

Treating Acute Lymphocytic Leukemia (ALL)

If you've been diagnosed with acute lymphocytic leukemia (ALL), your cancer care team will discuss your treatment options with you. Your options may be affected by the ALL subtype, as well as certain other prognostic factors, as well as your age and overall state of health.

(Note: This information is about acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see Leukemia in Children.)

How is acute lymphocytic leukemia treated?

The main types of treatment used for ALL include:

- Chemotherapy for Acute Lymphocytic Leukemia (ALL)
- Targeted Therapy for Acute Lymphocytic Leukemia (ALL)
- Immunotherapy for Acute Lymphocytic Leukemia (ALL)
- Surgery for Acute Lymphocytic Leukemia (ALL)
- Radiation Therapy for Acute Lymphocytic Leukemia (ALL)
- Stem Cell Transplant for Acute Lymphocytic Leukemia (ALL)

Common treatment approaches

Treatment of ALL typically lasts for about 2 years. It is often intense, especially in the first few months of treatment, so it's important that you are treated in a center that has experience with this disease.

The treatment approach for children with ALL can be slightly different from that used for adults. It's discussed separately in <u>Treatment of Children With Acute Lymphocytic</u>

Leukemia (ALL).

• Typical Treatment of Acute Lymphocytic Leukemia (ALL)

Who treats ALL?

Based on your treatment options, you may have different types of doctors on your treatment team. These doctors could include:

- A hematologist: a doctor who treats disorders of the blood
- A medical oncologist: a doctor who treats cancer with medicines

You might have many other specialists on your treatment team as well, including physician assistants, nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals.

Health Professionals Associated with Cancer Care

Making treatment decisions

It's important to discuss all of your treatment options and their goals and possible side effects, with your treatment team to help make the decision that best fits your needs. Some important things to consider include:

- Your age and overall health
- The type of ALL you have
- The likelihood that treatment will cure you (or help in some other way)
- Your feelings about the possible side effects from treatment

It's also very important to ask questions if there is anything you're not sure about.

In most cases ALL can progress quickly if not treated, so it's important to start treatment as soon as possible after the diagnosis is made. But if time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- Questions to Ask About Acute Lymphocytic Leukemia (ALL)
- <u>Seeking a Second Opinion</u>

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-ofthe art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

<u>Clinical Trials</u>

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

<u>Complementary and Integrative Medicine</u>

Help getting through cancer treatment

People with cancer need support and information, no matter what part of their journey they may be on. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Chemotherapy for Acute Lymphocytic

Leukemia (ALL)

- How is chemo given?
- Which chemo drugs are used to treat ALL?
- Possible side effects
- More information about chemotherapy

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

Chemotherapy (chemo) is the use of drugs to treat cancer. Chemo drugs travel through the bloodstream to reach cancer cells all over the body. This makes chemo useful for cancers such as leukemia that has spread throughout the body.

Chemo is the main treatment for just about all people with acute lymphocytic leukemia (ALL). Because of its potential side effects, chemo might not be recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemo.

How is chemo given?

Chemo treatment for ALL is typically divided into 3 phases:

- Induction, which is short and intensive, usually lasts about a month.
- **Consolidation (intensification)**, which is also intensive, typically lasts for a few months.
- **Maintenance (post-consolidation)**, which is less intensive, typically lasts for about 2 years.

During the more intensive phases of treatment, people can often have serious side effects from chemo, so they might need to spend time in the hospital. For more on the different phases of treatment, see Typical Treatment of Acute Lymphocytic Leukemia.

Chemo is typically given in cycles, with each period of treatment followed by a rest period to allow the body time to recover.

Most often, chemo drugs are injected into a vein (IV), into a muscle, or under the skin, or are taken by mouth. These drugs enter the blood and can reach leukemia cells all over the body.

Most chemo drugs have trouble reaching the area around the brain and spinal cord, so chemo may need to be injected into the cerebrospinal fluid (CSF) to kill cancer cells in that area. This is called **intrathecal chemo**. Intrathecal chemo can be given during a <u>spinal tap</u>² or by using a special catheter called an Ommaya reservoir.

Which chemo drugs are used to treat ALL?

