage the kidneys.

HLA typing

A human leukocyte antigen (HLA) is a protein found on the surface of most cells. It plays an important role in your body's immune response. HLAs are unique to each person. They mark your body's cells. Your body detects these markers to tell which cells are yours. In other words, all your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

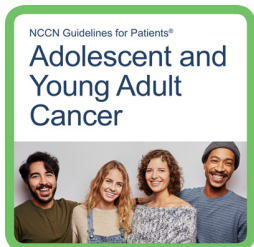
HLA typing is a test that detects a person's HLA type. This test is done before a donor (allogeneic) blood stem cell transplant. To find a donor match, your proteins will be compared to the donor's white blood cells to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood samples from you and your blood relatives will be tested first.

Fertility (all genders)

Treatment such as chemotherapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your care team how cancer and cancer treatment might change your fertility. To preserve your fertility, you may need to take action before starting cancer treatment. Those who want to have children in the future should be referred to a fertility specialist to discuss the options before starting treatment.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren't really sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation in adolescents and young adults can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Changes in fertility

Treatment might cause your fertility to be temporarily or permanently impaired or interrupted. This temporary loss of fertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Talk to your care team about your concerns and if you are planning a pregnancy.

Preventing pregnancy

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. Hormonal birth control may or may not be recommended, so ask your doctor about options such as intrauterine devices (IUDs) and barrier methods. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge.

Those with ovaries

Those who can become pregnant will have a pregnancy test before starting treatment. Cancer treatment can hurt the developing baby if you are or become pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. If you are pregnant or breastfeeding at the time of your cancer diagnosis, certain treatments will need to be avoided.

Menstruation, menses, menstrual flow, or your “period” may stop during treatment, but often returns within 2 years after treatment in those 35 years of age and under. It is still possible to become pregnant even though you might not have a period. Therefore, birth control is recommended during and after treatment. Consult your doctor for the best time to plan a pregnancy.

Those with testicles

Cancer and cancer treatment can damage sperm. Therefore, use contraception (birth control) such as condoms to prevent pregnancy during and immediately after cancer treatment.

Tissue tests

An aspirate or a biopsy is the removal of a sample of tissue or group of cells for testing. A diagnosis of ALL is confirmed using a bone marrow aspirate and bone marrow biopsy.

Bone marrow tests

Leukemia starts in the bone marrow. To diagnose ALL, samples of bone marrow must be removed and tested before starting any treatment. Your sample should be reviewed by a pathologist who is an expert in the diagnosis of ALL. This review is often referred to as histology, histopathology, or hematopathology review. The pathologist will note the overall appearance and the size, shape, and type of your cells.

There are 2 types of bone marrow tests that are often done at the same time:

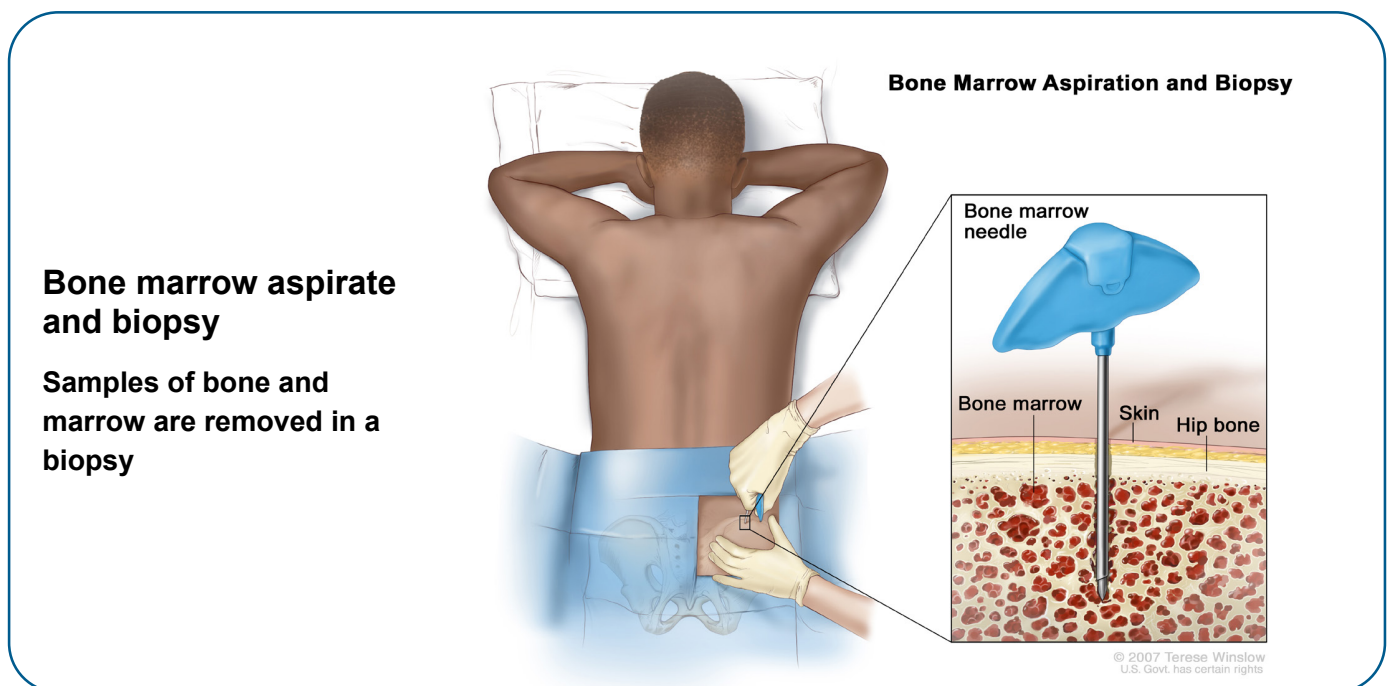
- Bone marrow aspirate
- Bone marrow biopsy

Your bone marrow is like a sponge holding liquid and cells. An aspirate takes some of the liquid and cells out of the sponge, and a biopsy takes a piece of the sponge.

For many, this is a painful procedure. Your care team will try to make you as comfortable as possible. The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. For an aspirate, a hollow needle will be pushed through your skin and into the bone. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be used to remove a core sample. You may feel bone pain at your hip for a few days. Your skin may bruise.

Flow cytometry

Flow cytometry is a laboratory method used to detect, identify, and count specific cells. Flow cytometry involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine



measures the number of cells, things like the size and shape of the cells, and other unique features of cells.

A complete blood test can count the number of white blood cells, but it cannot detect the subtle differences between different types of blood cancers. Immunophenotyping can detect these subtle differences. Flow cytometry can detect these subtle differences. The most common use of flow cytometry is in the identification of markers on cells, particularly in the immune system (called immunophenotyping).

Immunophenotyping

Immunophenotyping uses antibodies to detect the presence or absence of white blood cell antigens called biomarkers. These antigens are proteins that can be found on the surface of or inside white blood cells. Certain biomarkers are targeted in ALL treatment.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cells. The cells are then studied using a microscope.

Genetic risk testing

You might be thinking why did I get cancer? Most of the time, the answer is one cell made a mistake when dividing and then a cancer formed. Some, however, have a predisposition or have something in their DNA (genetic material) that makes them more likely to develop cancer. Understanding whether you have a cancer predisposition condition can sometimes affect your cancer treatment, but more often, it can affect screening for other

cancers. Therefore, identifying a cancer predisposition condition is important.

Genetic testing is done using blood or saliva (spitting into a cup). The goal is to look for gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, family members might carry these mutations. Tell your care team if there is a family history of cancer.

A genetic risk assessment will identify if you carry a cancer risk and if you may benefit from genetic testing, additional screening, or preventive interventions. Depending on the genetic risk assessment, you might undergo genetic testing and genetic counseling.

Leukemia predisposition syndromes

A family history of leukemia can affect treatment. A skin punch biopsy might be done if a predisposition condition is suspected. If your blood was tested at diagnosis, you would see the genetic changes of the leukemia. Therefore, a skin punch biopsy is used. In this procedure, a small piece of skin and connective tissue is removed to get DNA that hasn't been altered by ALL. This will be used to see if you inherited genes that increase your risk of leukemia. Leukemia predisposition syndrome can affect how your body responds to treatment. Blood and saliva can be used when ALL cells disappear (in remission). Biological family members who are possible hematopoietic cell donors might be tested for leukemia predisposition syndrome.

While it can be confusing, just know that testing done to look for an inherited gene (germline) mutation or an inherited risk of

cancer is different than genetic testing done specifically on cancer cells or testing to look for proteins produced by cancer cells.

Genetic and biomarker testing

Genetic and biomarker tests are used to learn more about your type of ALL, to target treatment, and to determine the likely path your cancer will take (prognosis). This genetic testing is different from family history genetic testing. ALL genetic testing looks for changes only in the leukemia cells that have developed over time, and not changes in the rest of your body's cells. Biomarker testing includes tests of genes or their products (proteins) and identifies the presence or absence of mutations and certain proteins. It is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing.

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes are coded instructions for the proteins your cells make. Most genes contain information about a specific protein. A mutation is when something goes wrong in the genetic code. Proteins are written like this: BCR. Genes are written in italics like this: *BCR*

ALL cells sometimes have changes in genes and chromosomes that can be seen under a microscope or found with other tests.

Mutations

ALL cells can have changes in genes and chromosomes. Mutation testing looks for these changes or abnormalities that are unique to ALL cells. Examples of such changes are called deletion, insertion, amplification, translocation (rearrangement), and point mutation.

