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GUIDELINES
FOR PATIENTS®

2023

Pediatric Acute Lymphoblastic Leukemia



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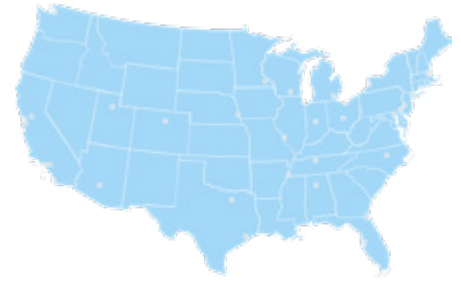
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About the NCCN Guidelines for Patients®



Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).



Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Acute Lymphoblastic Leukemia, Version 1.2023 – November 9, 2022.

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National Comprehensive Cancer Network (NCCN) and NCCN Foundation
3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462 USA

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ALL basics

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Acute lymphoblastic leukemia (ALL) is the most common cancer diagnosed in children. It is a fast-growing cancer that starts in lymphocytes, a type of white blood cell. Treatment depends on the type of ALL, age at diagnosis, and other factors. Pediatric refers to ALL found in infants, children, and young adults.

Blood

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

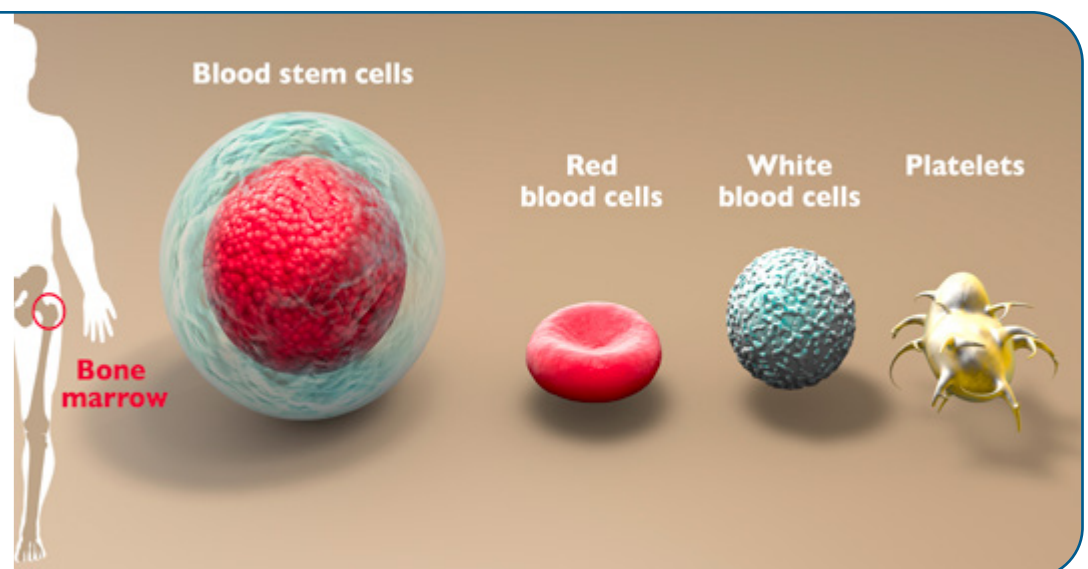
- Red blood cells (erythrocytes)
- White blood cells (leukocytes), which include granulocytes, monocytes, and lymphocytes
- Platelets (thrombocytes)

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 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!

Blood stem cells

Bone marrow contains stem cells. A blood stem cell is an immature cell that can develop into a red blood cell, white blood cell, or platelet.



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:

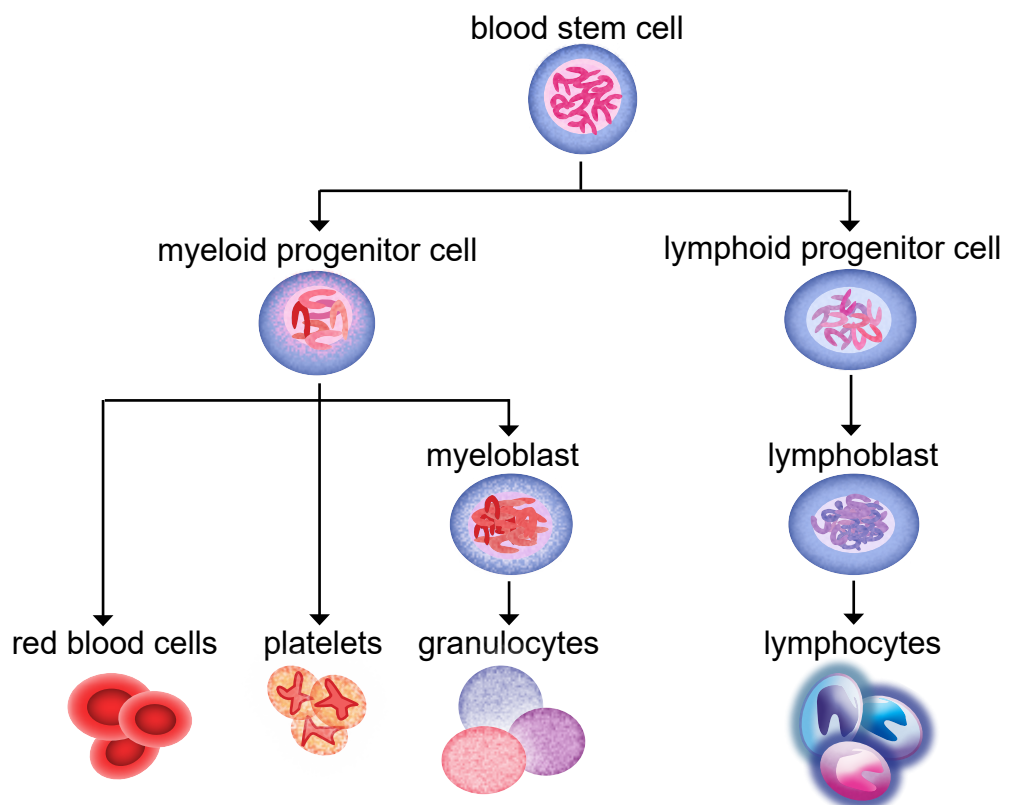
- Lymphoid progenitor cells form into lymphoblasts that mature into lymphocytes
- Myeloid progenitor cells form into myeloblasts and other non-lymphoid blood cells

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 a type of white blood cell called 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.

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.

Pediatric ALL

Pediatric refers to ALL found in infants, children, and young adults. “Pediatric” includes anyone 18 years of age or under, and certain adolescents and young adults (AYAs) over 18 years of age. AYAs are those 15 to 39 years of age at the time of initial cancer diagnosis. An AYA can be treated in pediatric or adult centers depending on the type of cancer. This book applies to AYAs who are 30 years of age or under and are being treated at a pediatric cancer center.

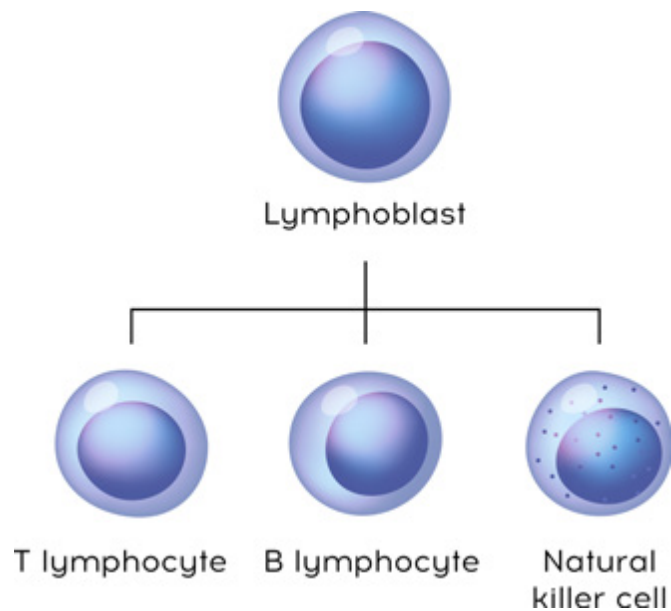
More information for AYAs seeking ALL treatment at an adult cancer center can be found at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Those with pediatric ALL should be treated at experienced pediatric leukemia centers.