Chemo for ALL uses a combination of anti-cancer drugs. The most commonly used chemo drugs include:

- Vincristine or liposomal vincristine (Marqibo)
- Daunorubicin (daunomycin) or doxorubicin (Adriamycin)
- Cytarabine (cytosine arabinoside, ara-C)
- L-asparaginase or PEG-L-asparaginase (pegaspargase or Oncaspar)
- 6-mercaptopurine (6-MP)
- Methotrexate
- Cyclophosphamide
- Prednisone
- Dexamethasone
- Nelarabine (Arranon)

People typically get several of these drugs at different times during the course of treatment, but they do not get all of them.

Possible side effects

Chemo drugs can affect some normal cells in the body, which can lead to side effects. The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. Common side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation

Chemo drugs also affect the normal cells in bone marrow, which can lower blood cell counts. This can lead to:

- Increased risk of infections (from having too few normal white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue and shortness of breath (from having too few red blood cells)

Most side effects from chemo go away once treatment is finished. Low blood cell counts can last weeks, but then should return to normal. There are often ways to lessen chemo side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your cancer care team about medicines to help reduce side effects, and let your doctor or nurse know when you do have side effects so they can be managed effectively.

Low white blood cell counts: Some of the most serious side effects of chemo are caused by low white blood cell counts.

You may get **antibiotics** and drugs that help prevent fungal and viral infections before before you have signs of infection or at the earliest sign that an infection may be developing (such as a fever).

Drugs known as **growth factors**, such as filgrastim (Neupogen), pegfilgrastim (Neulasta), and sargramostim (Leukine), are sometimes given to increase the white blood cell counts after chemo, to help lower the chance of infection. However, it's not clear if they have an effect on treatment success.

There are also steps that you can take to lower your risk of infection, such as washing your hands often. These are discussed in <u>Infections in People With Cancer³</u>.

Low platelet counts: If your platelet counts are low, you may be given drugs or platelet transfusions to help protect against bleeding.

Low red blood cell counts: Shortness of breath and extreme fatigue caused by low red blood cell counts (anemia) may be treated with drugs or with red blood cell transfusions.

Decisions about when a patient can leave the hospital are often influenced by their blood counts. Some people find it helpful to keep track of their counts. If you are interested in this, ask your doctor or nurse about your blood cell counts and what these numbers mean.

Side effects of specific drugs: Certain drugs might cause specific side effects. For example:

- **Cytarabine** (ara-C), especially when used at high doses, can cause dryness in the eyes and can affect certain parts of the brain, which can lead to problems with coordination and balance.
- Vincristine can damage nerves, which can lead to numbness, tingling, or weakness in hands or feet.
- Anthracyclines (such as **daunorubicin** or **doxorubicin**) can damage the heart, so the total dose needs to be watched closely, and these drugs might not be used in someone who already has heart problems.

Other organs that could be damaged by certain chemo drugs include the kidneys, liver, testicles, ovaries, and lungs. Doctors and nurses carefully monitor treatment to reduce the risk of these side effects as much as possible. If serious side effects occur, the chemo may have to be reduced or stopped, at least for a time.

Second cancers: One of the most serious side effects of ALL therapy is an increased risk of getting <u>acute myeloid leukemia</u>⁴ (AML) at a later time. This occurs in a small portion of patients after they have received certain chemo drugs. Less often, people cured of leukemia may later develop <u>non-Hodgkin lymphoma</u>⁵ or other cancers. Of course, the risk of getting these <u>second cancers</u>⁶ must be balanced against the obvious benefit of treating a life-threatening disease such as leukemia with chemotherapy.

Tumor lysis syndrome: This side effect of chemo is most common in patients who have large numbers of leukemia cells in the body, so it is seen most often in the first (induction) phase of treatment. When chemo kills the leukemia cells, they break open and release their contents into the bloodstream. This can overwhelm the kidneys, which aren't able to get rid of all of these substances at once. Excess amounts of certain minerals can also affect the heart and nervous system. This can often be prevented by giving extra fluids during treatment and by giving certain drugs, such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see <u>Chemotherapy</u>⁷.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁸.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children.html</u>
- 2. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> <u>staging/how-diagnosed.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-</u> <u>counts/infections.html</u>
- 4. <u>www.cancer.org/cancer/types/acute-myeloid-leukemia.html</u>
- 5. www.cancer.org/cancer/types/non-hodgkin-lymphoma.html
- 6. <u>www.cancer.org/cancer/survivorship/long-term-health-concerns/second-cancers-in-adults.html</u>
- 7. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 8. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Appelbaum FR. Chapter 98: Acute Leukemias in Adults. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Jain N, Gurbuxani S, Rhee C, Stock W. Chapter 65: Acute Lymphoblastic Leukemia in Adults. In: Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weitz J, Anastasi J, eds. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, Pa: Elsevier; 2013.