- ✓ **Amplification** – When a part or whole chromosome or gene is increased (for example, duplicated) such as intrachromosomal amplification of chromosome 21 (*iAMP21*)
- ✓ **Deletion** – When part of a chromosome or gene is missing such as PTEN or IKZF1
- ✓ **Insertion** – When a new part of a chromosome or gene is included
- ✓ **Inversion** – Switching of parts within one chromosome
- ✓ **Point mutation** – When part of a gene is changed
- ✓ **Chromosome translocation and gene rearrangement** – Switching of parts between 2 chromosomes. When described at the chromosome level, it is called a translocation. When described at the gene level, it is called rearrangement. For example, the chromosome translocation is written as t(12;21)(p13.2;q22.1) and its gene rearrangement is written as *ETV6::RUNX1*.

ALL mutation testing

A sample of your blood or bone marrow will be studied to see if the ALL cancer cells have any specific mutations. This is separate from the genetic testing for mutations that you may have inherited from your biological parents.

ALL cells can have changes in genes and chromosomes. Mutation testing using methods such as karyotype, fluorescence in situ hybridization (FISH), polymerase chain reaction (PCR), and next-generation sequencing (NGS) are used to look for these changes or abnormalities. Some mutations may determine the type of treatment given.

Karyotype

A karyotype is a picture of chromosomes. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. A karyotype will show extra, missing (deletion), translocated, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow or blood must be used.

FISH

Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. FISH can look for mutations that are too small to be seen with other methods. It can only be used for known changes. Since this test doesn't need growing cells, it can be performed on either a bone marrow or blood sample. Sometimes, a bone marrow sample is needed to get all the information the care team needs to help plan your treatment.

PCR

A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of one's DNA or RNA (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for next-generation sequencing (NGS). This is important when testing for treatment response or remission. A real-time or reverse transcriptase (RT-PCR) PCR is used to look for gene rearrangements such as *BCR::ABL1*

Next-generation sequencing

Next-generation sequencing (NGS) is a method used to determine a portion of a person's DNA sequence. It shows if a gene has any mutations that might affect how the gene works. NGS looks at the gene in a more detailed way than other methods, and can find mutations that other methods might miss.

Translocations and rearrangements

Translocation is a switching of parts between two chromosomes. If this is explained at the gene level, it is called rearrangement. The Philadelphia chromosome occurs with translocation between chromosomes 9 and 22 and is written as $t(9;22)(q34;q11.2)$ in the chromosome level and *BCR::ABL1* in the gene level. The detailed explanation is shown in the image on the next page.

Other common translocations in ALL include $t(v;11q23.3)$ written as *KMT2A*-rearranged and $t(12;21)(p13.2;q22.1)$ written as *ETV6::RUNX1*.

Philadelphia chromosome

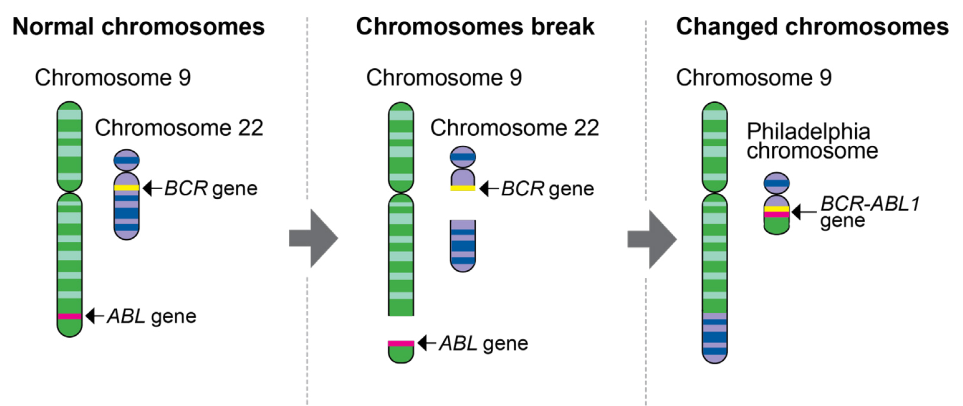
In the Philadelphia chromosome, a piece of chromosome 9 and a piece of chromosome 22 break off and trade places with each other. These pieces create a new, abnormal chromosome 22 that contains a small part of chromosome 9. This new, abnormal chromosome 22 is referred to as the Philadelphia chromosome. You might see it written as Ph-positive (Ph+).

Chromosomes have many genes. One piece of chromosome 9 contains a gene called *ABL1*. One piece of chromosome 22 contains a gene called *BCR*. When these genes fuse together on chromosome 22, a new *BCR::ABL1* gene is formed. This translocation is also shown as t(9;22). *BCR::ABL1* makes a new protein that leads to uncontrolled cell growth. *BCR::ABL1* is not found in normal blood cells. It is not passed down from biological parents to children.

Testing takes time. It might take days or weeks before all test results come in.

Philadelphia chromosome

The Philadelphia chromosome is formed by a translocation between parts of chromosomes 9 and 22. It contains the abnormal *BCR::ABL1* fusion gene.



Imaging tests

Imaging tests take pictures of the inside of one's body to look for sites with leukemia. Leukemia can spread outside the bloodstream to lymph nodes, liver, spleen, and skin. It rarely spreads to the lining of the brain and spinal cord. Imaging tests can also show areas of infection or bleeding, which may impact your care.

A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. The doctor will discuss the results with you. While these reports are available to you through your portal, please wait to discuss these results with the doctor.

Contrast material

Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. Contrast might be taken by mouth (oral) or given through a vein (IV). The contrast is not permanent and will leave the body in one's urine after the test. The types of contrast vary and are different for CT and MRI.

Tell your care team if you have had allergic reactions to contrast in the past, especially to iodine or shellfish like shrimp. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

Brain CT

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the same body part from different angles. All the images are combined to make

one detailed three-dimensional (3D) picture. A CT of the brain is used to look for bleeding. Contrast should not be used.

Brain MRI

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. A device will be placed around your head that sends and receives radio waves. An MRI can show if the outer layer of the brain is swollen. Swelling caused by leukemia is called leukemic meningitis. Contrast should be used.

A closed MRI has a capsule-like design where the magnet surrounds you. An open MRI has a magnet top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be sure to talk to your care team about it. Also, tell your doctor if there is any metal in your body.

PET scan

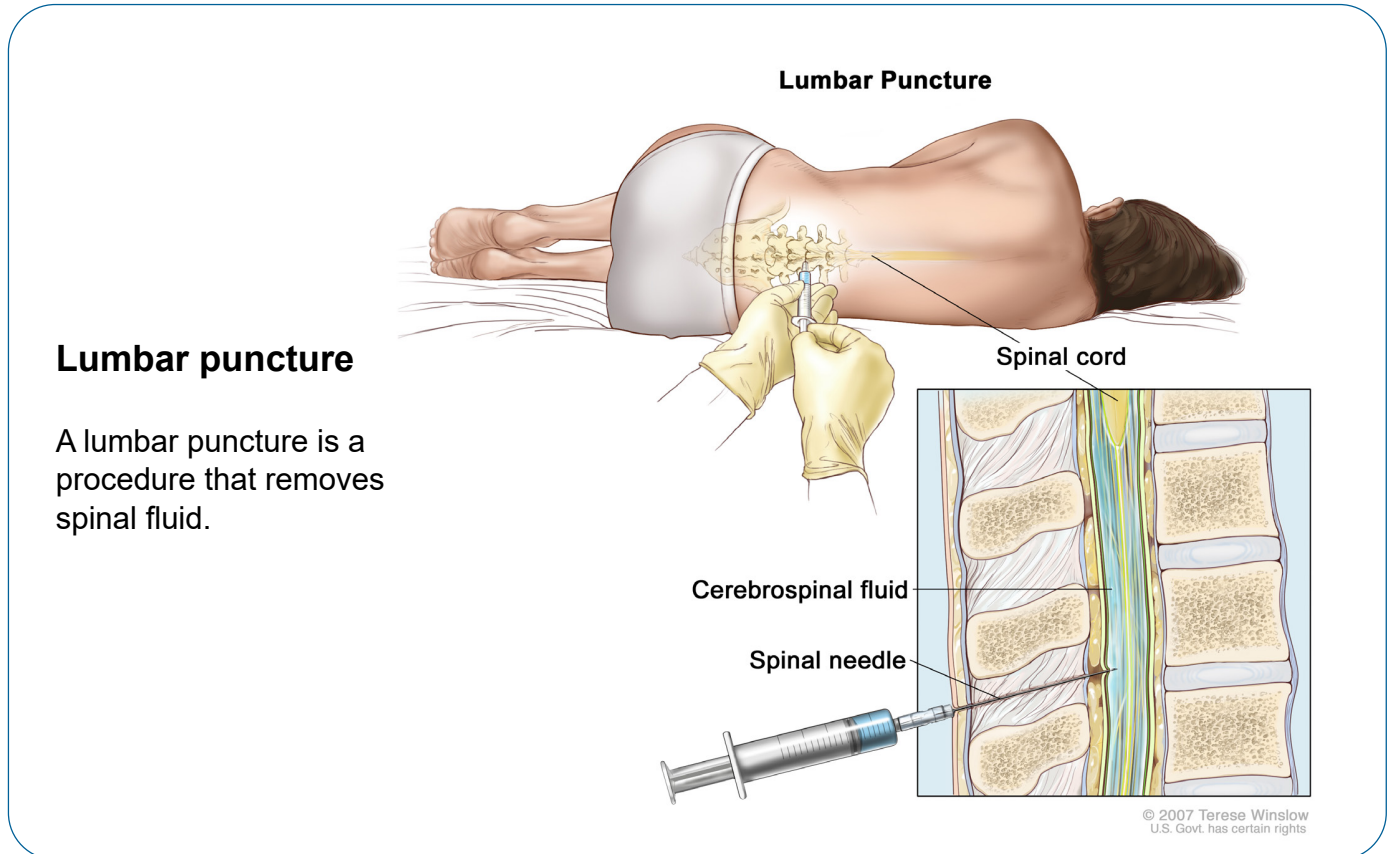
A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and if they are using sugar produced by your body to grow. Cancer cells show up as bright spots on PET scans because they use sugar more quickly than other cells. However, not all cancer cells will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot. When a PET scan is combined with CT, it is called a PET-CT scan. It may be done with one or two machines depending on the cancer center.