Lymphocytes

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



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.
- 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.
- Pediatric ALL is the most common cancer diagnosed in children. “Pediatric” includes anyone 18 years of age or under.
- There is more than one type of pediatric ALL. It is based on the type of lymphocyte, genetic mutations, and other features.



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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Testing for ALL

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

Test results

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

Keep these things in mind:

- Write down questions and take notes during appointments. Don't be afraid to ask your child's care team questions. Get to know your child's care team and help them get to know you and your child.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer your child has.
- Organize your child's 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 child's 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 child's pediatrician informed of changes to this list.



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 child's specific type of cancer. It will be helpful if you have a new doctor or get 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 (eg, blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your child's 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!

- 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.

Guide 1

Possible tests and procedures

Medical history and physical exam

Bone marrow aspirate and biopsy

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

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

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

Pregnancy testing, fertility counseling, and preservation as needed

CT and MRI of head with contrast, if neurologic symptoms

Chest x-ray to rule out mediastinal (in between the lungs) mass

Whole body PET/CT if lymphoblastic lymphoma suspected

Lumbar puncture (LP) with intrathecal (IT) chemotherapy

Testicular exam, including scrotal ultrasound as needed

Screen for opportunistic infections as needed

Assessment of left ventricular heart function (echocardiogram or cardiac nuclear medicine scan) in those who will receive anthracyclines as part of treatment plan

Pharmacogenomic testing as needed

Predisposition syndromes:

- Down syndrome is an important ALL predisposition syndrome
- For hypodiploid ALL, germline *TP53* mutation testing
- Other germline mutation testing

General health tests

Medical history

A medical history is a record of all health issues and treatments your child has had in their 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 medicines, herbals, or supplements they take. Some supplements interact with and affect medicines that your child's doctor may prescribe. Tell your child's doctor about any symptoms they have. A medical history, sometimes called a health history, will help determine which treatment is best for your child.

Physical exam

During a physical exam, a health care provider may:

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

Family history

Some cancers and other diseases can run in families. Your child's 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.

Leukemia predisposition syndrome

Certain genetic changes, or mutations, can increase a person's chances of developing cancer. These changes, known as hereditary cancer syndromes, can be passed down from parent to child if related by blood. If your child is a blood relative, their doctor should do a thorough family history and ask if anyone in your family has had leukemia. If there is a concern for a leukemia predisposition syndrome, your child might be referred to a genetic counselor or geneticist. Since blood-related family members are often bone marrow donors, it is important to rule out leukemia predisposition syndrome.

Testicular exam

ALL can spread to the testicles and cause them to swell or become more firm than usual. A testicular exam is a complete physical exam of the groin and the genitals, which are the penis, scrotum, and testicles. A doctor will feel the organs and check for lumps, swelling, shrinking, and other signs of ALL.

Dental exam

The health of your teeth and gums is important. Some treatments can cause dental problems. Therefore, it is important for your child to see a dentist before and during treatment.

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of blood, which is removed through a needle placed into a vein. Some of the possible blood tests you or your child might have are described next.

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. These tests are known together as a coagulation panel or disseminated intravascular coagulation (DIC) panel. An impaired clotting process is common in leukemia. This is called coagulopathy. Your child may have bleeding and bruises or blood clots.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. Red blood cells carry oxygen throughout your body, white blood cells fight infection, and platelets control bleeding.

Differential

There are 5 main types of white blood cells: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of white blood cell (WBC). It also checks if the counts are in balance with each other and whether leukemia cells (blasts) are present.

Chemistry profile

A chemistry profile or panel measures the levels of different substances released in your blood by the liver, bone, and other organs. When ALL is present, the chemistry panel can be abnormal.

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.

HLA typing

Human leukocyte antigens (HLAs) are proteins found on the surface of most cells. They play 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 blood test that detects a person's HLA type. This test is done before a donor (allogeneic) blood stem cell transplant.

Most children with pediatric ALL do not need a transplant and, therefore, will not have HLA typing. To find a donor match, your child's proteins will be compared to the donor's proteins to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your child's body will reject the donor cells or the donor cells will react against their body. Blood or tissue samples from your child and your child's blood relatives will be tested first.

Lactate dehydrogenase

Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is an enzyme found in most cells. Dying cells release LDH into blood. Fast-growing cells, such as tumor cells, also release LDH.

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 or the bile ducts might be blocked.

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. The 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. Since we absorb phosphate from the foods that we eat, your child might be given a medicine called a phosphate binder to prevent phosphate levels from rising too high.

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

Potassium

Blood plasma has a low level of potassium and a high level of sodium, but inside cells are high levels of potassium and low levels of sodium. When many cells are breaking down at the same time, the level of potassium in the blood can go up. The difference in levels of potassium inside and outside of cells is very important to certain processes such as the electrical signals in the heart. Very high levels of potassium in the blood can cause dangerous heart rhythms.

Pregnancy test

Those who can become pregnant will be given a pregnancy test before treatment begins.

Screen for opportunistic infections

An opportunistic infection is an infection that happens because someone's immune system is not working normally. Drug treatment for ALL can weaken the body's natural defense against infections. Your child will be monitored for opportunistic infections, as needed.

If not treated early, infections can be fatal. Infections can be caused by bacteria, fungus, or viruses. Antibiotics can treat bacterial infections. Antifungal medicines can treat fungal infections. Your child may be given antiviral drugs to prevent viral infections.

Tumor lysis syndrome panel

Cancer treatment causes cell death. In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. Changes in creatinine, potassium, phosphate, and uric acid levels can be signs of TLS. These levels are watched closely when your child is first diagnosed. They may receive medicine and intravenous fluids to help prevent the levels from getting too high.

Uric acid

Uric acid is released by cells when DNA breaks down. It is a normal waste product that dissolves in your blood and is filtered by the kidneys where it leaves the body in the urine. Too much uric acid in the body is called hyperuricemia. It can be caused by a fast turnover of white blood cells. High uric acid might be a side effect of treatment. Very high levels of uric acid in the blood can damage the kidneys. Uric acid levels are watched with other tumor lysis syndrome levels.

Fertility (all genders)

Treatment with chemotherapy and other forms of systemic therapy can affect fertility, the ability to have children. Ask your child's care team how cancer and cancer treatment might change your child's fertility. To preserve 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, if possible. It is not always possible to see a fertility specialist before starting treatment.

More information on fertility preservation can be found in *NCCN Guidelines for Patients: Adolescent and Young Adult Cancer* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](https://www.nccn.org/patientguidelines) app.



Changes in fertility

Treatment might cause your child's fertility to be temporarily impaired or interrupted. This temporary loss of fertility is related to age at time of diagnosis, treatment type(s), treatment dose, and treatment length.

Preventing pregnancy during treatment

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. Therefore, becoming pregnant or having one's partner become pregnant during treatment should be avoided. Hormonal birth control may or may not be recommended. Ask 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 your child or teen is or becomes pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. If your child or teen is pregnant or breastfeeding at the time of cancer diagnosis, certain treatments will need to be avoided.

Menstruation, menses, menstrual flow, or “period” may stop during treatment, but often returns within 2 years after treatment. It is still possible to become pregnant even without having a period. Therefore, birth control is recommended for those who are sexually active during and after treatment.

Those with testicles

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

Imaging tests

Imaging tests take pictures of the inside of one's body to look for cancer deposits. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your child's 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. Your child will not have all of the tests listed.

Chest x-ray

An x-ray is a type of radiation. In small doses, it is used to make pictures of the inside of the body. A chest x-ray is used to look for a mediastinal mass, which forms in the space between the lungs. This area includes the heart, aorta, esophagus, thymus, trachea, lymph nodes, and nerves.

CT scan

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

Contrast

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. 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 the doctors if your child has had allergic reactions to contrast in the past, especially to iodine or shellfish like shrimp. This is important. Your child might be given medicines to avoid the effects of those allergies. Contrast might not be used if your child has a serious allergy or if their kidneys aren't working well.

MRI scan

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. During the test, your child will likely be asked to hold their breath for 10 to 20 seconds as the technician collects the images. Young children who require an MRI but cannot hold still easily may be given sedation to get a good quality picture.

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 your child has claustrophobia (a dread or fear of enclosed spaces), be sure to talk to their doctor about it. Also, tell your child's doctor if they have any metal in their 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.

Scrotal ultrasound

A 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. The images are recorded on a computer.