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Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: A comprehensive review and 2017 update. *Blood Cancer J.* 2017;7(6):e577.

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Targeted Therapy for Acute Lymphocytic Leukemia (ALL)

- Targeted drugs for ALL with the Philadelphia chromosome (Ph+ ALL)
- Immunotherapy drugs for ALL
- More information about targeted therapy

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

Targeted therapy drugs work by attacking specific parts of cancer cells. They are different from standard chemotherapy (chemo) drugs. They sometimes work when chemo doesn't, and they often have different side effects. Some of these drugs can be useful in certain cases of acute lymphocytic leukemia (ALL).

Targeted drugs for ALL with the Philadelphia chromosome (Ph+ALL)

In about 1 out of 4 adult patients with ALL, the leukemia cells have the **Philadelphia chromosome**. This is an abnormal chromosome formed by the swapping of genetic material between chromosomes 9 and 22, which creates a new gene called *BCR-ABL*. Cells with the *BCR-ABL* gene make an abnormal protein that helps the cells grow.

Drugs called **tyrosine kinase inhibitors** (**TKIs**) have been developed to attack this protein. Examples include:

- Imatinib (Gleevec[®])
- Dasatinib (Sprycel[®])
- Nilotinib (Tasigna[®])
- Ponatinib (Iclusig[®])
- Bosutinib (Bosulif[®])

In patients with Ph+ ALL, adding a TKI to chemo helps increase the chance that the leukemia will go into remission. Continuing on one of these drugs can also help keep the leukemia from coming back. If one TKI doesn't work (or is no longer working), another one might be tried.

These drugs are taken daily as pills.

Common **side effects** include diarrhea, nausea, muscle pain, fatigue, and skin rashes. These are generally mild. A common side effect is swelling around the eyes or in the hands or feet. Other possible side effects include lower red blood cell and platelet counts at the start of treatment. All of these side effects can get worse at higher than usual doses of the drug. Other, more serious side effects can occur as well, depending on which drug is used.

Immunotherapy drugs for ALL

Some of the immunotherapy drugs used to treat ALL might also be considered forms of targeted therapy, because they work by attaching to specific parts of leukemia cells. Examples include:

- Blinatumomab (Blincyto)
- Inotuzumab ozogamicin (Besponsa)

For more information on these drugs, see Immunotherapy for Acute Lymphocytic Leukemia (ALL).

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

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Appelbaum FR. Chapter 98: Acute Leukemias in Adults. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Jain N, Gurbuxani S, Rhee C, Stock W. Chapter 65: Acute Lymphoblastic Leukemia in Adults. In: Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weitz J, Anastasi J, eds. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, Pa: Elsevier; 2013.

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Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: A comprehensive review and 2017 update. *Blood Cancer J.* 2017;7(6):e577.

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Immunotherapy for Acute Lymphocytic Leukemia (ALL)

- Monoclonal antibodies
- CAR T-cell therapy
- More information about immunotherapy

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

Immunotherapy is the use of medicines to help a patient's own immune system recognize and destroy cancer cells more effectively. Some types of immunotherapy are now being used to treat acute lymphocytic leukemia (ALL) in certain situations.

Monoclonal antibodies

Antibodies are proteins made by the body's immune system to help fight infections. Man-made versions of these proteins, called <u>monoclonal antibodies</u>², can be designed to attack a specific target, such as a protein on the surface of leukemia cells.

Blinatumomab (Blincyto)

Blinatumomab is a special kind of monoclonal antibody because it can attach to 2 different proteins at the same time. One part of blinatumomab attaches to the CD19 protein, which is found on B cells, including some leukemia and lymphoma cells. Another part attaches to CD3, a protein found on immune cells called T cells. By binding to both of these proteins, this drug brings the cancer cells and immune cells together, which is thought to cause the immune system to attack the cancer cells.