Lumbar puncture

Leukemia can travel to the fluid that surrounds the spine or brain. This may cause symptoms. In order to know if leukemia cells are in your spinal fluid, a sample must be taken and tested to rule out a central nervous system (CNS) disease.

A lumbar puncture (LP) is a procedure that removes spinal fluid. It is also called a spinal tap. A lumbar puncture may also be used to inject cancer drugs into spinal fluid. This is called intrathecal (IT) chemotherapy.

During a spinal tap, you will be lying down or sitting on an exam table. If lying down, your knees must be tucked up near your chest. If sitting, you must lean forward toward your knees. The lower part of your back over your spine will be numbed. Next, a thin needle will be inserted between your spinal bones. You may feel some pressure. After the sample is taken, it will be sent to a lab for testing.



Heart tests

Heart or cardiac tests are used to see how well your heart works. These tests might be used to monitor treatment side effects. You might be referred to a cardiologist.

Electrocardiogram

An electrocardiogram (ECG or EKG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged corrected QT interval (or QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an ECG. Certain treatments for ALL can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

Echocardiogram

An echocardiogram (or echo) uses sound waves to make pictures. For this test, small patches will be placed on your chest to track your heartbeat. Next, a wand (called a transducer) with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen on a screen. The pictures will be recorded for future viewing.

An echocardiogram is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart every time it beats. In low ejection fraction, the amount of blood pumping from the left side of the heart is lower than normal.

MUGA

A multigated acquisition (MUGA) scan is used to evaluate the pumping function of your heart. During the test, a small amount of radiotracer is injected into a vein. A special camera, called a gamma camera, will create computer-generated movie images of your beating heart.

MUGA scan might show low ejection fraction. This is when the amount of blood pumping from the left side of the heart is lower than normal.

Key points

- Results from blood tests, bone marrow aspirate and biopsy, and imaging studies will determine your treatment plan.
- An aspirate or biopsy is the removal of a sample of tissue or group of cells for testing. A diagnosis of ALL is confirmed using a bone marrow aspirate and bone marrow biopsy.
- Genetic tests are used to learn more about your type of ALL, to target treatment, and to determine the likely path your cancer will take (prognosis).
- Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment and prognosis.
- HLA typing should be done in those with newly diagnosed ALL for whom allogeneic (donor) hematopoietic cell transplant (HCT) is an option.
- Imaging tests are used to look for sites of infection, bleeding, and leukemia that might have spread outside the bloodstream.
- Heart or cardiac tests might be needed to test how well your heart works.
- A lumbar puncture (LP) may be done to look for leukemia in spinal and brain fluid.
- Online patient portals are a great way to access your test results.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

3

Treating ALL

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There is more than one treatment for ALL. This chapter presents an overview of the types of treatment and what to expect. Not everyone will receive the same treatment.

Care team

Treating ALL takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of health care and psychosocial care professionals from different professional backgrounds who have knowledge (expertise) and experience in your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, the care team might include the following:

- **A diagnostic radiologist** interprets the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places intravenous (IV) ports for treatment.
- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer

diagnosis, staging, and information about biomarker testing.

- **A medical oncologist** treats cancer in adults using systemic therapy.
- **A radiation oncologist** prescribes and delivers radiation therapy to treat cancer.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners (NPs) and physician assistants (PAs)** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.
- **Palliative care nurses, advanced practice providers (APPs),** and physicians help provide an extra layer of support with cancer-related care.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.

- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **A research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

Your physical, mental, and emotional well-being are important. Help other team members understand:

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

Treatment overview

ALL is not treated the same for everyone. As the body ages, it can have difficulty tolerating higher doses or more intense cancer treatments. In addition to age, your overall health, general level of fitness (performance status), and genetic risk play a role in treatment decisions. Some cancers are treated more aggressively than others. An intensive therapy might have more side effects or be of a higher dose than a less intensive therapy. An intensive therapy is not necessarily better. Remission or a complete response is still possible in lower-intensity treatments.

There are always risks with treatment. Talk with your care team about the risks and why a treatment might be better for you. Find out how treatment might affect the quality and length of life. Your preferences about treatment are also important.

Systemic therapy works throughout the body. Chemotherapy is a type of systemic therapy. It is the backbone of ALL treatment and is often combined with other drug therapies.

Systemic therapy, fluids, and blood products might be given through:

- Central venous access device (CVAD)
- Peripheral intravenous line (PIV)

You will likely get either a catheter or a port to deliver chemotherapy and other treatments. A catheter is a thin, long tube that is often placed in the chest. This goes into a large vein and stays there until treatment is complete. A port is a small, round disc that is usually placed in the chest.

CVAD

A central venous access device (CVAD) and central venous catheter (CVC or central line) are devices inserted into the body through a vein. This makes it easier to give fluids, blood products, medicine, and other therapies directly into the bloodstream. While generally safe, there are risks for infection and blood clots. The device may be a catheter (examples include Hickman and Broviac) or port (port-a-cath or mediport). Ask which option is best based on the treatment you will be receiving.

A central venous catheter (CVC) is a thin, long tube that is often placed in the chest and goes into a large vein, such as the neck (jugular) veins or the veins under the collarbone (subclavian). The part of the CVC used to attach to fluids or medicine is visible outside of the body at all times.

A port is a small, round disc that is usually placed in the chest, with a catheter underneath the skin that goes from the disc to a large vein, such as the neck (jugular) veins or the veins under the collarbone (subclavian). When the port is needed to give fluids or medications, a needle is placed through the skin on the chest to “access” the port. Once the fluid or medication has been given, the needle is removed (“deaccessed”) and the port just looks like a bump underneath the skin.

Both devices are inserted during a minor surgery and remain in the body until treatment is complete. Once the CVC or port-a-cath is removed, the skin will heal. There may be a scar.

PICC

A peripherally inserted central catheter (PICC or PICC line) is a long, thin tube that’s inserted through a vein in the arm or leg and passed through to the larger veins near the heart.

PIV

A peripheral intravenous line (PIV) is a small, short plastic catheter that is placed through the skin into a vein, usually in the hand, elbow, or foot. A PIV can be used to give fluids, medicines, and certain chemotherapies.

Warnings about herbal supplements and drug interactions

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction. It is critical to speak with your care team about any supplements you may be taking.

Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- St. John’s Wort
- Antioxidants

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC)

drugs, herbals, or supplements you are taking.
Bring a list with you to every visit.

Steroids

All ALL treatments include steroids. Steroid is the short name for corticosteroid. Steroids are human-made versions of hormones made by the adrenal glands. The adrenal glands are small structures found near the kidneys, which help regulate blood pressure and reduce inflammation. Steroids also are toxic to lymphoid cells and are an important part of pediatric ALL chemotherapy. Steroids can cause short-term and long-term side effects. The type of steroids used to treat ALL are called corticosteroids or glucocorticoids. Corticosteroids are not the same as the steroids used by some athletes.

Steroids can cause short- and long-term side effects. Ask your care team about possible side effects.

Chemotherapy

Chemotherapy is the standard of care for treating ALL. Chemotherapy kills fast-dividing cells throughout the body, including cancer cells. You will be monitored throughout treatment for side effects or other unwanted (adverse) reactions. All chemotherapy drugs may cause severe, life-threatening, or fatal reactions.

Chemotherapy can be given as follows:

- **Oral (PO)** – taken by mouth either as a liquid or pill
- **Subcutaneous (SQ)** – given under the skin

- **Intramuscular (IM)** – uses a needle to inject medicine in the muscle of the arm or leg (like the flu shot)
- **IV (intravenous) infusion** – given through a vein using IV push, gravity infusion, or infusion pump. In an IV push, a drug is injected quickly over a few minutes. With a gravity infusion, medicine is put into a bag that hangs on a pole, and the pressure of gravity delivers the medicine into the IV line at a safe and steady rate. In an IV infusion, chemotherapy flows through a tube attached to the catheter. The flow may be controlled by a machine called an IV pump. Most IV chemotherapy is given through a port, CVC, or PICC, but some can be given through PIVs.
- **Intrathecal (IT)** – given into the spinal fluid. In addition to other forms of chemotherapy, everyone with pediatric ALL will have chemotherapy injected into the cerebrospinal fluid (CSF) to kill any leukemia cells that might have spread to the brain and spinal cord. This treatment is given through a lumbar puncture (spinal tap).

Types of chemotherapy

There are many types of chemotherapy used to treat ALL. Often chemotherapies are combined. This is called multiagent chemotherapy or a multiagent regimen. Each chemotherapy works to kill cancer cells in a different way, which helps prevent the cancer from coming back. Each type of chemotherapy can also cause different side effects. Talk to the care team about the types of chemotherapy you are getting, when you will get them, and what side effects to expect.

For examples of the main types of chemotherapy drugs (agents) used to treat ALL, **see Guide 2**.

Other types of chemotherapy may be used depending on your type of leukemia and how ALL responds to therapy.

Guide 2

Systemic therapy examples

Chemotherapy examples

- Asparaginase (Pegaspargase, Calaspargase, Oncaspar, Erwinaze, Rylaze)
- Cyclophosphamide
- Cytarabine (Cytosar-U)
- Daunorubicin (Cerubidine)
- Doxorubicin (Adriamycin)
- 6-MP (6-mercaptopurine)
- Methotrexate
- Nelarabine (Arranon)
- Thioguanine (Tabloid)
- Vincristine (Oncovin, Vincasar)

TKI examples

- Bortezomib (Velcade)
- Bosutinib (Bosulif)
- Dasatinib (Sprycel)
- Imatinib (Gleevec)
- Nilotinib (Tasigna)
- Ponatinib (Iclusig)
- Ruxolitinib (Jakafi)

Immunotherapy examples

- Blinatumomab (Blincyto)
- Daratumumab (Darzalex)
- Inotuzumab ozogamicin (Besponsa)
- Tisagenlecleucel (Kymriah)
- Brexucabtagene autoleucel (Tecartus)

Targeted therapy

Targeted therapy is a form of systemic therapy that focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive.