Lumbar puncture

A lumbar puncture (LP) is a procedure that removes spinal fluid. It is also called a spinal tap. A lumbar puncture at diagnosis is used to rule out a central nervous system (CNS) disease. Leukemia can travel to the cerebrospinal fluid (CSF) that surrounds the spine or brain. This may cause symptoms. In order to look for leukemia cells in your child's spinal fluid, a sample must be taken and tested. A lumbar puncture is also used to inject cancer drugs into spinal fluid. This is called intrathecal (IT) chemotherapy. All treatment plans include IT chemotherapy.

Heart tests

Electrocardiogram

An electrocardiogram (ECG or EKG) shows electrical changes in the heart. It reveals information about heart rate and rhythm. For this test, small patches will be placed on your child's chest to track their heartbeat.

Echocardiogram

An echocardiogram (or echo) uses sound waves to see how well the heart is working. A wand (called a transducer) with gel on its tip will be slid across part of your child's bare chest. Their beating heart will be seen on a screen. The pictures will be recorded for future viewing.

Cardiac nuclear medicine scan

A nuclear heart scan is an imaging test that uses special cameras and a radioactive substance called a tracer to create pictures of the heart. The tracer is injected into the blood and travels to the heart.

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 to confirm the disease and to see how well treatment is working. For many, this is a painful procedure. The care team will try to make your child as comfortable as possible. In some places, sedation or anesthesia is provided during this procedure. Discuss the options with the care team.

A hematologist is a doctor who specializes in blood diseases and cancers. A hematopathologist is a doctor who specializes in blood diseases by looking at cells under a microscope. The hematopathologist will study the results of various blood and bone marrow tests and write a report that will be sent to your child's doctor.

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. An aspirate takes some of the liquid out of the sponge, and a biopsy takes a piece of the sponge.

Samples are usually taken from the back or front of the hip bone (pelvis). Your child will likely lie on their belly, back, or side. Their doctors will first clean and give sedation or numb the skin and outer surface of the bone. For an aspirate, a hollow needle will be pushed

through their 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. Your child may feel bone pain at your hip for a few days. Their 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 proteins on the surface of thousands of cells.

A blood test can count the number of white blood cells, but it cannot detect the subtle differences between different types of blood cancers. 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 (said immuno-feeno-typing) uses antibodies to detect the presence or absence of white blood cell antigens. These antigens are proteins that can be found on the surface of or inside white blood cells. They are called markers or biomarkers. Certain biomarkers are targeted in ALL treatment. Immunophenotyping is used to pinpoint the type of ALL.

Based on immunophenotype, ALL can be placed into 2 general groups:

- B-cell ALL
- T-cell ALL

B-ALL

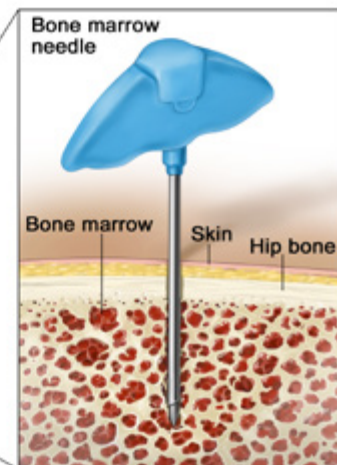
B-ALL is the most common type of pediatric ALL. It starts in immature cells (lymphoblasts) that would normally develop

Bone marrow aspirate and biopsy

Samples of bone and marrow are removed in a biopsy



Bone Marrow Aspiration and Biopsy



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into B-lymphocytes. Subtypes include early precursor B-cell (early pre-B-cell) and pre-B-cell. Mature B-cell ALL (Burkitt lymphoma) is a rare subtype and is treated differently.

T-ALL

T-ALL starts in lymphoblasts that would normally develop into T-cell lymphocytes. This type is less common. Early T-cell precursor (ETP-ALL) is a distinct subtype of T-ALL that is typically treated the same as other subtypes of T-ALL.

Biomarker tests

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. A mutation is when something goes wrong in the genetic code.

Biomarker testing is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing. It includes tests of genes or their products (proteins) and identifies the presence or absence of mutations and certain proteins. Proteins are written like this: BCR. Genes are written with italics like this: *BCR*.

For a list of ALL subtypes and some of the genetic abnormalities found in pediatric ALL, see **Guide 2**.

ALL mutation testing

A sample of your child's blood or bone marrow will be used to see if the ALL cancer cells have any specific mutations. This is separate from the genetic testing for mutations that your child may have inherited from you, if blood-related.

ALL cells can have changes in genes and chromosomes. Mutation testing using methods such as karyotype, FISH, PCR, and next-generation sequencing (NGS) are used to look for these changes or abnormalities. Your child may be placed into a risk group based on the types of genetic abnormalities found. Some mutations may determine the type of treatment your child needs. Their care team will explain any genetic abnormalities or mutations and how it may affect their risk and treatment.

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. For example, the probes attach to the *BCR* gene and the *ABL1* gene. The *BCR::ABL1* gene is detected when the colors of the probes overlap by translocation. A translocation is the switching of parts between two chromosomes. The *BCR::ABL1* translocation can also be written as t(9;22).

FISH can look for translocations that are too small to be seen with other methods. It can only be used for known changes. It cannot detect all the possible changes found with a karyotype. 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 your child's doctor needs to help plan their care.

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 NGS. A real-time or reverse transcriptase (RT) is a type of PCR used to look for *BCR::ABL1*.

Guide 2 ALL subtypes

	<ul style="list-style-type: none"> • B-ALL or B-cell acute lymphoblastic lymphoma (B-LBL) • Not otherwise specified (NOS) • Hyperdiploidy (leukemia cells with 51 to 67 chromosomes) • Hypodiploidy (leukemia cells with fewer than 44 chromosomes) • Intrachromosomal amplification (too many copies) of a portion of chromosome 21 (iAMP21)
<p>B-ALL subtypes</p>	<p>Any of the above subtypes with:</p> <ul style="list-style-type: none"> • t(9;22)(q34.1;q11.2) translocation that results in <i>BCR::ABL1</i> • t(v;11q23.3) translocation that results in <i>KMT2A</i> rearranged • t(12;21)(p13.2;q22.1) translocation that results in <i>ETV6::RUNX1</i> • t(1;19)(q23;p13.3) translocation that results in <i>TCF3::PBX1</i> • t(5;14)(q31.1;q32.3) translocation that results in <i>IGH::IL3</i> • Other translocations and gene abnormalities are possible such as rearrangements of <i>DUX4</i>, <i>MEF2D</i>, <i>ZNF384</i>, and <i>NUTM1</i>; <i>IG::MYC</i> fusion; and <i>PAX5alt</i> and with <i>PAX5</i> p.P80R <p><i>BCR::ABL1</i>-like ALL (Ph-like ALL)</p> <ul style="list-style-type: none"> • Gene fusions and mutations that activate tyrosine kinase pathways and includes gene fusions involving <i>ABL1</i>, <i>ABL2</i>, <i>CRLF2</i>, <i>CSF1R</i>, <i>EPOR</i>, <i>JAK2</i>, or <i>PDGFRB</i> and mutations involving <i>CRLF2</i>, <i>FLT3</i>, <i>IL7R</i>, <i>SH2B3</i>, <i>JAK1</i>, <i>JAK3</i>, and <i>JAK2</i> (in combination with <i>CRLF2</i> gene fusions).
<p>T-ALL subtypes</p>	<ul style="list-style-type: none"> • T-ALL or T-cell acute lymphoblastic lymphoma (T-LBL) • Not otherwise specified (NOS) • Early T-cell precursor (ETP) acute lymphoblastic leukemia (ETP-ALL or ETP T-ALL)

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.

ALL cells can have changes in genes and chromosomes. Mutation testing looks for these changes or abnormalities. By testing karyotype, FISH, RT-PCR, and NGS, chromosome or gene abnormalities that are unique to ALL cells are found. Examples of such changes are called deletion, insertion, amplification, translocation (rearrangement), and point mutation.

Deletions

When part of a chromosome or gene is missing, it is called a deletion.

Insertions

When a new part of a chromosome or gene is included, it is called an insertion.

Amplifications

When a part or whole chromosome or gene is increased (for example, duplicated), it is called an amplification.