This drug is used to treat some types of B-cell ALL, typically after chemotherapy has been tried. It is given into a vein (IV) as a continuous infusion over 28 days. It may be repeated again for more cycles with 2 weeks off in between. Because of certain serious side effects that occur more often during the first few times it is given, the patient usually needs to be treated in a hospital or clinic for the beginning of at least the first 2 cycles.

The most common **side effects** are fever, headache, swelling of the feet and hands, nausea, tremor, rash, constipation, and low blood potassium levels. It can also cause low white blood cell counts, which increase the risk of serious infection.

This drug can also cause neurologic problems, such as seizures, difficulty in speaking or slurred speech, passing out, confusion, and loss of balance.

Some patients have serious reactions while this drug is being infused. Symptoms can include feeling lightheaded or dizzy (due to low blood pressure), headache, nausea, fever or chills, shortness of breath, and/or wheezing. Let your healthcare team know if you develop any of these symptoms, as this reaction can be life-threatening. If you do have a reaction, the drug will be stopped while the reaction is treated.

Inotuzumab ozogamicin (Besponsa)

This drug is an anti-CD22 antibody linked to a chemotherapy drug. B cells (including some leukemia cells) usually have the CD22 protein on their surface. The antibody acts like a homing signal, bringing the chemo drug to the leukemia cells, where it enters the cells and kills them when they try to divide into new cells.

This drug is used to treat some types of B-cell ALL, typically after chemotherapy has been tried. It is given as an infusion into a vein (IV), once a week for 3 or 4 weeks in a row. This may be repeated for more cycles.

The most common **side effects** are low levels of blood cells (with increased risks of infection, bleeding, and fatigue), fever, nausea, headache, abdominal (belly) pain, and high blood levels of bilirubin (a substance in bile).

Less common but more serious side effects can include:

- Severe liver damage, including veno-occlusive disease (blockage of veins in the liver)
- Reactions during the infusion (similar to an allergic reaction). You will likely be given medicines before each infusion to help prevent this.
- Serious or life-threatening infections, especially in people who have already had a stem cell transplant
- Changes in the rhythm of the heart

CAR T-cell therapy

For this treatment, immune cells called **T cells** are removed from the person's blood and genetically altered in the lab to have specific receptors (called **chimeric antigen receptors**, or **CARs**) on their surface. These receptors can attach to proteins on leukemia cells. The T cells are then multiplied in the lab and given back into the blood, where they can seek out the leukemia cells and attack them.

To make this treatment, T cells are removed from the blood during a process called *leukapheresis*. Blood is removed through an IV line and goes into a machine that removes the T cells. The remaining blood then goes back into the body. This typically takes a few hours, and it might need to be repeated. The cells are then frozen and sent to a lab, where they are turned into CAR T cells and are multiplied. This can take a few weeks.

For the treatment itself, the patient typically gets chemo for a few days to help prepare the body. Then they get the CAR T cells as an infusion into a vein (IV). Because this treatment can have serious side effects (see below), it is only given in medical centers that have special training with this treatment.

Brexucabtagene autoleucel (Tecartus, also known as brexu-cel) is approved to treat adults with B-cell ALL that has come back or is no longer responding to other treatments.

Tisagenlecleucel (Kymriah, also known as tisa-cel) is approved for use in children and young adults up to age 25 to treat B-cell ALL that has come back or is no longer responding to treatment.

Side effects of CAR T-cell therapy

This treatment can have serious or even life-threatening side effects, which is why it

needs to be given in a medical center that has special training in its use.

Cytokine release syndrome (CRS): CRS happens when T cells release chemicals (cytokines) that ramp up the immune system. This can happen within a few days to weeks after treatment, and it can be life-threatening. Symptoms can include:

- High fever and chills
- Trouble breathing
- Severe nausea, vomiting, and/or diarrhea
- Severe muscle or joint pain
- Feeling dizzy or lightheaded

Nervous system problems: This drug can have serious effects on the nervous system, which can result in symptoms such as:

- Headaches
- Changes in consciousness
- Confusion or agitation
- Seizures
- Trouble speaking and understanding
- Loss of balance

Other serious side effects: Other possible side effects can include:

- Serious infections
- Low blood cell counts, which can increase the risk of infections, fatigue, and bruising or bleeding

It's very important to report any side effects to the health care team right away, as there are often medicines that can help treat them.

To learn more about this type of treatment, see <u>CAR T-Cell Therapies</u>³.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>⁴.

To learn about some of the side effects listed here and how to manage them,

see Managing Cancer-related Side Effects⁵.