You will be monitored throughout treatment for side effects or other unwanted (adverse) reactions. As with other systemic therapies, targeted therapy may cause severe, life-threatening, or fatal reactions.

Tyrosine kinase inhibitor

A tyrosine kinase inhibitor (TKI) is a type of targeted therapy that blocks the signals that cause cancer to grow and spread. TKIs might be used alone or in combination with other systemic therapies like chemotherapy.

Tyrosine kinases are proteins in cells that are important for many cell functions. The protein made by the *BCR::ABL1* gene is a tyrosine kinase. It moves or transfers chemicals, called phosphates, from one molecule to another. TKIs block this transfer, which stops uncontrolled cell growth in ALL.

TKIs are slightly different from one another, but they generally work in a similar way. They may cause different side effects. You might not be given a certain TKI if you have a health condition, such as lung or heart issues, or certain ALL-related mutations.

For examples of TKIs that might be used to treat ALL, **see Guide 2**.

Immunotherapy

The immune system is the part of the body that fights infection. Our immune system also is supposed to attack cancer cells when they first develop. Sometimes cancer cells escape the natural defense of our immune system. Immunotherapy is drug therapy that acts like your immune system. Some types of immunotherapy can increase the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Other types of immune therapy are drugs that work similarly to our immune system. Immunotherapy can be given alone or with other types of treatment. As with other treatments, there is the potential for complications and life-threatening reactions.

Antibody therapy

Antibody therapy uses antibodies to help the body fight cancer, infection, or other diseases. Antibodies are proteins made by the immune system that bind to specific markers on cells or tissues. There are different types of antibody therapy. One type is called monoclonal antibodies (mAbs). mAbs used in cancer treatment may kill cancer cells directly, block development of tumor blood vessels, or help the immune system kill cancer cells. Other types of antibody therapy include bispecific T-cell engagers (BiTEs). BiTEs connect cancer cells to normal immune cells to improve the way normal immune cells fight the cancer.

- Blinatumomab (Blincyto) allows normal T cells to attack cancerous B cells by bringing them close together. Blinatumomab is a BiTE.
- Inotuzumab ozogamicin (Besponsa) binds to CD22 on leukemia cells then releases a toxic agent once it's inside the cells.

CD19-targeting CAR T-cell therapy

CD19-directed genetically modified autologous T-cell immunotherapy (CD19-targeting CAR T-cell therapy) or anti-CD19 CAR T-cell therapy is made from your own T cells. T cells will be removed from your body, and in the lab, a CAR (chimeric antigen receptor) will be added to them. This programs the T cells to find cancer cells. The programmed T cells will be infused back into your body to find and kill cancer cells. Not everyone will need this type of treatment.

Tisagenlecleucel (Kymriah) and Brexucabtagene autoleucel (Tecartus) are a type of CD19-targeting CAR T-cell therapy.

More information on CAR T-cell therapy can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Radiation therapy

Radiation therapy (RT) uses high-energy radiation from photons, electrons, x-rays, or protons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of time. Radiation therapy can be given alone or with certain systemic therapies. It may be used as supportive care to help ease pain or discomfort caused by cancer.

- Those with leukemia in the central nervous system may receive radiation to the brain area called **cranial irradiation**. The areas of the brain targeted for ALL radiation treatment are different from areas targeted for brain metastases of solid tumors.
- Those with testicular disease may receive radiation to the testes called **testicular irradiation**.
- **Total body irradiation (TBI)** is radiation of the whole body given before bone marrow transplant.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of treating cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II trials** study how well the drug or approach works against a specific type of cancer.
- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom you trust. Keep in

mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Do I have to pay to be in a clinical trial?

Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.



Finding a clinical trial

In the United States

NCCN Cancer Centers

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

The U.S. National Library of Medicine (NLM)

clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

[cancer.gov/contact](https://www.cancer.gov/contact)

Hematopoietic cell transplant

A hematopoietic cell transplant (HCT) replaces hematopoietic stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy as part of the transplant process. A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. You might hear it called a stem cell transplant (SCT) or a bone marrow transplant (BMT). This book will refer to it as HCT. HCTs are performed in specialized centers.

There are 2 types of HCTs:

- **Autologous** – stem cells come from you.
- **Allogeneic** – stem cells come from a donor who may or may not be related to you. Only an allogeneic HCT is used as a possible treatment in ALL.

Allogeneic transplant

An allogeneic hematopoietic cell transplant (alloHCT) uses healthy stem cells from a donor. The donor may or may not be related to you. Before an HCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune system so your body won't kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

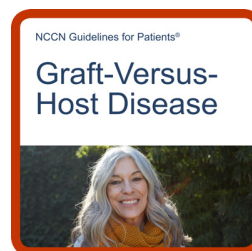
After conditioning, you will receive a transfusion of the healthy stem cells from a donor matched to you. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form.

This is called engraftment. It usually takes about 2 to 4 weeks. Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. Transfusions are also possible. A red blood cell transfusion is used to prevent bleeding and to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding. While waiting for the cells to engraft, you will likely feel tired and weak.

Possible side effects

Every treatment has side effects. You will be monitored for infections, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack your normal, healthy tissue. There are treatments for GVHD. Ask your care team about the possible side effects or complications of HCT and how this might affect your quality and of life.

More information on GVHD can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Supportive care overview

Supportive care will be specific to your needs. Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. It might include pain relief, palliative care, emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Best supportive care, supportive care, and palliative care are often used interchangeably.

It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment. Some potential side effects and procedures are described next. They are not listed in order of importance. Some side effects are very rare.

Side effects

All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant. ALL treatment can cause a number of side effects. Some are very serious.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects. You will be monitored closely for side effects.

Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. When treatment leads to remission (or no evidence of disease), you will need follow-up or survivorship care for late effects. During survivorship care you will still have a care team, but it will look different. Seek out peer support groups, whether online or in-person.

It is important to tell the care team about all side effects so they can be managed.

Side effects

Anemia, neutropenia, and thrombocytopenia

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not have enough healthy blood cells, resulting in less oxygen being carried to your cells. You might tire easily if you are anemic.
- **Neutropenia** is a decrease in neutrophils, a type of white blood cell. This puts you at risk for infection.
- **Thrombocytopenia** is a condition where there are not enough platelets found in the blood. This puts you at risk for bleeding.

Blood clots

Cancer treatment can cause blood clots to form. This can block blood flow and oxygen in the body. Blood clots can break loose and travel to other parts of the body causing stroke or other problems.

Cytokine release syndrome

Cytokine release syndrome (CRS) is a condition that may occur after treatment with some types of immunotherapy, such as monoclonal antibodies and CAR T cells. It is caused by a large, rapid release of cytokines from immune cells affected by the immunotherapy. Signs and symptoms of CRS include fever, muscle aches, nausea, headache, rash, fast heartbeat, low blood pressure, and trouble breathing.

Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- The time and dose of all medicines
- When pain starts and ends or lessens
- Where you feel pain
- A description of your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- A rating of your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- Does pain get in the way of you doing the things you enjoy?

Diarrhea

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It is important to drink lots of fluids.

Difficulty eating

Sometimes side effects from surgery, cancer, or its treatment might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining weight.

Distress

Depression, anxiety, and sleeping problems are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you may be feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of

treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet and physical activity can help. You might be referred to a nutritionist or dietitian to help with fatigue.

Hand-foot syndrome

Hand-foot syndrome is a common side effect of chemotherapy. Small amounts of chemotherapy leak out of very small blood vessels called capillaries in the palms of the hands and soles of the feet. It causes redness, swelling, and pain. Sometimes blisters appear. You will want to protect your hands and feet by applying moisturizer or lotion.

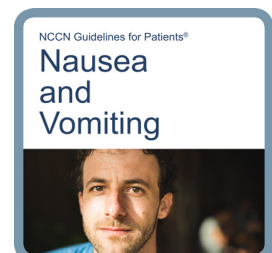
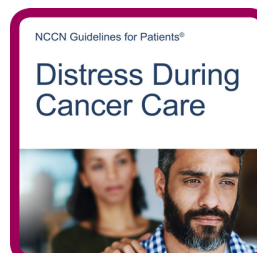
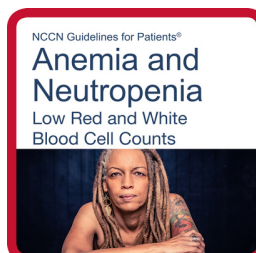
High blood pressure

High blood pressure (HBP or hypertension) occurs when the force of blood flowing through your blood vessels is consistently too high. This can cause headaches and vision problems. If left untreated, HBP can cause heart problems and stroke. Steroids can cause HBP. Medicine might be used to control HBP.

High blood sugar

One possible side effect of steroids is high blood sugar or hyperglycemia. Glucose (sugar found in the blood) will be measured. Insulin might be needed to control high blood sugar.

More information on supportive care is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Hypersensitivity, allergy, and anaphylaxis

Certain treatments can cause an unwanted reaction. Hypersensitivity is an exaggerated response by the immune system to a drug or other substance. This can include hives, skin welts, and trouble breathing. An allergy is an immune reaction to a substance that normally is harmless or would not cause an immune response in most people. An allergic response may cause harmful symptoms such as itching or inflammation (swelling). Anaphylaxis or anaphylactic shock is a severe and possible life-threatening allergic reaction.