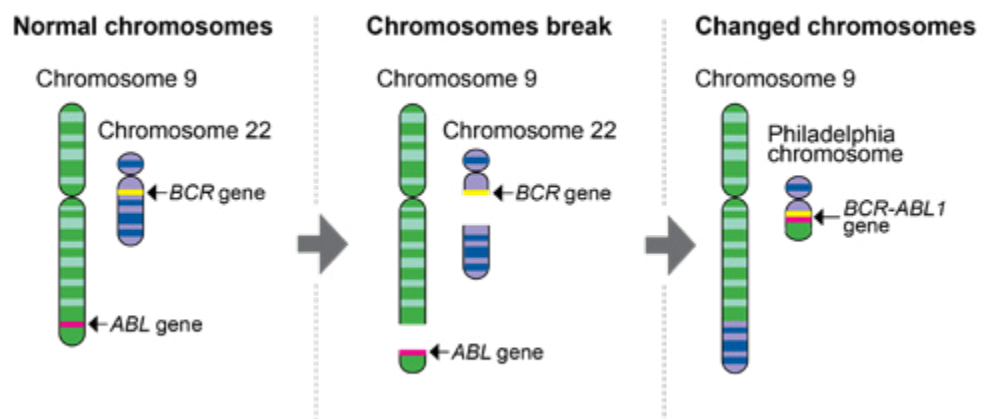
Translocations and rearrangements

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 chromosome 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 below.

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

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



Point mutations

When part of a gene is changed, it is called a point mutation.

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 parents to children.

Keep these things in mind

- Take care of yourself. This is a stressful time. Make an appointment to see your doctor. Seek out and ask for support. Support can be a friend, relative, neighbor, or coworker.
- This will be a confusing time. You will hear a lot of unfamiliar words. Start conversations with questions and about your concerns.
- Encourage your child to interact with their health care team, to ask questions, and to talk about how they feel.
- Teach your teen how and when to take their medicine, what to do if their medicine is low, how to refill a prescription, how to manage side effects, and who to call if they have questions about their medicine or treatment.
- Explain to your child or teen why taking medicine is important. Create a chart so they can keep track of when to take medicine or use an electronic device to schedule a reminder.
- Treating pediatric ALL is complex. Not everyone responds to treatment the same way. Some do better than expected. Others do worse. A treatment response takes time.
- Celebrate treatment milestones and other events. Find ways to engage your child. Explore new interests together.

Genetic and genetic risk testing

Genetic testing is done using skin, blood (when ALL cells disappear), 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 child's doctor if there is a family history of cancer.

There are 3 major types of genetic testing:

- **Cytogenetic** - to examine whole chromosomes
- **Biochemical** - to measure proteins produced by genes
- **Molecular** - to look for small DNA or gene mutations and/or gene fusions

While it can be confusing, just know that testing done to look for an inherited gene mutation or an inherited risk of cancer is different than genetic testing done on cancer cells or testing to look for proteins produced by cancer cells.

Risk groups

Treatment options for B-ALL are based on age, white blood cell counts at diagnosis, and results of tests done on leukemia cells to look for gene or chromosome changes. The presence of certain mutations can sometimes predict how ALL will respond to certain types of treatment. How ALL responds to treatment and if minimal residual disease (MRD) remains after treatment are also important. Your child might be placed into a risk group based on risk factors.

Risk factors include:

- Age
- White blood cell (WBC) count at diagnosis
- Gene or chromosome mutations, translocations, deletions, and rearrangements
- Response to therapy often expressed as minimal residual disease
- Predisposition syndrome
- Down syndrome

Risk groups and treatment planning are based on testing lymphoblasts in bone marrow or blood for specific genetic abnormalities.

Age

ALL tends to be more aggressive in infants and those 10 years of age and over. Infants are those under the age of 12 months (1 year).

WBC

A WBC greater than 50,000/ μ L at initial diagnosis is considered high risk.

B-ALL genetic risk groups

Your child will be placed into an initial risk group based on the genetic features (mutations) found in the leukemia cells. Some genetic mutations respond better to treatment. Unfavorable risk features are more of a challenge to treat. At certain treatment milestones, risk group might be reassessed by considering response to treatment.

Hyperdiploidy

In hyperdiploidy, leukemia cells have more than 50 chromosomes. Normal cells have 46 chromosomes.

Hypodiploidy

In hypodiploidy, leukemia cells have fewer than 44 chromosomes. Normal cells have 46 chromosomes.

Leukemia predisposition syndrome

Some hereditary cancer syndromes can be passed down from parent to child. A family history of leukemia can affect treatment. If a predisposition condition is suspected, your child might have a skin punch biopsy. If their 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 your child has inherited genes that increase their risk of leukemia. Leukemia predisposition syndrome can affect how your child's body responds to treatment. Blood and saliva can be used when ALL cells disappear (in remission).

Down syndrome

In Down syndrome, there is an extra chromosome 21. Instead of two chromosomes, there are three. There are challenges treating ALL in those with Down syndrome.

Pharmacogenomic testing

Pharmacogenomics (said farma-co-gee-nome-icks) is the study of how genes affect a person's response to drugs. How well your child's body absorbs (metabolizes) drugs is an important factor in treatment. Not everyone receives the same dose. Your child's age, weight, and other factors play a role in the dose they receive. Therefore, they may have a test to find the best starting dose of certain drugs. This test looks for genes that help to guide dosing decisions.

Two examples are as follows, which are related to chemotherapy with 6-mercaptopurine and 6-thioguanine:

- Thiopurine methyltransferase (*TPMT*)
- Nudix hydrolase 15 (*NUDT15*)

Based on the results of the test, your child might start certain types of chemotherapy at a lower dose to avoid severe myelosuppression. In myelosuppression, bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets. This is supposed to happen with certain chemotherapies. However, since those with a genetic mutation in *TPMT* or *NUDT15* may have more severe myelosuppression, they may be started on lower doses to prevent this from happening.

Key points

- Results from blood tests, bone marrow aspirate and biopsy, and imaging studies will determine the 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.
- Immunophenotyping is used to pinpoint the type of pediatric ALL.
- Your child might be placed into a risk group before starting treatment. Risk might be reassessed between stages of treatment.
- Factors that can affect treatment include age, white blood cell count at diagnosis, gene or chromosome mutations, response to treatment, predisposition syndrome, and Down syndrome.
- Cancer treatment can affect fertility.
- Blood tests check for signs of disease, how well organs are working, and treatment results. Blood clotting tests will also be done.
- Imaging tests are used to look for sites of infection, bleeding, and leukemia that might have spread outside the bloodstream.
- Heart or cardiac tests are used to see how well your child's heart works. These tests might be used to monitor treatment side effects.
- Leukemia can travel to the cerebrospinal fluid (CSF) that surrounds the spine or brain. It can also travel to sites outside of the blood such as the testicles.

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

3

Treatment overview

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There is more than one treatment for pediatric 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 child's type of cancer. This team is united in the planning and implementing of your child's treatment. Ask who will coordinate your child's care.

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

Depending on your child's 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 plans 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 child's clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your child's hands-on care, like giving systemic therapy, managing your child's care, answering questions, and helping your child 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 child's 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 child's physical, mental, and emotional well-being are important. Work with your child to help other team members understand:

- How your child may be feeling
- What your child may need
- What is working for your child and what is not

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

Overview

Chemotherapy is a type of systemic drug therapy that kills fast-dividing cells throughout the body, including cancer cells and normal cells. Chemotherapy is the backbone of pediatric ALL treatment and is often combined with other drug therapies.

Chemotherapy, fluids, and blood products might be given through:

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

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 for your child based on the treatment they 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 for your child 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 child's care team about any supplements they may be taking.

Some examples include:

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

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 child's care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements your child is 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.

Chemotherapy

Chemotherapy is the standard of care for treating pediatric ALL. Chemotherapy kills fast-dividing cells throughout the body, including cancer cells. Children and young adults can tolerate higher doses than adults. However, with higher doses there are side effects. Your child 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 multi-agent chemotherapy or a multi-agent 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 your child is getting, when your child will get them, and what side effects to expect.

These are the main types of chemotherapy drugs (agents) used to treat pediatric ALL:

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

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

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.

Your child 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. Your child might not be given a certain TKI if they have a health condition, such as lung or heart issues, or certain mutations.

Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

TKIs that might be used to treat pediatric ALL:

- Dasatinib (Sprycel)
- Imatinib (Gleevec)
- Nilotinib (Tasigna)
- Ponatinib (Iclusig)
- Ruxolitinib (Jakafi)

There are other types of targeted therapies available to treat ALL. Whether or not one is available or would be helpful for your child depends on your child's subtype of ALL and what types of genetic changes your child's ALL cells have.