Hyperlinks

- 1. www.cancer.org/cancer/types/leukemia-in-children.html
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-</u> <u>types/immunotherapy/monoclonal-antibodies.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/car-t-cell1.html</u>
- 4. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html

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Surgery for Acute Lymphocytic Leukemia (ALL)

Placement of a central venous catheter

Placement of an Ommaya reservoir

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

Surgery has a very limited role in the treatment of acute lymphocytic leukemia (ALL). Because leukemia cells are spread widely throughout the bone marrow and blood, it isn't possible to cure this type of cancer with surgery. Aside from a possible lymph node biopsy², surgery rarely has a role even in the diagnosis of ALL, as this is typically done with a bone marrow aspiration and biopsy³.

The main role for surgery in ALL is to insert catheters (tubes) into the body to make it easier to give chemotherapy (chemo), which is the main treatment for ALL.

Placement of a central venous catheter

Often before chemo is about to start, surgery is often needed to insert a small plastic tube, called a <u>central venous catheter</u>⁴ (CVC), central line, or venous access device (VAD), into a large vein (usually in the chest). The end of the tube stays just under the skin or sticks out in the chest area or upper arm.

The CVC is left in place during treatment (often for many months) to give intravenous (IV) drugs such as chemo and to take blood samples. This lowers the number of needle sticks needed during treatment. It is very important to learn how to care for the device to keep it from getting infected.

Placement of an Ommaya reservoir

Giving chemo directly into the fluid that surrounds the brain and spinal cord (cerebrospinal fluid or CSF) is often a part of the treatment of ALL. In this treatment, called **intrathecal chemo**, the medicines can be given through a lumbar puncture (spinal tap) or through an Ommaya reservoir.

An Ommaya reservoir is a dome-like device attached to a catheter, which is put in place during a surgical procedure. The dome part sits under the skin of the scalp, with the catheter going through a small hole in the skull and into one of the spaces (ventricles) in the brain.

Intrathecal chemo can be given by placing a needle through the skin and into the dome . The chemo goes through the catheter and into the CSF in the ventricle, and then

circulates through the area around the brain and spinal cord.

An Ommaya reservoir allows a person to get intrathecal chemo without having to get repeated spinal taps. CSF can also be withdrawn from the Ommaya reservoir to check for leukemia cells and signs of infection.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children.html</u>
- 2. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> <u>staging/how-diagnosed.html</u>
- 3. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> staging/how-diagnosed.html
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html</u>

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Radiation Therapy for Acute

Lymphocytic Leukemia (ALL)

- Side effects
- More information about radiation therapy

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

Radiation therapy uses high-energy radiation to kill cancer cells. It is not usually part of the main treatment for people with acute lymphocytic leukemia (ALL), but it is used in certain situations:

- Radiation is sometimes used to treat leukemia that has spread to the brain and spinal fluid, or to the testicles.
- Radiation to the whole body is often an important part of treatment before a bone marrow or peripheral blood stem cell transplant (see High-dose Chemotherapy and Stem Cell Transplant for Acute Lymphocytic Leukemia).
- Radiation is used (rarely) to help shrink a tumor if it is pressing on the trachea (windpipe) and causing breathing problems. But chemotherapy is often used instead, as it may work more quickly.
- Radiation can also be used to reduce pain in an area of bone invaded by leukemia, if chemotherapy hasn't helped.

External beam radiation therapy, in which a machine delivers a beam of radiation to a specific part of the body, is the type of radiation used most often for ALL. Before your treatment starts, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session, called **simulation**, usually includes getting <u>imaging tests</u>² such as CT or MRI scans.

Radiation treatment is much like getting an x-ray, but the radiation is much stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. The number of treatments you get depends on the reason radiation therapy is being used.

Side effects

The **possible sideeffects** of radiation therapy depend on where the radiation is aimed.

They include:

- Fatigue (tiredness)
- Skin changes in the treated area, which can range from mild redness to burning and peeling
- Hair loss in the area being treated
- Nausea and vomiting (if the head or belly is being treated)
- Diarrhea (if the belly or pelvis is being treated)
- Mouth sores and trouble swallowing (if the head and neck area are being treated)
- Headaches (if the head is being treated)
- Lowered blood cell counts, which can lead to fatigue and shortness of breath (from low red blood cell counts), bleeding or bruising (from low platelet counts), and an increased risk of infection (from low white blood cell counts)

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u>³.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

- 1. www.cancer.org/cancer/types/leukemia-in-children.html
- 2. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Stem Cell Transplant for Acute Lymphocytic Leukemia (ALL)

- Types of stem cell transplants
- Practical points
- · More information about stem cell transplant

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see Leukemia in Children¹.)