Infection

Infections occur more frequently and are more severe in those with a weakened immune system. Drug treatment for ALL can weaken the body's natural defense against infections. If not treated early, infections can be fatal.

Neutropenia, a low number of white blood cells, can lead to frequent or severe infections. When someone with neutropenia also develops a fever, it is called febrile neutropenia (FN). With FN, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections. FN is a side effect of some types of systemic therapy.

Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You will be given medicine to prevent nausea and vomiting.

Neurocognitive or neuropsychological effects

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration, memory, and thinking. Survivors are at risk for neurotoxicity and might be recommended for neuropsychological testing. Neuropsychology looks at how the health of your brain affects your thinking and behavior. Neuropsychological testing can identify your limits and a health care professional can create a plan to help with these limits.

Neuropathy

Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by cancer or cancer treatment. Most of the time, neuropathy goes away after treatment.

Neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Seizures and confusion can occur. If ALL treatment includes methotrexate, then you will be monitored for methotrexate neurotoxicity (MTX). Neurotoxicity, such as seizures and confusion, can be seen with immunotherapy, as well.

Organ issues

Treatment might cause your kidneys, liver, heart, and pancreas to not work as well as they should.

Osteonecrosis

Osteonecrosis, or avascular necrosis, is death of bone tissue due to lack of blood supply. It is a possible side effect of steroids and most often affects weight-bearing joints, such as the hip and/or knee.

Pain

Tell your care team about any pain or discomfort. You might meet with a pediatric pain or palliative care specialist to manage pain. Bone pain and vincristine-associated neuropathic pain are common in ALL.

Pneumonia

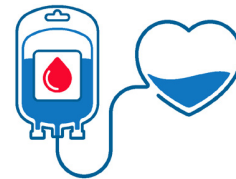
Pneumocystis pneumonia is a serious infection caused by the fungus *Pneumocystis jirovecii*. Since those with ALL are at high risk, medicine will be given throughout treatment to prevent this type of pneumonia.

Tumor lysis syndrome

Tumor lysis syndrome (TLS) causes an imbalance of substances in blood. There are different treatments for TLS. Treatment depends on what substances are out of balance and how well your kidneys are working. Sometimes, TLS can cause too much potassium in your blood. Treatment might include hemodialysis or hemofiltration. A machine will filter your blood.

Weight gain

Weight gain is one side effect of high-dose steroids. This can be uncomfortable and cause distress. It is important to maintain muscle mass. Find a physical activity you enjoy. Ask your care team what can be done to help manage weight gain.



Transfusions

A transfusion is a common procedure to replace blood or blood components (red blood cells or platelets). It is given through an intravenous line (IV), a tiny tube that is inserted into a vein with a small needle.

- ✓ The whole process can take about 1 to 4 hours, depending on how much blood is needed
- ✓ Most transfusions use blood from a donor. This is preferred in ALL.
- ✓ Blood transfusions are usually very safe. Donated blood is carefully tested, handled, and stored.
- ✓ Most people's bodies handle blood transfusions very well. But, like any medical procedure, there are some risks. Speak with your care team for specific information about the risks.
- ✓ Systemic therapy can affect how bone marrow makes new blood cells. Some people getting treatment for cancer might need a transfusion of red blood cells or platelets.

Supportive care

Antibiotics and treatment

For infection, antibiotics (for bacterial infection), antifungal medicine (for fungal infection), and antiviral drugs (for viral infection) are used. These medications can be used to prevent infections called prophylaxis.

Dialysis

Leukemia cells and chemotherapy sometimes cause damage to the kidneys. If the damage is severe, you may need dialysis. Dialysis is the process of filtering blood when the kidneys are unable. There are different types of dialysis. Hemodialysis and hemofiltration remove waste and water by circulating blood outside the body through an external filter.

Hyperleukocytosis and leukapheresis

Hyperleukocytosis (leukostasis) is an extremely high lymphoblast count. Sometimes those with hyperleukocytosis need to have a machine remove lymphoblasts from the blood in a process called leukapheresis. In leukapheresis, you may be connected to a machine called an apheresis machine. The machine separates white blood cells (leukocytes) from other blood cells. Once the excess leukocytes are removed, the blood is returned to your body.

Transfusions

Blood transfusions are common during ALL treatment. A transfusion is a slow injection of blood products such as red blood cells or platelets into a vein. Over time, the body may begin to reject blood transfusions.

Most blood transfusions come from blood banks and are collected from strangers who donate blood. Sometimes, family members ask if they can donate blood for a family member with ALL. Typically, we do not want to transfuse blood products collected from family members. Your doctor can explain why it is safer to use blood products from strangers than members of your own family.

Get to know your care team and help them get to know you.

Key points

- Treatment decisions should involve a multidisciplinary team (MDT) of health care and psychosocial care professionals from different fields of medicine who have knowledge (expertise) and experience with your type of cancer.
- Steroids are part of all ALL regimens.
- Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and normal cells. Chemotherapy is the backbone of ALL treatment and is often combined with other drug therapies.
- Targeted therapy focuses on specific or unique features of cancer cells.
- Immunotherapy uses the immune system to find and destroy cancer cells.
- A hematopoietic cell transplant (HCT) replaces damaged bone marrow stem cells with healthy stem cells. You might hear it called a stem cell transplant (SCT) or bone marrow transplant (BMT).
- Clinical trials study how safe and helpful tests and treatments are for people. Many ALL standard of care treatment regimens are the result of clinical trials.
- All cancer treatments can cause unwanted health issues called side effects. You will be monitored for side effects, infection, and other treatment-related issues.
- Supportive care is health care that relieves symptoms of side effects caused by cancer or its treatment and improves quality of life. Supportive care is always given.
- Some side effects, called late effects, may take years to appear. Risk for late effects will depend on the type(s) of cancer treatment given, and the dose and the length of time of treatment. It is important to go to follow-up appointments.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

4

Treatment phases

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The goal of treatment is a complete response or complete remission. Treatment will be in phases. Each phase has a different name depending on the treatment plan your care team is using. All treatment plans include an induction phase, which aims to put leukemia into remission. After (post) induction, there will be multiple phases to rid the body of any remaining leukemia cells. Maintenance phase helps prevent relapse.

In complete response all of the following are true:

- No lymphoblasts are found in blood.
- Less than 5% of blasts are found in bone marrow when looking at the sample under a microscope. This means that there are fewer than 5 blasts out of every 100 blood cells.
- No signs and symptoms of cancer outside the bone marrow. This is called extramedullary disease and includes lymph nodes, spleen skin, gums, testicles, and central nervous system (CNS).
- Blood recovery.

In an incomplete blood count recovery or incomplete response (CRi), the platelet count or absolute neutrophil count (ANC) has not yet returned to normal. ANC is an estimate of the body's ability to fight infections, especially bacterial infections.

Types of response

There are different types of treatment response. When there are no signs of cancer, it is called a complete response (CR) or complete remission. This does not always mean that ALL has been cured. Remission can be short-term (temporary) or long-lasting (permanent).

A diagnosis of ALL is based on the presence of 20 percent (20%) or more lymphoblasts in the bone marrow. This means that at least 1 out of every 5 marrow cells are lymphoblasts. However, in some cases a diagnosis of ALL is possible with less than 20% blasts. Treatment aims to reduce the number of blasts.

Phases of treatment

In general, there are several phases of intense chemotherapy followed by a longer phase of maintenance chemotherapy. Treatment phases may include induction, after induction or post-induction phases, and maintenance. However, not all doctors use the same terms when discussing treatment. The number of phases and the type chemotherapy given depend on the type of leukemia, as well as how you respond to the first phases of treatment.

Induction

Induction is the first phase of treatment. You will likely spend time in the hospital for part of this treatment. Treatment is a multi-drug combination of chemotherapies (called multiagent chemotherapy) and steroids.

The goal of induction is a complete response (CR) or remission. In CR, less than 5% of blasts remain at the end of induction. When induction does not lead to a complete response, it could be a sign that this cancer is very difficult to treat. In many subtypes, how ALL responds to initial treatment affects prognosis.

After induction, bone marrow aspirate and biopsy are used to look for a complete response and to measure the amount of leukemia cells that might remain called minimal residual disease.

Minimal residual disease

In minimal or measurable residual disease (MRD) very sensitive lab tests, such as flow cytometry, PCR, or NGS, find leukemia cells in bone marrow that cannot be seen under a microscope. Not all MRD can be found with tests. Treatment aims to reduce the amount of MRD.

What do I need to know?

Induction phase is the most stressful part of treatment. There is uncertainty, fear, and confusion. In addition, there will be a lot of tests, appointments, and disruption to routine. Lastly, you will hear a lot of unfamiliar words to describe a complex disease. Seek out support groups at your local hospital, through social media, or from those listed in the back of this book. Look to friends, relatives, neighbors, and coworkers for social support. Support services



Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- ✓ Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- ✓ Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- ✓ Create folders for insurance forms, test types (blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

such as counseling are also available. Ask the treatment team for more information. They are there to help.

Post-induction

After induction, there are multiple phases of intensive chemotherapy. These post-induction phases are needed to rid the body of any leukemia cells that might remain called minimal residual disease (MRD) and aim to prevent cancer from returning. You might hear a post-induction phase called consolidation. The time spent in post-induction phases and the intensity of the drug regimen will vary. It will be based on factors such as age, how well ALL responds to treatment, and risk factors.

Maintenance

Maintenance chemotherapy is the final, and longest, stage of treatment ALL. Treatment is less intensive than prior chemotherapy. It usually lasts at least 2 years and is outpatient. The goal is to lower the risk of relapse.

What do I need to know?

It is very important to continue taking medicine as prescribed and not miss or skip any doses.

This helps to prevent relapse. Ask your treatment team for help if you have trouble paying for medicine or trouble remembering to take your medicine.