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 (Blinicyto) 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) is 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](https://www.nccn.org/patientguidelines) 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 at diagnosis may receive radiation to the brain area.
- Those with testicular disease at diagnosis that remains after induction therapy may receive radiation to the testes.

Cranial irradiation

In cranial irradiation, the areas of the brain targeted for ALL radiation treatment are different from areas targeted for brain metastases of solid tumors.

Total body irradiation

Total body irradiation (TBI) is radiation of the whole body given before bone marrow transplant.

Testicular irradiation

Since ALL can sometimes be found in the testicles, radiation therapy might be given to this area.



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. Only a small number of those with pediatric ALL will receive an HCT.

There are 2 types of HCTs:

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

The timing of an HCT depends upon donor availability and your child's health at the time of potential HCT.

Allogeneic transplant

An allogeneic transplant (alloHCT) uses healthy stem cells from a donor. The donor may or may not be related to your child. 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 child's body will accept and won't kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

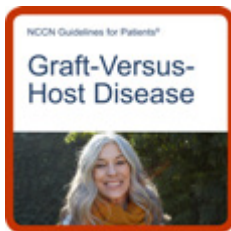
The timing of a hematopoietic cell transplant (HCT) depends upon donor availability and your child's health at the time of potential HCT.

After conditioning, your child will receive a transfusion of the healthy stem cells from a donor that has been matched to them. 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 child's bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. Until then, your child will have little or no immune defense. Your child 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 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, your child will likely feel tired and weak.

Possible side effects

Every treatment has side effects. Your child will be monitored for infections, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack normal, healthy tissue. There are treatments for GVHD.

Ask your child's doctor about the possible side effects or complications of HCT and how this might affect your child's quality 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.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting 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 of care treatments and clinical trials. Talk to your child's doctor about whether a clinical trial may make sense for your child.

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 of care 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 for your child outside of the clinical trial at any time.

Start the conversation

Don't wait for your child's doctor to bring up clinical trials. Start the conversation and learn about all of your child's treatment options. If you find a study that your child may be eligible for, ask the treatment team if your child meets the requirements. If your child has already started standard treatment they may not be eligible for certain clinical trials. Try not to be discouraged if your child 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. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll your child.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial,

care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Keep a pain diary

A pain diary is a written record that helps you keep track of when your child has pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your child's pain with their 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 your child feels pain
- A description of your child's 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 your child from falling asleep at night? Does pain wake your child up in the night?
- A rating your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- Does pain get in the way of your child doing the things they enjoy?

Supportive care overview

Supportive care will be specific to your child's 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. When possible, allow your child to tell their care team about how they 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 eat well, drink plenty of fluids, play, move, and do things so your child feels energized. Strength is needed 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 child's health. Others may just be unpleasant. Pediatric ALL treatment can cause a number of side effects. Some are very serious.

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

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

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 child's 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), your child will need follow-up or survivorship care for late effects. During survivorship care your child will still have a care team, but it will look different. Your child will need support. Seek out peer support groups, whether online or in-person.

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.

Diarrhea

Diarrhea is frequent and watery bowel movements. Your child's 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 your child to feel not hungry or sick to their stomach (nauseated). Your child 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 child's care team if your child has trouble eating or maintaining weight.

Distress

Depression, anxiety, and sleeping problems are common and are a normal part of cancer diagnosis. Talk to your child's care team and with those whom you feel most comfortable about how your child may be feeling. There are services, people, and medicine that can help your child. 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 child's care team know how your child is feeling and if fatigue is getting in the way of them doing the things they enjoy. Eating a balanced diet and physical activity can help. Your child 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 child's 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.

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

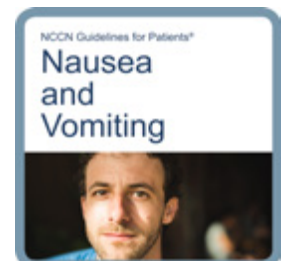
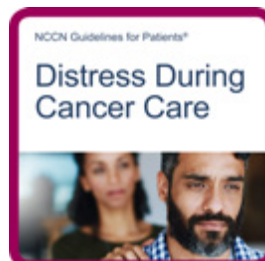
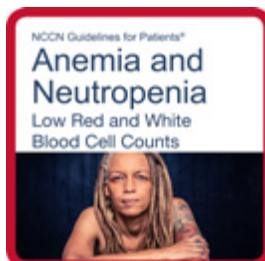
Infections occur more frequently and are more severe in those with a weakened immune system. Drug treatment for ALL can weaken the body's natural defense against infections. If not treated early, infections can be fatal.

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 child's 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. Your child will be given medicine to prevent nausea and vomiting.

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.



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 your child 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 child's kidneys, liver, heart, and pancreas to not to 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. Your child 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 child's kidneys are working. Sometimes, TLS can cause too much potassium in your child's blood. Treatment might include hemodialysis or hemofiltration. A machine will filter your child's 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. Help your child to find an activity they enjoy. Ask your child's care team what can be done to help manage weight gain.

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, your child 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, your child 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 child's body.



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 child's 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.

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.

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 child's type of cancer.
- Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and normal cells. Chemotherapy is the backbone of pediatric ALL treatment and is often combined with other drug therapies.
- Steroids are part of all ALL regimens.
- 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. Your child 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.

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 child's 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.

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.

In complete response all of the following are true:

- No lymphoblasts are found in blood
- Less than 5% 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 (extramedullary disease, which includes lymph nodes, spleen skin, gums, testicles, and central nervous system)
- Blood recovery
- Cancer has not returned in 4 weeks

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.

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 your child responds to the first phases of treatment.

Induction

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

The goal of induction is a complete response (CR) or remission. In CR, less than 5% 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 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?

Parents and caregivers say the 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. Your child or teen

will also need their own support network. Their network will look different than yours. Support services 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 in pediatric ALL. Treatment is less intensive than prior chemotherapy. It is given at an outpatient location. The goal is to lower the risk of relapse.

What do I need to know?

It is very important for your child to continue taking their medicine as prescribed and not miss or skip any doses. This helps to prevent relapse.

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 child's CNS at the time of diagnosis, they may need more IT chemotherapy or radiation to the brain.

Surveillance and monitoring

Surveillance watches for any changes in your child's condition, which includes monitoring for disease and side effects.

Tips for preparing your child for treatment

- ✓ Remain relaxed and calm
- ✓ Explain what to expect
- ✓ Use simple language
- ✓ Encourage questions
- ✓ Answer questions truthfully
- ✓ It's okay to say, "I don't know"

Refractory disease

When leukemia remains in high levels at the end of induction (EOI) and then does not respond to post-induction 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.

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. Help your child or teen find their own support network. It will likely look different than yours.



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%.

Relapse

When leukemia returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. Relapse happens in about 1 out of 5 cases. Ask the care team about your child's specific risk of relapse. 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 (CNS) or testicles called isolated extramedullary relapse, or a combination of both.

Key points

- The goal of treatment is a complete response.
- Induction is the first phase of treatment. Your child 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 child's 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-negative or Ph-like B-ALL

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This chapter is for those with Philadelphia chromosome-negative (Ph-) B-ALL or Philadelphia chromosome-like (Ph-like) B-ALL. A clinical trial is the preferred treatment for both Ph- and Ph-like B-ALL.

Overview

Ph-negative (Ph-) and Ph-like B-ALL do not have the Philadelphia chromosome or the *BCR::ABL1* gene. Before starting treatment, your child will be placed into a risk group. Risk is based on white blood cell (WBC) count and age at diagnosis.

- Standard risk is for those with a WBC less than 50,000/mm³ and who are between 1 and 10 years of age.
- High risk is for those with a WBC higher than 50,000/mm³ or who are less than 1 year of age or 10 years of age and older.

For both risk groups, induction will be chemotherapy given through a clinical trial or as standard of care. A clinical trial is preferred, but if one is not available, or you prefer for your child to not be treated as part of a clinical trial, the best-known treatment for your child's type of ALL will be used. This is called standard of care. Ask your child's care team what treatment options are available.

All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy. After induction is complete, your child's risk group will be reassessed before starting consolidation.

Ph- treatment

Ph- B-ALL is the most common type of B-ALL. It is treated with induction, post-induction phases, and maintenance therapy.