Standard doses of chemotherapy (chemo) aren't always able to cure acute lymphocytic leukemia (ALL). Even though higher doses of chemo drugs might be more effective, they can't be given because they could severely damage the bone marrow, which is where new blood cells are formed. This could lead to life-threatening infections, bleeding, and other problems due to low blood cell counts.

A <u>stem cell transplant</u>² (SCT) allows doctors to use higher doses of chemo (sometimes along with radiation) to kill the cancer cells. After these treatments are finished, the patient gets an infusion (transplant) of blood-forming stem cells to restore their bone marrow.

Blood-forming stem cells used for a transplant are obtained either from the blood, from the bone marrow, or from a baby's umbilical cord blood. Most often, stem cells from the blood are used.

Types of stem cell transplants

The main types of stem cell transplants are:

- Allogeneic stem cell transplant, in which the stem cells come from someone else. This is the preferred type of transplant when treating ALL.
- Autologous stem cell transplant, in which the patient gets back their own cells

Allogeneic transplant: A donor's tissue type (also known as the HLA type) needs to closely match the patient's tissue type to help prevent the risk of major problems with the transplant. The best donor is often a close relative, such as a brother or sister, if they have the same tissue type as the patient. If there are no siblings with a good match, the cells may come from an HLA-matched, unrelated donor – a stranger who has volunteered to donate their cells. Some patients cannot have this kind of transplant because a matching donor isn't available.

The use of allogeneic transplant is also limited by its side effects, which are often too severe for people who are older or who have other health problems. One option that may help patients who can't have an allogeneic transplant because of age or health issues is to use lower doses of chemo and radiation that don't completely destroy the cells in their bone marrow. This is known as a **non-myeloablative** or **reducedintensity transplant**. This kind of SCT relies on the donor cells to kill the leukemia cells, instead of the chemo and radiation. This is not a standard treatment for ALL, and is being studied to determine how useful it may be.

Autologous transplant: A patient's own stem cells are removed from their bone marrow or blood. They are frozen and stored while the person gets treatment (high-dose chemotherapy and/or radiation). A process called **purging** may be used in the lab to try to remove any leukemia cells in the samples. The stem cells are then put back (reinfused) into the patient's blood after treatment.

An autologous transplant may be an option for patients who can't have an allogeneic transplant because they don't have a matched donor, or for some other reason. One problem with autologous transplants is that leukemia is a disease of the bone marrow and blood, so even after purging, there is a danger of giving the patient back leukemia cells with the stem cells.

Another reason that allogeneic transplants are preferred is because of the **graft-versus-leukemia** effect. When the donor immune cells are infused into the body, they may recognize any remaining leukemia cells as being foreign to them and attack them. This effect doesn't happen with an autologous SCT.

Practical points

A stem cell transplant is an intensive and complex treatment that can cause life-

threatening side effects. If your doctor thinks you might benefit from a transplant, you should discuss what kind you will have, the possible side effects, and how long it may take for you to recover. Stem cell transplants should be done at a hospital where the staff has experience with the procedure and with managing the recovery phase.

More information about stem cell transplant

To learn more about stem cell transplants, including how they are done and their potential side effects, see <u>Stem Cell Transplant for Cancer³</u>.

For more general information about side effects and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

- 1. www.cancer.org/cancer/types/leukemia-in-children.html
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-</u> <u>transplant.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-</u> <u>transplant.html</u>
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Typical Treatment of Acute Lymphocytic Leukemia (ALL)

- Induction
- Consolidation (intensification)
- Maintenance
- Response rates to ALL treatment
- What if the leukemia doesn't respond or comes back after treatment?

(**Note:** This information is about treating acute lymphocytic leukemia (ALL) in adults. To learn about ALL in children, see <u>Leukemia in Children</u>¹.)

