

# **Treating Childhood Leukemia**

If your child has been diagnosed with leukemia, your child's treatment team will discuss the options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

#### How is childhood leukemia treated?

The main treatment for most childhood leukemias is chemotherapy. For some children with higher risk leukemias, high-dose chemotherapy may be given along with a stem cell transplant. Other treatments might also be used in special circumstances.

- Surgery for Childhood Leukemia
- Radiation Therapy for Childhood Leukemia
- Chemotherapy for Childhood Leukemia
- Targeted Therapy Drugs for Childhood Leukemia
- Immunotherapy for Childhood Leukemia
- High-dose Chemotherapy and Stem Cell Transplant for Childhood Leukemia

#### **Common treatment approaches**

After leukemia is diagnosed and <u>tests</u> have been done to determine its <u>type</u> and <u>subtype</u>, your child's cancer care team will discuss the treatment options with you. The most important factor in choosing a treatment is the type of leukemia, but <u>other factors</u> also play a role.

Treatment of acute forms of childhood leukemia (ALL or AML) is usually very intensive, so it's important that it takes place in a center that specializes in treating childhoodso i been dlay i c.3

- Immediate Treatment for Childhood Leukemia
- Treatment of Children with Acute Lymphocytic Leukemia (ALL)
- Treatment of Children With Acute Myeloid Leukemia (AML)
- Treatment of Children with Acute Promyelocytic Leukemia (APL)
- Treatment of Children with Juvenile Myelomonocytic Leukemia (JMML)
- Treatment of Children with Chronic Myeloid Leukemia (CML)

#### Who treats leukemia in children?

Children and teens with leukemia and their families have special needs. These needs can be met best by cancer centers for children and teens, working closely with the child's primary care doctor. These centers offer the advantage of being treated by teams of specialists who know the differences between cancers in adults and those in

#### Thinking about taking part in a clinical trial

Today, most children and teens with cancer are treated at specialized children's cancer centers. These centers offer the most up-to-date-treatment by conducting clinical trials (studies of promising new therapies). Children's cancer centers often conduct many clinical trials at any one time, and in fact most children treated at these centers take part in a clinical trial as part of their treatment. Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to newer

Your child's cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services can also be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help. For children and teens with cancer and their families, other specialists can be an important part of care as well. 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 trained specialists.

- Finding Help and Support When Your Child Has Cancer
- Programs & Services

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.

# Immediate Treatment for Childhood Leukemia

Some children are critically ill when they are first diagnosed with leukemia. For example:

- They might have a shortage of normal white blood cells, which might lead to very serious <u>infections</u><sup>1</sup>.
- They might have low levels of platelets or clotting factors in the blood, which can cause severe bleeding.

These problems must often be addressed before treatment of the leukemia can begin. Antibiotics, blood growth factors, and <u>transfusions of platelets and red blood cells</u>,<sup>2</sup> or procedures to lower white blood cell counts (for leukostasis) might be needed to treat or help prevent some of these conditions.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/side-effects/infections.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html</u>

## References

Horton TM, Steuber CP. Overview of the treatment of acute lymphoblastic leukemia in children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/overview-of-the-treatment-of-acute-lymphoblastic-leukemia-in-children-and-adolescents on December 29, 2018.

Tarlock K, Cooper TM. Acute myeloid leukemia in children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/acute-myeloid-leukemia-in-children-and-adolescents on December 29, 2018.

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# **Surgery for Childhood Leukemia**

- · Placing a central venous catheter
- More information about Surgery

Surgery has a very limited role in treating childhood leukemia. Because leukemia cells

of cancer with surgery. Aside from a possible <u>lymph node biopsy</u><sup>1</sup>, surgery rarely has any role even in diagnosing leukemia, since this is usually done with a bone marrow aspirate and biopsy can usually diagnose leukemia.

## Placing a central venous catheter

Often before chemotherapy is about to start, surgery is needed to insert a small plastic tube, called a <u>central venous catheter (CVC) or venous access<sup>2</sup>device (VAD)<sup>3</sup></u>, into a large blood vessel. 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 chemotherapy and to take blood samples. This lowers the number of needle sticks needed during treatment. It's very important for parents to learn how to care for the catheter to keep it from getting infected.

## More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u><sup>4</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>5</sup>.

# **Hyperlinks**

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

#### References

children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/overview-of-the-treatment-of-acute-lymphoblasticleukemia-in-children-and-adolescents on December 29, 2018.

# Radiation Therapy for Childhood Leukemia

• Radiation to the whole body is often an important part of treatment before a stem cell transplant (see High-Dose Chemotherapy and Stem Cell Transplant).

How is radiation therapy given?

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# **Chemotherapy for Childhood Leukemia**

- Possible side effects of chemo
- More information about chemotherapy

Chemotherapy (chemo) is the main treatment for most childhood leukemias. This is treatment with anti-cancer drugs that are given in a vein (IV), in a muscle, in the cerebrospinal fluid (CSF) around the brain and spinal cord, or are taken by mouth. Except when given in the CSF, chemo drugs enter the bloodstream and reach all areas of the body, making this treatment very useful for cancers such as leukemia.

Leukemia is treated with combinations of several chemo drugs. Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover.

In general, treatment for acute myeloid leukemia (AML) uses higher doses of chemo over a shorter period of time (usually less than a year), and treatment for acute lymphocytic leukemia (ALL) uses lower doses of chemo over a longer period of time (usually 2 to 3 years).