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.

Post-induction

Before starting post-induction phases of treatment, your child will be placed into a risk group. Risk is based on a variety of factors. A risk group will determine the treatment with the best chance of leukemia going into remission and not relapsing in the future. Treatment may be partially based on genetic analysis and whether there is minimal residual disease (MRD) at the end of induction. A hematopoietic cell transplant (HCT) might be an option if MRD continues to remain positive.

Maintenance

Maintenance chemotherapy is after post-induction. This is usually the longest phase of therapy and is less intense than previous phases.

Ph-like treatment

Ph-like is a subtype of B-ALL with specific genetic changes that may be considered high risk. There are a number of possible mutations in Ph-like ALL, making it difficult to treat. Ph-like ALL might be referred to as *BCR::ABL1*-like ALL.

Induction

Many induction treatment regimens are part of ongoing clinical trials. Induction is a combination of therapies. All treatment regimens include systemic and/or intrathecal therapy to prevent CNS disease. During induction, your child's blood will be tested for genetic mutations. This information is used to choose the best systemic therapy for post-induction phases.

Post-induction

When cancer remains after induction, it is called MRD-positive (MRD+). Depending on the type of genetic mutation(s) found, tyrosine kinase inhibitors (TKIs) may be added to chemotherapy or as part of a clinical trial for post-induction phases of treatment.

Maintenance

Maintenance chemotherapy is given when no minimal residual disease remains (MRD-).

MRD+ after induction

Treatment response will be measured after completing induction. The goal is a complete response (CR). Tests will look for minimal residual disease (MRD). When MRD is found, it is called MRD-positive (MRD+). A certain low level of MRD may be permissible (called a threshold), but it depends on the treatment. Ask your child's care team what this might mean.

Treatment

MRD+ is treated with a clinical trial or chemotherapy. A clinical trial is preferred, if available.

If MRD remains negative (MRD-) after the first post-induction phase of chemotherapy, then your child will continue chemotherapy, followed by maintenance chemotherapy.

If MRD remains positive (MRD+) after first post-induction phase chemotherapy, options include:

- Clinical trial (preferred)
- Chemotherapy
- Targeted therapy
- Immunotherapy

A hematopoietic cell transplant (HCT) can be considered as the next treatment option for those whose MRD becomes negative. If MRD is continuously positive, then a different treatment might be given from the list above.

Surveillance and monitoring

During maintenance or after an HCT, your child will be monitored for signs of recurrence called relapse. **See Guide 3.**

Guide 3 Surveillance and monitoring		
Surveillance	1 year after treatment	<p>→</p> <p>Every 1 to 2 months</p> <ul style="list-style-type: none"> • Physical exam with testicular exam • Complete blood count (CBC) with differential • Liver function tests (LFTs) until normal
	2 years after treatment	<p>→</p> <p>Every 2 to 6 months</p> <ul style="list-style-type: none"> • Physical exam with testicular exam • CBC with differential
	3 years after treatment	<p>→</p> <p>Every 6 to 12 months or as needed</p> <ul style="list-style-type: none"> • Physical exam, including testicular exam • CBC with differential
Procedures and biomarker testing	<ul style="list-style-type: none"> • Bone marrow aspirate and cerebrospinal fluid (CSF) for suspected relapse • 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"> • Echocardiogram as needed • Neuropsychological testing as needed • Monitor weight (those with history of childhood ALL are at increased risk of developing obesity) • 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 	

First relapse

First relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission (a complete response) again. This is not always possible. Treatment options are based on the time from initial diagnosis to relapse and if there is extramedullary disease (cancer outside of the bone marrow and blood).

Cancer can return in the bone marrow called isolated medullary relapse, outside the bone marrow called isolated extramedullary relapse, or a combination of both called combined relapse. Extramedullary relapse is cancer found in the central nervous system or testicles.

Isolated extramedullary relapse requires systemic therapy to prevent relapse in bone marrow. Likewise, isolated medullary relapse requires intrathecal treatment to prevent cancer in the central nervous system.

Treatment for B-ALL first relapse will be based on your prior therapy and length of time from initial diagnosis to relapse. Most treatment paths lead to a hematopoietic cell transplant (HCT).

Early and late first relapse

Treatment options for early or late first relapse include a clinical trial or systemic therapy. A clinical trial is preferred, if available.

Early relapse is:

- Less than 36 months (3 years) from initial diagnosis for isolated or combined bone marrow relapse OR
- Less than 18 months from initial diagnosis for isolated extramedullary relapse

Late relapse is:

- 36 months (3 years) or more from initial diagnosis for isolated or combined bone marrow relapse OR
- 18 months or more from initial diagnosis for isolated extramedullary relapse

First relapse after HCT

Treatment options for a relapse that occurs after an HCT include:

- Clinical trial (preferred) using systemic therapy
- Standard of care systemic therapy
- Blinatumomab
- Tisagenlecleucel
- Inotuzumab ozogamicin

Treatment response will be checked before starting consolidation.

- If there is a complete response, then a second HCT might follow.
- If there is less than a complete response, then treatment might be one of the options listed above.

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+.

Multiple relapse or refractory

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.

Treatment options include:

- Clinical trial (preferred)
- Chemotherapy
- Blinatumomab
- Tisagenlecleucel
- Inotuzumab ozogamicin

Treatment response will be checked before starting consolidation.

- If there is a complete response, then a hematopoietic cell transplant (HCT) will follow.
- If there is less than a complete response, then treatment might be an alternative therapy and/or best supportive or palliative care.

Key points

- Both Ph-negative (Ph-) and Ph-like B-ALL do not have the Philadelphia chromosome. However, Ph-like B-ALL is very similar to Ph-positive (Ph+) B-ALL. Ph- B-ALL is the most common type of B-ALL.
- Induction is a combination of systemic therapies. A clinical trial is the preferred treatment, if available.
- All treatment regimens include systemic and/or intrathecal (IT) therapy to prevent central nervous system (CNS) disease.
- When cancer remains after induction, it is called MRD-positive (MRD+).
- MRD+ is treated with a clinical trial (preferred) or post-induction chemotherapy.
- During maintenance or after a hematopoietic cell transplant (HCT), your child will be monitored for signs of recurrence called relapse.
- First relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission again. A clinical trial is the preferred treatment, if available.
- Relapse can happen more than once. With each relapse the goal of treatment is a complete response or remission.
- Treatment after a complete response in relapsed disease is often an HCT. The timing of an HCT depends upon donor availability and your child's health at the time of potential HCT.

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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.

Treatment

Ph+ B-ALL is less common than other types of B-ALL. Treatment aims to stop the activity of the BCR::ABL fusion protein. Although Ph+ B-ALL is considered high risk, there are effective treatments. Treatment is usually an intensive combination of systemic therapies that include tyrosine kinase inhibitors (TKIs). Treatment can be done as part of a clinical trial, which is preferred 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. 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. 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.

Post-induction

Before starting post-induction phases of treatment, your child will be placed into a risk group. Risk is based on a variety of factors. A risk group will determine the treatment with the best chance of leukemia going into remission and not relapsing in the future. Treatment options may be partially based on if there is minimal residual disease (MRD) at the end of induction. When leukemia cells remain, it is called MRD+. A hematopoietic cell transplant (HCT) might be an option if MRD continues to remain positive or a different TKI might be used.

Maintenance

Maintenance is given after post-induction phases of treatment. This is usually the longest phase of therapy and is less intense than previous phases. TKIs are given throughout maintenance until therapy is complete.

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.

Mutation testing will be done before starting treatment. Treatment options for Ph+ B-ALL relapse include:

- Clinical trial (preferred)
- Chemotherapy
- A different type of TKI than used before might be added to chemotherapy
- Blinatumomab
- Tisagenlecleucel
- Inotuzumab ozogamicin (not FDA approved for children)

Most treatment paths lead toward a hematopoietic cell transplant (HCT). The goal is to achieve an MRD-negative result before an HCT. If less than a complete response, then treatment options include an alternative therapy and/or best supportive or palliative care. In some cases, an HCT might be considered in those who are MRD+. The timing of an HCT depends upon donor availability and your child's health at the time of potential HCT.

Multiple relapse

Ph+ B-ALL can relapse multiple times. With each relapse the goal of treatment is a complete response (CR), typically followed by an HCT. 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.