CNS disease

Treatment to prevent ALL from spreading to the central nervous system (CNS) is called CNS prophylaxis or prophylactic treatment. CNS prophylaxis is typically given throughout all phases of treatment.

All treatment plans include intrathecal (IT) chemotherapy. IT chemotherapy is injected into spinal fluid. Some treatments include intrathecal treatment throughout therapy, whereas others do not include it in later phase maintenance therapy. Options for IT chemotherapy include intrathecal methotrexate or a combination of IT methotrexate, cytarabine, and hydrocortisone (known as triple IT chemotherapy). If ALL is found in your CNS at the time of diagnosis, you may need more IT chemotherapy or radiation to the brain.

Standard of care is the best-known way to treat particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.



Surveillance and monitoring

Monitoring or surveillance watches for any changes in your condition. **See Guide 3.**

Disease progression

When the percentage of ALL increases in blood or bone marrow during treatment, it is called progressive disease. Disease progression also occurs when the number of blasts within the blood or bone marrow increase by at least 25%.

Guide 3 Surveillance and monitoring

Surveillance	1 year after treatment	→	Every 1 to 2 months <ul style="list-style-type: none"> • Physical exam • Complete blood count (CBC) with differential • Liver function tests (LFTs) until normal
	2 years after treatment	→	Every 2 to 6 months <ul style="list-style-type: none"> • Physical exam • CBC with differential
	3 years after treatment	→	Every 6 to 12 months or as needed <ul style="list-style-type: none"> • Physical exam • CBC with differential
Procedures and biomarker testing	<ul style="list-style-type: none"> • Bone marrow aspirate as needed every 3 to 6 months for at least 5 years • Biomarker and other testing might include: <i>BCR::ABL1</i>, flow cytometry, FISH, chromosome, and minimal residual disease (MRD) testing. 		
Monitoring for late effects	<ul style="list-style-type: none"> • See <i>Long-Term Follow-up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers from the Children’s Oncology Group (COG)</i> at survivorshipguidelines.org • See <i>NCCN Guidelines for Patients: Survivorship Care for Cancer-Related Late and Long-Term Effects</i> at NCCN.org/patientguidelines • See <i>NCCN Guidelines for Patients: Adolescent and Young Adult Cancer</i> at NCCN.org/patientguidelines 		

Relapse

When leukemia returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. This is not always possible. A relapse is very serious. It is important to ask about prognosis.

Those with relapsed ALL are placed into risk groups. Length of first complete remission (CR1) and site of relapse are two important factors. Relapse can occur in the bone marrow called isolated medullary relapse, in areas outside of the marrow or blood such the brain or testicles called isolated extramedullary relapse, or a combination of both. In general, those with a later relapse, 3 or more years after starting treatment, have the best prognosis

Refractory disease

When leukemia remains and does not respond to treatment, it is called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about prognosis.

Key points

- The goal of treatment is a complete response.
- Induction is the first phase of treatment. You will likely spend time in the hospital for part of this treatment.
- Post-induction therapy is the second phase of treatment. It is needed to kill any cancer cells called minimal residual disease (MRD) that might be left after induction.
- Maintenance therapy is the final phase of treatment. The goal is to lower the risk of relapse.
- Central nervous system (CNS) prophylaxis is given to everyone to prevent ALL from spreading to the brain and spinal fluid.
- Monitoring watches for any changes in your condition.
- ALL that returns after remission is called relapse. To prevent relapse, it is important to take medicine as prescribed and not miss or skip any doses.
- When ALL does not respond to treatment or stops responding to treatment, it is called refractory or resistant cancer.

5

Ph-positive B-ALL

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In Ph-positive (Ph+) B-ALL, tests show the presence of the Philadelphia chromosome. Treatment is usually an intensive combination of systemic therapies.

Ask your care team which regimen is preferred for your subtype of ALL and what to expect from treatment.

Overview

Ph+ B-ALL is less common than other types of B-ALL. Treatment aims to stop the activity of the BCR::ABL fusion protein. Treatment is usually an intensive combination of systemic therapies that include tyrosin kinase inhibitors (TKIs). Systemic therapies work throughout the body. Treatment can be done as part of a clinical trial when available, or as part of a standard of care regimen.

Induction

Many induction treatment regimens are part of ongoing clinical trials. Induction is a combination of systemic therapies. All treatment regimens include systemic and/or intrathecal (IT) therapy to prevent central nervous system (CNS) disease. Typically, TKIs are added in the middle of induction for those who are found to be Ph+, whether they are being treated as part of a clinical trial or with a standard of care regimen.

There are 3 induction options:

- Clinical trial
- TKI with chemotherapy
- TKI with steroid

There are a many TKIs and chemotherapies used to treat ALL. Talk with your care team about which treatment might be best for you.

Treatment response will be measured after completing induction. The goal is a complete response (CR). In less than a CR, cancer remains. Treatment for less than a CR can be found in the relapsed or refractory disease section.

After a CR, tests will look for minimal residual disease (MRD). When MRD is found, it is called MRD-positive (MRD+).

Consolidation

After a complete response (remission), consolidation is based on if any minimal residual disease (MRD) remains.

MRD+

Persistent or rising MRD is treated with one of the following:

- Blinatumomab with or without TKI
- Multiagent chemotherapy with TKI
- TKI

After consolidation, a hematopoietic cell transplant (HCT) might be an option. The timing of an HCT depends upon donor availability and your health at the time of potential HCT. An HCT is not an option for everyone. You might be given a TKI after an HCT.

MRD-

If MRD is negative (MRD-), options are:

- Multiagent chemotherapy with TKI
- TKI
- Blinatumomab with TKI
- HCT in some cases

Maintenance

Maintenance is the last phase of treatment given after a complete response and when no minimal residual disease is found. This is usually the longest phase of therapy and is less intense than previous phases. TKIs are given throughout maintenance until therapy is complete. It is very important to continue to take your medicine as prescribed and not miss any doses.

Surveillance and monitoring

During maintenance or after a hematopoietic cell transplant, you will be monitored for signs of recurrence called relapse.

Relapsed or refractory disease

Relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission again. Cancer can return in the bone marrow called isolated medullary relapse, outside the bone marrow called isolated extramedullary relapse, or a combination of both (combined relapse). Extramedullary relapse can occur in the central nervous system or testicles. Location of relapse will impact treatment.

Relapse can happen more than once. With each relapse the goal of treatment is a complete response or remission. When cancer returns only in the bone marrow, it is called isolated medullary relapse. When cancer is found in the central nervous system and testicles, but not in the bone marrow or blood, it is called isolated extramedullary relapse. In this case, systemic therapy is needed to prevent relapse in bone marrow.

When leukemia remains and does not respond to treatment, it is called refractory.

Before starting treatment for relapsed or refractory disease, you will have ABL1 kinase domain mutation testing.

Treatment options for relapsed or refractory disease include:

- Clinical trial
- TKI with or without chemotherapy
- TKI with or without steroid
- Blinatumomab with or without TKI
- Inotuzumab ozogamicin with or without TKI
- Tisagenlecleucel (for those under 26 years of age with refractory B-ALL disease or in those who have had 2 or more relapses and no response with 2 TKIs)
- Brexucabtagene autoleucel (following therapy that included TKIs)

Most treatment paths for relapsed or refractory disease lead toward a hematopoietic cell transplant (HCT). The goal is to achieve an MRD-negative result before an HCT. The timing of an HCT depends upon donor availability and your health at the time of potential HCT.

Key points

- In Ph-positive (Ph+) B-ALL, tests show the presence of the Philadelphia chromosome.
- Induction is either a clinical trial or systemic therapy.
- All treatment regimens include systemic and/or intrathecal (IT) therapy to prevent central nervous system (CNS) disease.
- Treatment response will be measured after completing induction. The goal is a complete response (CR).
- After a CR, tests will look for minimal residual disease (MRD). When MRD is found, it is called MRD-positive (MRD+).
- Treatment for MRD+ aims to reduce the amount of MRD.
- During maintenance or after a hematopoietic cell transplant (HCT), you will be monitored for signs of recurrence called relapse.
- Relapse can happen more than once. With each relapse the goal of treatment is a complete response or remission.
- The timing of an HCT depends upon donor availability and your health at the time of potential HCT.

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Ph-negative B-ALL

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Philadelphia chromosome-negative (Ph-) B-ALL is the most common type of B-ALL. Treatment is a clinical trial or systemic therapy.

gene. It is the most common type of B-ALL. Induction will either be a clinical trial or systemic therapy. All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy. Treatment response will be measured after completing induction. Consolidation is based on if tests find minimal residual disease (MRD).

Before starting treatment, you will be placed in a risk group based on genetic and biomarker mutations found in your Ph- B-ALL. **See Guide 4.**

Overview

Ph-negative (Ph-) does not have the Philadelphia chromosome or the *BCR::ABL1*

Guide 4

Ph- B-ALL: Risk groups based on genetic and biomarker testing

Good risk features	Hyperdiploidy (leukemia cells with 51 to 65 chromosomes). <ul style="list-style-type: none"> • Triple trisomy of chromosomes 4, 10, and 17 are among trisomies that have the most favorable outcome
	t(12;21)(p13;q22): <i>ETV6::RUNX1</i> fusion
Poor risk features	Hypodiploidy (leukemia cells with less than 44 chromosomes)
	<i>KMT2A</i> rearranged (t[4;11] or others)
	t(v;14q32) /IgH
	t(9;22)(q34;q11.2): <i>BCR::ABL1</i>
	Complex karyotype (5 or more chromosome abnormalities)
	<i>BCR::ABL1</i> -like (Ph-like) ALL <ul style="list-style-type: none"> • JAK-STAT (<i>CRLF2r</i>, <i>EPORr</i>, <i>JAK1/2/3r</i>, <i>TYK2r</i>, mutations of <i>SH2B3</i>, <i>IL7R</i>, <i>JAK1/2/3</i>) • ABL class (rearrangements of <i>ABL1</i>, <i>ABL2</i>, <i>PDGFRA</i>, <i>PDGFRB</i>, <i>FGFR1</i>) • Other (<i>NTRKr</i>, <i>FLT3r</i>, <i>LYNr</i>, <i>PTK2Br</i>)
	Intrachromosomal amplification of chromosome 21 (iAMP21)
t(17;19): <i>TCF3::HLF</i> fusion	
Alterations of <i>IKZF1</i>	

Induction

Many induction treatment regimens are part of ongoing clinical trials. Induction is a combination of systemic therapies. Systemic therapies work throughout the body. All treatment regimens include systemic therapy and/or intrathecal therapy (injected into the spinal fluid) to prevent CNS disease.