The main treatment for acute lymphocytic leukemia (ALL) in adults is typically long-term chemotherapy (chemo). In recent years, doctors have begun to use more intensive chemo regimens, which has led to more responses to treatment. But these regimens are also more likely to cause side effects, such as low white blood cell counts. Patients may need to take other drugs to help prevent or treat these side effects.

Treatment typically takes place in 3 phases:

- Induction (remission induction)
- Consolidation (intensification)
- Maintenance

The total treatment usually takes about 2 years, with the maintenance phase taking up most of this time. Treatment may be more or less intense, depending on the <u>subtype of ALL and other prognostic factors</u>².

ALL can spread to the area around the brain and spinal cord. Sometimes this has already occurred by the time ALL is first diagnosed. This spread is found when the doctor does a <u>lumbar puncture³</u> (spinal tap) and leukemia cells are found in the cerebrospinal fluid (CSF), the liquid that surrounds the brain and spinal cord. The treatment of this is discussed below.

Even if leukemia cells aren't found in the CSF at diagnosis, it's possible that they might spread there later on. This is why an important part of treatment for ALL is **central nervous system (CNS) prophylaxis** – treatment that lowers the risk of the leukemia spreading to the area around the brain or spinal cord. This is also described in more

detail below.

Induction

The goal of induction chemo is to get the leukemia into <u>remission (complete remission)</u>⁴. This means that leukemia cells are no longer found in bone marrow samples (on a <u>bone marrow biopsy</u>⁵), the normal marrow cells return, and the blood counts return to normal levels. But a remission is not necessarily a cure, as leukemia cells may still be hiding somewhere in the body.

Induction chemo usually lasts for a month or so. Different combinations of chemo drugs might be used, but they typically include:

- Vincristine
- Dexamethasone or prednisone
- An anthracycline drug such as doxorubicin (Adriamycin) or daunorubicin

Based on the patient's <u>prognostic factors</u>⁶, some regimens may also include cyclophosphamide, L-asparaginase (or pegaspargase), and/or high doses of methotrexate or cytarabine (ara-C) as part of the induction phase.

For ALL patients whose leukemia cells have the **Philadelphia chromosome**, a targeted drug such as imatinib (Gleevec) or dasatinib (Sprycel) is often included as well.

For patients who are older (typically over 65) or who have other serious health conditions, many of the same drugs are used for induction, although the doses of the drugs might need to be reduced.

This first month of treatment is intensive and requires frequent visits to the doctor. You may spend some or much of this time in the hospital, because serious infections or other complications can occur. It's very important to take all medicines as prescribed. Sometimes complications can be serious enough to be life-threatening, but with recent advances in supportive care (nursing care, nutrition, antibiotics, growth factors, red blood cell and platelet transfusions⁷ as needed, etc.), these are much less common than in the past.

Most often, leukemia goes into remission with induction chemotherapy. But because leukemia cells may still be hiding somewhere in the body, further treatment is needed.

CNS treatment or prophylaxis: Treatment needs to be given either to keep the leukemia cells from spreading to the CNS (CNS prophylaxis), or to treat the leukemia if

it has already spread to the CNS. This is often started during induction and continued through the other phases of treatment. It may include one or more of the following:

- Chemo injected directly into the CSF (called intrathecal chemotherapy). The drug used most often is methotrexate, but sometimes cytarabine or a steroid such as prednisone may be used as well. Intrathecal chemo can be given during a <u>lumbar</u> <u>puncture</u>⁸ (spinal tap) or through an Ommaya reservoir (as discussed in the surgery section).
- High-dose IV methotrexate, cytarabine, or other chemo drugs
- Radiation therapy to the brain and spinal cord

Consolidation (intensification)

If the leukemia goes into remission, the next phase often consists of another fairly short course of chemo, using many of the same drugs that were used for induction therapy. This typically lasts for a few months. Usually the drugs are given in high doses so that the treatment is still fairly intense. CNS prophylaxis/treatment is typically continued at this time.

A targeted drug like imatinib is also continued for patients whose leukemia cells have the Philadelphia chromosome.

Some patients in remission, such as those who have certain subtypes of ALL or other poor prognostic factors, are still at high risk for the leukemia relapsing (coming back). Instead of standard chemo, doctors may suggest an allogeneic stem cell transplant (SCT) at this time, especially for those who have a brother or sister who would be a good donor match. An autologous SCT may be another option. The possible risks and benefits of a stem cell transplant need to be weighed carefully for each patient based on their own case, as it's not clear that they are helpful for every patient. Patients considering this procedure should think about having it done at a center that has done a lot of stem cell transplants.