Key points

- In Ph-positive (Ph+) B-ALL, tests show the presence of the Philadelphia chromosome.
- 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 including a TKI. All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy.
- Relapse is the return of cancer after a period of remission. The goal of treatment is to achieve remission (a complete response) again.
- 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 child's health at the time of potential HCT.



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7

T-ALL

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T-ALL includes a group of cancers that start in T-cell lymphocytes.
T-ALL is less common than B-ALL.
Treatment options include a clinical trial or chemotherapy.

Treatment

It is recommended that T-ALL be treated in a clinical trial when possible. If a clinical trial is not available, your child will be treated with the best known regimen. All treatment regimens include systemic therapy and/or intrathecal therapy (injected into the spinal fluid) to prevent CNS disease.

The overall treatment plan for T-ALL is the same as Ph- B-ALL, with induction, post-induction phases, and maintenance. In some phases, medicine doses and timing may be different than for B-ALL. Some phases may also include medicines that work well for T-ALL, but those with B-ALL do not receive it. In T-ALL, the goal is to be in complete remission at the end of the first post-induction phase, rather than at the end of induction.

Induction

Many induction treatment regimens are part of ongoing clinical trials. A bone marrow aspirate will be done at the end of induction to see how the leukemia responded to therapy. In T-ALL, not achieving a complete response at the end of induction does not affect risk group or prognosis the way it does in B-ALL.

Tips for parents and caregivers

- ✓ Take breaks, exercise, eat, and rest
- ✓ Ask for help
- ✓ Let others help
- ✓ Seek out a support network
- ✓ Use your support network
- ✓ Help your child or teen find their own support network.
- ✓ Explore new interests together.

Post-induction

Everyone with T-ALL will receive a first post-induction phase treatment before being placed into a risk group. Risk is based on a variety of factors. A risk group will determine the treatment with the best chance of leukemia going into remission and not relapsing in the future. Another bone marrow aspirate might be done if minimal residual disease was found earlier. A hematopoietic cell transplant (HCT) might be an option if MRD remains positive.

Maintenance

Maintenance is given after post-induction phases of therapy and is less intense than previous phases.

First relapse

T-ALL often returns within 2 years of diagnosis. When cancer returns after remission, it is called relapse. 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.

Treatment will likely include a combination of drugs. If relapse is more than 3 years after initial diagnosis, then the same induction regimen might be used again.

Treatment options for a first relapse:

- Clinical trial (preferred)
- Chemotherapy
- Targeted therapy

Complete response

If treatment causes a complete response (CR), then your child will continue with the same treatment. A clinical trial is an option. The next step would be a hematopoietic cell transplant (HCT).

Less than a complete response

If treatment does not cause a complete response, then a different treatment will be given. It might include a clinical trial or chemotherapy.

The best-known treatment for your child's type of ALL will be used. This is called standard of care. Standard of care is based on past clinical trials. Many ALL standard of care treatment regimens are the result of clinical trials. There may be more than one treatment regimen that is considered standard of care. Ask your child's care team what treatment options are available.



Multiple relapse

Relapse can happen multiple times. With each relapse the goal of treatment is a complete response.

Treatment options include:

- Clinical trial (preferred)
- Chemotherapy
- Targeted therapy

Treatment response will be checked before starting consolidation.

- If there is a complete response, usually a hematopoietic cell transplant (HCT) will follow.
- If less than a complete response, then treatment might be an alternative therapy and/or best supportive or palliative care.

Refractory

When cancer remains, it is called MRD-positive (MRD+). When leukemia remains and does not respond to treatment, it is called refractory or resistant disease. 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 for refractory disease or disease that continues to be MRD+ after consolidation include chemotherapy, a clinical trial, or an HCT.

Key points

- T-ALL includes a group of cancers that start in T-cell lymphocytes. T-ALL is less common than B-ALL.
- It is recommended that T-ALL be treated in a clinical trial, when possible. Chemotherapy is also a treatment option. All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy.
- The goal of treatment is a complete response (CR).
- After a CR or a hematopoietic cell transplant (HCT), your child will be monitored for signs of recurrence or relapse.
- When cancer returns or relapses, treatment is a clinical trial (preferred) or chemotherapy. 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 child's 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 disease. Treatment for refractory disease might include chemotherapy, a clinical trial, or an HCT.

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Infant ALL

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ALL treatment for infants is different than other age groups. Infants are children under 12 months of age.

Interfant induction

Interfant induction is the first phase of treatment for infants. “Interfant” refers to the name of the clinical trials that showed that this was an effective and safe way to treat infant ALL. You do not have to be enrolled in a clinical trial to have Interfant induction. However, enrolling in a clinical trial may be the best choice for your child.

There are 2 treatment options:

- Clinical trial (preferred)
- Interfant induction

Interfant induction is a multi-drug therapy that might include prednisone, dexamethasone, vincristine, cytarabine, daunorubicin, pegaspargase, or methotrexate. Blinatumomab might be added. Other systemic therapies might be used. All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy. Systemic therapy works throughout the body. IT therapy is injected into the spinal fluid.

Post-induction

The goal of post-induction treatment is to rid the body of any remaining leukemia cells. Treatment is based on the status of a gene called *KMT2A* (11q23). If *KMT2A* is

found to be abnormal, it is called *KMT2A*-rearranged. There are 2 risk groups for *KMT2A*-rearranged: high or intermediate. When *KMT2A* rearrangement is not found, it is considered standard risk.

***KMT2A*-rearranged**

For *KMT2A*-rearranged, post-induction treatment will be based on Interfant intensive chemotherapy. The Interfant intensive phases are a multi-drug treatment. After these intensive phases, maintenance chemotherapy or hematopoietic cell transplant (HCT) may be considered.

Not *KMT2A*-rearranged

Post-induction treatment options include:

- Clinical trial (preferred)
- Standard of care chemotherapy using non-infant ALL regimens
- Standard of care using Interfant chemotherapy

Maintenance

Maintenance chemotherapy 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 therapy or after an HCT, your child will be monitored for signs of recurrence called relapse. If cancer returns, treatment can be found under B-ALL or T-ALL first relapse. For surveillance and monitoring tests, **see Guide 3**.

Key points

- Infants are children under 12 months of age.
- There are special treatment regimens for infants.
- Treatment options include a clinical trial, multi-drug therapy chemotherapy, and possibly a hematopoietic cell transplant (HCT).
- All regimens include central nervous system (CNS) prophylaxis with systemic therapy and/or intrathecal (IT) therapy.
- Post-induction phases are based on the status of a gene called *KMT2A* (11q23) and response to previous therapy.
- Maintenance chemotherapy is given to prevent the return or spread of ALL.
- During maintenance or after an HCT, your child will be monitored for signs of recurrence called relapse.



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Making treatment decisions

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It's important to be comfortable with the cancer treatment your child receives. This starts with having an open and honest conversation with your child's care team.

You have a voice

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

Treatment decisions are very personal. What is important to you and your child 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 your child is and the activities that are important to them

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 child's care team.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there might be time to have another doctor review your child's 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 child's records sent to the doctor they will see for a 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

Some possible questions to ask your child's care team are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your and your child's goals for treatment and find out what to expect from treatment.

Questions about diagnosis and testing

1. What subtype of pediatric ALL does my child have? What does this mean in terms of prognosis and treatment options?
2. Is there a cancer center or hospital nearby that specializes in this type and subtype of cancer?
3. How soon will we know the test results and who will explain them to us?
4. Will treatment start before the test results are in?
5. What will you do to make my child comfortable during testing? Should I or can I be in the room?
6. How can I talk to my child about what to expect?
7. Would you give us a copy of the pathology report and other test results?
8. How many bone marrow tests are needed? When are they done?
9. Are there any resources you would recommend that can help me explain to my child what is happening?

Questions about options

1. What will happen if we do nothing?
2. How do age, white blood cell (WBC) count, health, and other factors affect the options?
3. Which option is proven to work best for my child's ALL subtype, age, and other risk factors?
4. How will treatment affect my child's fertility? Should we see a fertility specialist before starting treatment?
5. Is my child a candidate for a hematopoietic cell transplant (HCT)?
6. Is my child a candidate for a clinical trial?
7. What are our options if the treatment stops working?
8. Are there any life-threatening side effects of this treatment?
9. Can we stop treatment at any time? What will happen?
10. How will we know when blood transfusions or antibiotics are needed?