Induction options include:

- Clinical trial
- Systemic therapy

Adults who are 65 years of age and over or those who have serious health conditions may opt for a palliative steroid instead of a clinical trial or systemic therapy. For AYAs, a pediatric-based treatment regimen is preferred.

Treatment response will be measured after completing induction. The goal is a complete response (CR). After a complete response, you will be monitored for minimal residual disease (MRD). When MRD is found, it is called MRD-positive (MRD+). In less than a CR, cancer remains. Treatment for less than a CR will follow relapsed or refractory section.

Consolidation

Consolidation options are based on if tests find minimal or measurable residual disease (MRD).

MRD+

In general, MRD positivity at the end of induction predicts a high chance of relapse.

Treatment for resistant or rising MRD is:

- Blinatumomab followed by a hematopoietic cell transplant (HCT)

MRD-

If no minimal residual disease (MRD-) is found, then you will continue chemotherapy or be given blinatumomab before starting maintenance therapy. An HCT may also be an option.

MRD unavailable

If MRD cannot be determined, then an HCT is an option. You could also continue chemotherapy or be given blinatumomab before starting maintenance therapy.

HCT

The timing of an HCT depends upon donor availability, length of remission, your social support, and your health at the time of potential HCT.

Maintenance

Maintenance therapy is given after consolidation with multiagent chemotherapy or blinatumomab. Maintenance is given to prevent the return or spread of ALL. It is usually a continuation of treatment, but might be at a lower dose.

Surveillance

During maintenance or after an HCT, you will be monitored for signs of recurrence.

Relapsed or refractory disease

Relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission again. Cancer can return in the bone marrow called isolated medullary relapse, outside the bone marrow called isolated extramedullary relapse, or a combination of both (combined relapse). Extramedullary relapse can occur in the central nervous system or testicles.

When leukemia remains and does not respond to treatment, it is called refractory.

Mutation testing and MRD assessment will be done before starting treatment.

Treatment options include:

- Clinical trial
- Blinatumomab
- Inotuzumab ozogamicin
- Tisagenlecleucel (for those under 26 years of age with refractory B-ALL disease or 2 or more relapses)
- Brexucabtagene autoleucel
- Chemotherapy

Most treatment paths lead toward a hematopoietic cell transplant (HCT). The goal is to achieve an MRD-negative result before an HCT. The timing of an HCT depends upon donor availability and your health at the time of potential HCT.

Multiple relapse

B-ALL can relapse multiple times. With each relapse the goal of treatment is a complete response (CR). This is not always possible.

Refractory

When leukemia remains and does not respond to treatment, it is called refractory or resistant. The cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about prognosis. Treatment options are the same as for relapse.

Treatment is needed to prevent ALL from spreading to the central nervous system (CNS). This is called CNS prophylaxis and everyone receives it.

Key points

- Ph-negative (Ph-) does not have the Philadelphia chromosome. It is the most common type of B-ALL.
- The goal of treatment is a complete response and to prevent the spread of cancer to areas outside the blood.
- Treatment is usually an intensive combination of systemic therapies. All treatment regimens include systemic therapy and/or intrathecal (IT) therapy to prevent central nervous system (CNS) disease.
- Relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission (a complete response) again.
- Cancer may be resistant at the start of treatment or it may become resistant during treatment. This is called refractory.
- For multiple relapse or refractory disease, the goal is to achieve an MRD-negative result before a hematopoietic cell transplant (HCT). An HCT is not an option for everyone.
- The timing of an HCT depends upon donor availability and your health at the time of potential HCT.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

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T-ALL

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T-ALL includes a group of cancers that start in T-cell lymphocytes. It is less common than B-ALL and is Philadelphia chromosome-negative (Ph-). Treatment options include a clinical trial or systemic therapy.

Treatment

T-ALL is Ph-negative (Ph-). It does not have the Philadelphia chromosome. It is recommended that T-ALL be treated in a clinical trial when possible.

Induction

Induction chemotherapy might include daunorubicin, vincristine, prednisone, and pegaspargase. All treatment regimens include systemic therapy and/or intrathecal (injected into the spinal fluid) therapy to prevent central nervous system (CNS) disease. Treatment response will be measured after completing induction. Tests will look for minimal residual disease (MRD).

Consolidation

Consolidation is a continuation of chemotherapy. Nelarabine might be added to a consolidation regimen. After consolidation, treatment response will be assessed.

Continuation therapy

The goal of extended maintenance or continuation therapy is to prevent cancer from returning (called a relapse) or spreading to the CNS or testicles, and to reduce the amount of MRD.

After continuation therapy, a hematopoietic cell transplant might be an option. However, the timing of an HCT depends upon donor availability and your health at the time of potential HCT.

Surveillance

After a complete response or an HCT, you will be monitored for signs of recurrence or relapse.

Relapse

T-ALL often returns. Relapse can occur in the bone marrow called isolated medullary relapse, in the testicles or central nervous system called isolated extramedullary relapse, or a combination of both. Isolated extramedullary relapse requires systemic therapy to prevent relapse in bone marrow.

Relapse treatment options:

- Clinical trial
- Systemic therapy

Treatments will likely include a combination of drugs. Relapse can happen multiple times. With each relapse the goal of treatment is a complete response or an MRD-negative result before an HCT.

Refractory disease

When leukemia remains and does not respond to treatment, it is called refractory or resistant. The cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about prognosis.

Refractory treatment options:

- Clinical trial
- Systemic therapy

The goal is to achieve an MRD-negative result before an HCT. However, in some cases an HCT might be considered in those who are MRD+.

Systemic therapy options for relapsed or refractory Ph- T-ALL can be found in **Guide 5**.

Your preferences about treatment are always important. Talk to your care team and make your wishes known.

Guide 5

Systemic therapy options: Relapsed and refractory T-ALL

Preferred

Nelarabine. Etoposide and cyclophosphamide might be added.

Other recommended

- Bortezomib with chemotherapy
- Daratumumab
- HiDAC (high-dose cytarabine)
- Mitoxantrone, etoposide, and cytarabine
- Venetoclax with chemotherapy
- Regimens used for relapsed/refractory Ph-negative B-ALL may be appropriate

Key points

- T-ALL includes a group of cancers that start in T-cell lymphocytes. T-ALL does not have the Philadelphia chromosome (Ph-).
- It is recommended that T-ALL be treated in a clinical trial when possible. Systemic therapy is also a treatment option.
- All treatment regimens include systemic therapy and/or intrathecal (IT) therapy to prevent central nervous system (CNS) disease. IT therapy is injected into the spinal fluid.
- The goal of treatment is a complete response (CR).
- After a CR or a hematopoietic cell transplant (HCT), you will be monitored for signs of recurrence or relapse.
- When cancer returns or relapses, the goal of treatment is to have another CR. After a CR, an HCT might follow. The timing of an HCT depends upon donor availability and your health at the time of potential HCT.
- Cancer may be resistant at the start of treatment or it may become resistant during treatment. This is called refractory.



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**Take our survey,
and help make the
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better for everyone!**

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8

Making treatment decisions

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- 63 Questions to ask
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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your care team.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your care team.

If you take the time to build a relationship with your care team, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see 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 second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Questions about diagnosis and testing

1. What subtype of ALL do I have?
2. What does my type of ALL mean in terms of prognosis and treatment options?
3. Is there a cancer center or hospital nearby that specializes in this type and subtype of cancer?
4. Should I consider treatment at a pediatric center?
5. Who will talk with me about the next steps? When?
6. Will treatment start before the test results are in?
7. What tests are needed?
8. What other tests do you recommend?
9. Would you give me a copy of the pathology report and other test results?
10. How many bone marrow tests are needed and when are they done?

Questions about options

1. What will happen if I do nothing?
2. Which option is proven to work best for my ALL subtype, age, white blood cell (WBC) count, overall health, and other factors?
3. How will treatment affect my fertility? Should I see a fertility specialist before starting treatment?
4. Am I a candidate for a hematopoietic cell transplant (HCT)?
5. Am I a candidate for a clinical trial?
6. What are the options if the treatment stops working?
7. Are there any life-threatening side effects of this treatment?
8. Can I stop treatment at any time? What will happen?
9. How long do I have to decide about treatment options?
10. Is there a social worker or someone who can help me decide about treatment?

Questions about treatment

1. Which treatment do you recommend and why?
2. Which treatment will give me the best quality of life?
3. Which treatment will extend life? By how long?
4. What should I expect from this treatment?
5. Will I have to go to the hospital or elsewhere for treatment?
6. How much will this treatment cost me?
7. Are there any programs to help pay for treatment?
8. What can I do to prevent or relieve side effects? What will you do?
9. Will I miss work during treatment? How much work?
10. How will you know when blood transfusions or antibiotics are needed?