Maintenance

After consolidation, the patient is generally put on a maintenance chemotherapy program of methotrexate and 6-mercaptopurine (6-MP). In some cases, this may be combined with other drugs such as vincristine and prednisone.

For ALL patients whose leukemia cells have the Philadelphia chromosome, a targeted

drug like imatinib is often included as well.

Maintenance usually lasts for about 2 years. CNS prophylaxis/treatment is typically continued at this time.

Response rates to ALL treatment

In general, about 80% to 90% of adults will have complete remissions at some point during these treatments. This means leukemia cells can no longer be seen in their bone marrow. Unfortunately, about half of these patients relapse, so the overall cure rate is in the range of 40%. Again, these rates can vary a lot, depending on the <u>subtype of ALL</u> and other prognostic factors⁹. For example, cure rates tend to be higher in younger patients.

What if the leukemia doesn't respond or comes back after treatment?

If the leukemia is **refractory** – that is, if it doesn't go away with the first treatment (which happens in about 10% to 20% of patients) – then newer or more intensive doses of chemo drugs may be tried, although they are less likely to work. Immunotherapy (monoclonal antibodies or CAR T-cell therapy) may be an option for patients with B-cell ALL. A stem cell transplant may be tried if the leukemia can be put into at least partial remission. <u>Clinical trials</u>¹⁰ of new treatment approaches may also be considered.

If leukemia goes into remission with the initial treatment but then comes back (**relapses** or **recurs**), it will most often do so in the bone marrow and blood. Occasionally, the brain or spinal fluid will be the first place it recurs.

In these cases, it is sometimes possible to put the leukemia into remission again with more chemotherapy (chemo), although this remission is not likely to last. The approach to treatment may depend on how soon the leukemia returns after the first treatment. If the relapse occurs after a long interval, the same or similar treatment may be used to try for a second remission. If the time interval is shorter, more aggressive chemo with other drugs may be needed.

Immunotherapy might be another option for some patients. For example, a monoclonal antibody or CAR T-cell therapy might be an option for some people with B-cell ALL.

ALL patients with the Philadelphia chromosome who were taking a targeted drug like imatinib (Gleevec) are often switched to a different targeted drug.

For patients with T-cell ALL, the chemo drug nelarabine (Arranon) may be helpful.

If a second remission can be achieved, most doctors will advise some type of stem cell transplant if possible.

If the leukemia doesn't go away or keeps coming back, eventually treatment with more chemo is unlikely to be helpful. If a stem cell transplant is not an option, a patient may want to consider taking part in a clinical trial of newer treatments.

Palliative treatment

At some point, it may become clear that further treatment, even in clinical trials, is extremely unlikely to cure the leukemia. At that time, the focus of treatment may shift to controlling the leukemia and its symptoms for as long as possible, rather than trying to cure it. This may be called <u>palliative treatment</u>¹¹ or **supportive care**. For example, the doctor may advise less intensive chemo to try to slow the leukemia growth instead of trying to cure it.

As the leukemia grows in the bone marrow it may cause pain. It's important that you be as comfortable as possible. Treatments that may be helpful include radiation and appropriate pain-relieving medicines. If medicines such as aspirin and ibuprofen don't help with the pain, stronger opioid medicines such as morphine are likely to be helpful.

Other common symptoms from leukemia are low blood counts and <u>fatigue</u>¹². Medicines or <u>blood transfusions</u>¹³ may be needed to help correct these problems. <u>Nausea</u>¹⁴ and loss of appetite can be treated with medicines and high-calorie food supplements. <u>Infections</u>¹⁵ that occur may be treated with antibiotics.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children.html</u>
- 2. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> staging/how-classified.html
- 3. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> staging/how-diagnosed.html
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- 5. www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-

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- 6. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> staging/how-classified.html
- 7. <u>www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html</u>
- 8. <u>www.cancer.org/cancer/types/acute-lymphocytic-leukemia/detection-diagnosis-</u> staging/how-diagnosed.html
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- 10. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 11. <u>www.cancer.org/cancer/managing-cancer/palliative-care.html</u>
- 12. <u>www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html</u>
- 13. <u>www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html</u>
- 14. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
- 15. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-</u> <u>counts/infections.html</u>

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