Questions about treatment

1. Which treatment do you recommend and why?
2. Which treatment will give my child the best quality of life?
3. Which treatment will extend life? By how long?
4. What should we expect from this treatment?
5. How long do we have to decide?
6. Will we have to go to the hospital or elsewhere for treatment?
7. Can we choose the days and times of treatment?
8. How much will this treatment cost? Are there any programs to help pay for treatment?
9. What can we do to prevent or relieve side effects? What will you do?
10. Will my child miss school or be able to be involved in sports, dance, or other extracurricular activities?

Questions about care team’s experience

1. What is your experience treating pediatric ALL?
2. What is the experience of those on your team?
3. Do you only treat pediatric 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 patients like my child (of the same age, gender, race) have you treated?
7. Will you be consulting with pediatric ALL experts to discuss my child’s 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 we expect? How will the side effects be controlled?
7. How long will my child 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 we have to wait for a hematopoietic cell transplant (HCT)?
3. What are the risks to myself and/or the donor?
4. How will the HCT affect my child's prognosis?
5. How will an HCT affect the quality and length of my child's life?
6. How long should my child expect to be in the hospital?
7. How will my child feel before, during, and after the HCT?
8. How many HCTs has this center done for those with this type of pediatric ALL?
9. Will my child 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 or send a message through the medical chart?
7. Will you stop treatment or change treatment if there are side effects?
8. What can we 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 my child will get another type of cancer?
3. Whom do we see for follow-up care? How often?
4. How often should my child see a dentist?
5. How often should my child see an eye doctor (ophthalmologist)?
6. What tests will my child have to monitor their health?
7. What vaccinations do you recommend?
8. What late effects should we look for?
9. What should we do if my child has trouble with work or school? Or difficulty focusing?
10. We are looking for a survivor support group. What support groups or other resources can you recommend?

Resources

Alex's Lemonade Stand Foundation

alexlemonade.org

American Association for Cancer Research (AACR)

aacr.org

American Cancer Society (ACS)

cancer.org/cancer/leukemia-in-children

American Society of Clinical Oncology (ASCO) for Young Adults and Teenagers

cancer.net

American Society of Hematology

hematology.org/education/patients

Be The Match®

bethematch.org

Blood & Marrow Transplant Information Network (BMT InfoNet)

bmtinfonet.org

CancerCare (also available en español)

cancercares.org

CancerFree Kids

cancerfreekids.org

Cancer Hope Network

cancerhopenetwork.org

Cancer Support Community

cancersupportcommunity.org/living-cancer

CaringBridge

caringbridge.org

Chemocare (also available en español)

chemocare.com

Children's National®

childrensnational.org

Children's Oncology Group (available in multiple languages)

survivorshipguidelines.org

CureSearch

curesearch.org

KidsHealth® (also available en español)

kidshealth.org

kidshealth.org/es/kids.html

MedlinePlus (also available en español)

medlineplus.gov

National Alliance for Mental Illness (NAMI)

nami.org

National Bone Marrow Transplant Link (nbmtLINK)

nbmtlink.org

National Cancer Institute (NCI) (also available en español)

cancer.gov/types/leukemia

National Coalition for Cancer Survivorship (NCCS)

canceradvocacy.org/toolbox

National Financial Resource Directory - Patient Advocate Foundation (PAF)

patientadvocate.org/explore-our-resources/national-financial-resource-directory

National Hospice and Palliative Care Organization (NHPCO)

caringinfo.org

OncoLink (also available en español)

oncolink.org

Patient Access Network Foundation

panfoundation.org

Pediatric Cancer Foundation of the Lehigh Valley

pcfiv.org

Radiological Society of North America

radiologyinfo.org

Society for Adolescent Health and Medicine (SAHM)

adolescenthealth.org/Resources/Resources-for-Adolescents-and-Parents

Stupid Cancer

stupidcancer.org

Testing.com

testing.com

The Leukemia & Lymphoma Society (LLS)

lls.org/leukemia/acute-lymphoblastic-leukemia/childhood-all

lls.org/PatientSupport

U.S. Department of Health & Human Services (HRSA) (available in multiple languages)

bloodstemcell.hrsa.gov

Young Adult Cancer Connection (YACC)

yacancerconnection.org

Young Survival Coalition (YSC)

youngsurvival.org



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Words to know

absolute neutrophil count (ANC)

The number of neutrophils, a type of white blood cell, in a blood sample. This number provides 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 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.

deoxyribonucleic acid (DNA)

Long strands of genetic information found inside cells.

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 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.

infant

A child under 12 months of age.

infection

An illness caused by germs.

infusion

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

Interfant induction

The first phase of treatment for those under 12 months of age.

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.

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 pediatric 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.

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.

pharmacogenomic

The study of how genes affect a person's response to drugs.

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

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.

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.

targeted therapy

A drug treatment that targets and attacks specific cancer cells.

T cell

A type of lymphocyte.

translocation

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

white blood cell (WBC)

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

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Acute Lymphoblastic Leukemia Version 1.2023. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

Tanya Fischer, MEd, MSLIS
Senior Medical Writer

Laura Phillips
Graphic Design Specialist

The NCCN Guidelines® for Pediatric Acute Lymphoblastic Leukemia Version 1.2023 were developed by the following NCCN Panel Members:

*Hiroto Inaba, MD, PhD/ Chair
St. Jude Children's Research Hospital/
The University of Tennessee
Health Science Center

*David Teachey, MD/ Vice-Chair
Abramson Cancer Center
at the University of Pennsylvania -
Children's Hospital of Philadelphia

Colleen Annesley, MD
Fred Hutchinson Cancer Center

Sandeep Batra, MD
Indiana University
Melvin and Bren Simon
Comprehensive Cancer Center

Jill Beck, MD
Fred & Pamela Buffett Cancer Center

Jong Chung, MD
UC Davis Comprehensive Cancer Center

*Susan Colace, MD, MSCI
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital
and Solove Research Institute

Stacy Cooper, MD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Kevin Curran, MD
Memorial Sloan Kettering Cancer Center

Mari Dallas, MD
Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center
and Cleveland Clinic Taussig Cancer Institute

Satiro De Oliveira, MD
UCLA Jonsson
Comprehensive Cancer Center

Kara Kelly, MD
Roswell Park Comprehensive Cancer Center

Carrie Kitko, MD
Vanderbilt-Ingram Cancer Center

Mira Kohorst, MD
Mayo Clinic Cancer Center

Norman Lacayo, MD
Stanford Cancer Institute

Cathy Lee-Miller, MD
Carbone Cancer Center
University of Wisconsin

Kathleen Ludwig, MD
UT Southwestern Simmons
Comprehensive Cancer Center

Luke Maese, DO
Huntsman Cancer Institute
at the University of Utah

Kris Mahadeo, MD, MPH
The University of Texas
MD Anderson Cancer Center

Kelly Maloney, M
University of Colorado Cancer Center

Valentina Nardi, MD
Massachusetts General Hospital
Cancer Center

Jenna Rossoff, MD
Robert H. Lurie Comprehensive
Cancer Center of Northwestern University
Ann & Robert H. Lurie Children's
Hospital of Chicago

*Laura Schuettepelz, MD, PhD
Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine

Bijal Shah, MD
Moffitt Cancer Center

Shilpa Shahani, MD
City of Hope National Medical Center

Lewis Silverman, MD
Dana-Farber Cancer Institute

Jessica Sun, MD
Duke Cancer Institute

Aman Wadhwa, MD
O'Neal Comprehensive
Cancer Center at UAB

*Victor Wong, MD
UC San Diego Moores Cancer Center -
Rady Children's Hospital of San Diego

Gregory Yanik, MD
University of Michigan Rogel Cancer Center

NCCN

Ryan Berardi, MSc
Guidelines Layout Specialist

Deborah Freedman-Cass, PhD
Manager, Guidelines Processes

* Reviewed this patient guide. For disclosures, visit [NCCN.org/disclosures](https://www.nccn.org/disclosures).

NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
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University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
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800.641.2422 • UH Seidman Cancer Center
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at the University of Utah
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The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

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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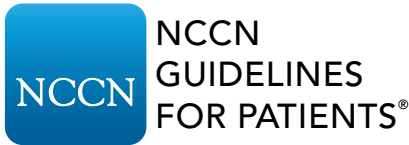
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877.936.8422 • vicc.org

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Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

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3025 Chemical Road, Suite 100
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