Questions about care team's experience

1. What is your experience treating ALL?
2. What is the experience of those on your team?
3. Do you only treat ALL? What else do you treat?
4. I would like to get a second opinion. Is there someone you recommend?
5. I would like another pathologist or hematopathologist to review the blood samples. Is there someone you recommend?
6. How many people like me (of the same age, gender, race) have you treated?
7. Will you be consulting with ALL experts to discuss my care? Whom will you consult?
8. How many procedures like the one you're suggesting have you done?
9. Is this treatment a major part of your practice?
10. How many of your patients have had complications? What were the complications?

Questions about clinical trials

1. What clinical trials are available?
2. What are the treatments used in the clinical trial?
3. What does the treatment do?
4. Has the treatment been used before? Has it been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect? How will the side effects be controlled?
7. How long will I be on the clinical trial?
8. Will we be able to get other treatment if this doesn't work?
9. How will you know the treatment is working?
10. Will the clinical trial cost me anything? If so, how much?

Questions about hematopoietic cell transplants

1. How do you find a donor?
2. How long will I have to wait for a hematopoietic cell transplant (HCT)?
3. What are the risks to myself and/or the donor?
4. How will the transplant affect my prognosis?
5. How will a transplant affect the quality and length of my life?
6. How long should I expect to be in the hospital?
7. How will I feel before, during, and after the transplant?
8. How many HCTs has this center done for those with this type of ALL?
9. Will I have more than one HCT?
10. What side effects may occur after an HCT?

Questions about side effects

1. What are the side effects of treatment?
2. How long will these side effects last?
3. Do any side effects lessen or worsen in severity over time?
4. What side effects should I watch for?
5. What side effects are expected and which are life-threatening?
6. When should I call the doctor? Can I text?
7. Will you stop treatment or change treatment if there are side effects?
8. What can I do to lessen or prevent side effects? What will you do?
9. What side effects are life-long and irreversible even after completing treatment?
10. What medicines may worsen side effects of treatment?

Questions about survivorship and late effects

1. What happens after treatment?
2. What are the chances ALL will return or that I will develop another type of cancer?
3. Whom do we see for follow-up care? How often?
4. How often should I see a dentist?
5. How often should I see an eye doctor (ophthalmologist)?
6. What tests will I have to monitor my health?
7. What late effects are caused by this treatment?
8. What late effects should I look for?
9. What should I do if I have trouble with work? Or difficulty focusing?
10. I am looking for a survivor support group. What support groups or other resources can you recommend?

Resources

Many of these resources are available en español and other languages.

Be The Match®

bethematch.org/one-on-one

Cancer Hope Network

cancerhopenetwork.org

MedlinePlus

medlineplus.gov

National Bone Marrow Transplant Link

nbmtlink.org

National Cancer Institute (NCI)

cancer.gov/types/leukemia

The Leukemia & Lymphoma Society (LLS)

lls.org/PatientSupport

Triage Cancer

triagecancer.org

U.S. Department of Health & Human Services (HRSA)

bloodstemcell.hrsa.gov



Words to know

absolute neutrophil count (ANC)

An estimate of the body's ability to fight infections, especially bacterial infections.

acute lymphoblastic leukemia (ALL)

A fast-growing cancer that causes too many immature white blood cells called lymphoblasts to be made.

adolescent and young adult (AYA)

People who are 15 to 39 years of age at the time of initial cancer diagnosis.

allogeneic

Donor who may or may not be related to you.

antibody

A protein made by a plasma cell (a type of white blood cell).

autologous

Stem cells that come from you.

B cell

A type of lymphocyte.

BCR::ABL1 protein

An abnormal protein that is made by the *BCR::ABL1* fusion gene and causes too many abnormal white blood cells to be made.

biopsy

A procedure that removes tissue samples.

blast

An immature blood cell. Also called lymphoblast.

blood stem cell

An immature blood-forming cell from which all other types of blood cells are made. Also called hematopoietic stem cell.

bone marrow

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

bone marrow aspirate

The removal of a small amount of liquid bone marrow to test for disease.

bone marrow biopsy

The removal of a small amount of solid bone and bone marrow to test for disease.

chemotherapy

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

chromosomes

Long strands that contain bundles of coded instructions in cells for making and controlling cells.

clinical trial

A study of how safe and helpful tests and treatments are for people.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the insides of the body.

consolidation

One of the post-induction phases of treatment.

contrast

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

cytogenetics

The study of chromosomes.

deoxyribonucleic acid (DNA)

Long strands of genetic information found inside cells.

Words to know

donor

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

extramedullary

Outside the bone marrow.

gene

Coded instructions in cells for making new cells and controlling how cells behave.

hematopathologist

A doctor who specializes in blood diseases by looking at cells under a microscope.

hematopoietic cell transplant (HCT)

A treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

hematologist

A doctor who's an expert in diseases of the blood.

hereditary

Passed down from biological parent to child through coded information in cells (genes).

human leukocyte antigen (HLA)

Special proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

hyperdiploidy

Leukemia cells with 51 to 67 chromosomes.

hypodiploidy

Leukemia cells with fewer than 44 chromosomes.

immune system

The body's natural defense against infection and disease.

immunotherapy

A treatment with drugs that help the body find and destroy cancer cells.

induction

The first phase of treatment.

infection

An illness caused by germs.

infusion

A method for delivering chemotherapy into the vein in a controlled manner.

interventional radiologist

A doctor who is an expert in imaging tests and using image-guided tools to perform minimally invasive techniques to diagnose or treat disease.

intravenous (IV)

A method of giving drugs by a needle or tube inserted into a vein.

leukapheresis

A procedure that separates leukocytes from the blood.

leukemia

A disease in which there are too many white blood cells.

liver function test (LFT)

A lab test that measures chemicals made or processed by the liver.

lymph node

A small, bean-shaped, disease-fighting structure.

lymphoblast

An immature lymphocyte. Also called blast.

lymphocyte

A type of white blood cell that is part of the immune system.

Words to know

lymphoid

Referring to a type of white blood cell called a lymphocyte.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

maintenance

Usually the last phase of ALL treatment.

medical oncologist

A doctor who is an expert in cancer drugs.

medullary

In the bone marrow.

minimal residual disease (MRD)

Small amount of ALL cells that remain after treatment. Detected by highly sensitive tests done on blood or bone marrow tissue. Sometimes called measurable residual disease.

mutation

An abnormal change.

myeloid

Referring to a type of white blood cell called a granulocyte.

myelosuppression

A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets.

natural killer (NK) cell

A type of lymphocyte.

neutrophil

A type of white blood cell that fights infections, especially bacterial and fungal infections.

oncologist

A doctor who is an expert in the treatment of cancer.

palliative care

Health care that includes symptom relief but not cancer treatment. Also sometimes called supportive care.

pathologist

A doctor who is an expert in testing cells and tissue to find disease.

pediatric

People who are 18 years of age or under at the time of initial diagnosis.

peripheral blood

Blood that circulates throughout the body.

Philadelphia chromosome (Ph)

An abnormal, short chromosome 22 that is formed when parts of chromosomes 9 and 22 switch with each other. The result is the *BCR::ABL1* fused gene.

platelet (PLT)

A type of blood cell that helps control bleeding. Also called thrombocyte.

polymerase chain reaction (PCR)

A lab process in which copies of a piece of DNA are made.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

post-induction

More intensive phases of chemotherapy that happen after induction and before maintenance.

predisposition syndrome

Certain genetic changes, or mutations, can increase a person's chances of developing cancer.

prognosis

The likely course and outcome of a disease.

Words to know

progression

The growth or spread of cancer after being tested or treated.

radiation therapy (RT)

A treatment that uses high-energy rays.

radiologist

A doctor who is an expert in imaging tests.

recurrence

The return of cancer after a cancer-free period.

red blood cell (RBC)

A type of blood cell that carries oxygen from the lungs to the rest of the body. Also called an erythrocyte.

refractory

A cancer that does not improve with treatment.

relapse

The return or worsening of cancer after a period of improvement.

regimen

A treatment plan that includes specific information about drug dose, when medicine is taken, and how long treatment will last.

remission

There are minor or no signs of a disease.

resistance

When cancer does not respond to a drug treatment.

scrotal ultrasound

Uses sound waves to make images of the scrotum. The scrotum is the pouch of skin at the base of the penis that contains the testicles.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

standard of care

The best known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care.

steroid

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

subtype

A smaller group within a type of cancer that is based on certain cell features.

supportive care

Health care that includes symptom relief but not cancer treatment. Also called palliative care or best supportive care.

surveillance

Testing that is done after treatment ends to check for the return of cancer.

systemic therapy

Treatment that works throughout the body.

T cell

A type of lymphocyte.

targeted therapy

A drug treatment that targets and attacks specific cancer cells.

translocation

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

tumor lysis syndrome (TLS)

A condition caused when waste released by dead cells is not quickly cleared out of the body.

tumor marker

A substance found in body tissue or fluid that may be a sign of cancer.

white blood cell (WBC)

A type of blood cell that helps fight infections in the body. Also called a leukocyte.

NCCN Contributors

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800.789.7366 • pennmedicine.org/cancer

**Case Comprehensive Cancer Center/
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Cleveland Clinic Taussig Cancer Institute**
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

**Dana-Farber/Brigham and Women's Cancer Center |
Massachusetts General Hospital Cancer Center**
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

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Salt Lake City, Utah
800.824.2073 • huntsmanccancer.org

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Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

**Robert H. Lurie Comprehensive Cancer Center
of Northwestern University**
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

**Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine**
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

**St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center**
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

**The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute**
Columbus, Ohio
800.293.5066 • cancer.osu.edu

**The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins**
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

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La Jolla, California

858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center

Los Angeles, California

310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family Comprehensive Cancer Center

San Francisco, California

800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center

Aurora, Colorado

720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center

Ann Arbor, Michigan

800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center

Madison, Wisconsin

608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center

Dallas, Texas

214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center

Nashville, Tennessee

877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital

New Haven, Connecticut

855.4.SMILOW • yalecancercenter.org

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#Reference From NCCN Guidelines