Some of the chemo drugs used to treat childhood leukemia include:

- Vincristine
- Daunorubicin, (daunomycin)
- Doxorubicin (Adriamycin)
- Idarubicin
- Cytarabine (cytosine arabinoside or ara-C)
- L-asparaginase, PEG-L-asparaginase (pegaspargase)
- Etoposide
- 6-mercaptopurine (6-MP)
- 6-thioguanine (6-TG)
- Methotrexate
- Mitoxantrone
- Cyclophosphamide

Cort35 292.5 Tm 324.5 Tm t1 0 0 1 95.35 291 0 0f0o4.5 Tm t1 0 Tm /F3 Sbis5.3r07.5 Tm /F2 12

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 treatment. These side effects can include:

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

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)
- Bruising and bleeding easily (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

The problems with blood cell counts are often caused by the leukemia itself at first. They might get worse during the first part of treatment because of the chemo, but they will probably improve as the leukemia cells are killed off and the normal cells in the bone marrow recover.

Most side effects usually go away when treatment is finished. There are often ways to reduce these side effects. For instance, drugs can be given to help prevent or reduce nausea and vomiting. Other drugs known as **growth factors** can be given to help keep the blood cell counts higher.

**Tumor lysis syndrome:** This side effect of chemo can happen in children who had large numbers of leukemia cells in the body before treatment. When chemo kills these 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. Too much of certain minerals can also affect the heart and nervous system. This problem can be prevented by making sure the child gets lots of fluids during treatment and certain drugs, such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

Some chemo drugs can also have other specific side effects. For example:

• Vincristine can damage nerves, which can lead to numbness, tingling, or weakness

in hands or feet (known as peripheral neuropathy).

• L-asparaginase and PEG-L-asparaginase can increase the risk of blood clots.

Some chemo drugs can also cause **late or long-term side effects**, such as effects on growth and development, effects on fertility later in life, or an increased risk of getting a second cancer (often AML). For more on this, see <u>Living as a Childhood Leukemia</u> <u>Survivor</u><sup>1</sup>.

Be sure to ask your child's doctor or nurse about any specific side effects you should watch for and about what you can do to help reduce these side effects.

Chemo given directly into the cerebrospinal fluid (CSF) around the brain and spinal cord (known as **intrathecal chemotherapy**) can have its own side effects, although these are not common. Intrathecal chemo may cause trouble thinking or even seizures in some children.

## More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see  $\frac{Chemotherapy}{2}^2$ .

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

# Hyperlinks

- 1. www.cancer.org/cancer/types/leukemia-in-children/after-treatment/follow-up.html
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

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Horton TM, Steuber CP. Overview of the treatment of acute lymphoblastic leukemia in children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/overview-of-the-treatment-of-acute-lymphoblastic-leukemia-in-children-and-adolescents on December 29, 2018.

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https://www.cancer.gov/types/leukemia/hp/child-all-treatment-pdq on December 29, 2018.

National Cancer Institute. Childhood Acute Myeloid Leukemia/Other Myeloid Malignancies Treatment (PDQ®)–Health Professional Version. Accessed at https://www.cancer.gov/types/leukemia/hp/child-aml-treatment-pdq on December 29, 2018.

Tarlock K, Cooper TM. Acute myeloid leukemia in children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/acute-myeloid-leukemia-in-children-and-adolescents on December 29, 2018.

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# Targeted Therapy Drugs for Childhood Leukemia

- BCR-ABL inhibitors for CML (and some cases of ALL)
- Gemtuzumab ozogamicin (Mylotarg) for AML
- Inotuzumab ozogamicin (Besponsa) for ALL

The most common

- Serious or life-threatening infections, especially in people who have already had a stem cell transplant
- Changes in the rhythm of the heart

# Differentiation agents for APL

Acute promyelocytic leukemia (APL) is different from other subtypes of AML in some important ways. The leukemia cells in APL (called blasts), have certain gene changes that stop them from maturing into normal white blood cells. Drugs called **differentiation agents** can help the blasts mature (differentiate) into normal white blood cells. Two of these drugs can be used to treat APL:

- All-trans-retinoic acid (ATRA, tretinoin)
- Arsenic trioxide (ATO)

**ATRA** is a form of vitamin A that is typically part of the initial treatment of APL. It is given either along with chemo or along with ATO. It can also be used during later phases of treatment.

Side effects of ATRA can include:

- Headache
- Fever
- Dry skin and mouth
- Skin rash
- Swollen feet
- Sores in the mouth or throat
- Itching
- Irritated eyes

It can also raise blood lipid levels (like cholesterol and triglycerides). Often blood liver test results become abnormal. These side effects often go away when the drug is stopped.

**Arsenic trioxide (ATO)** can act in a way similar to ATRA in patients with APL. It can be given with ATRA in the initial treatment of APL, but it is also helpful in treating APL that comes back after treatment with ATRA plus chemo.

Most side effects of ATO are mild and can include:

- Feeling tired
- Nausea
- Vomiting
- Diarrhea
- Belly pain
- Nerve damage (neuropathy), leading to numbness and tingling in the hands and feet

- Chimeric antigen receptor (CAR) T-cell therapy
- Monoclonal antibodies
- More information about immunotherapy

Immunotherapy is the use of medicines to help a person's own immune system recognize and destroy cancer cells. Many types of immunotherapy are being studied for use against childhood leukemia, and some are now coming into use.

# Chimeric antigen receptor (CAR) T-cell therapy

For this treatment, immune cells called **T cells** are removed from the child'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 child's blood, where they can seek out the leukemia cells and attack them.

## Tisagenlecleucel (Kymriah)

This is a type of CAR T-cell therapy that targets the CD19 protein on certain leukemia cells. It can be used to treat childhood acute lymphoblastic leukemia (ALL) that has come back after treatment or that is no longer responding to treatment.

To make this treatment, T cells are removed from the child's 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 process can take a few weeks.

For the treatment itself, the child typically gets chemotherapy for a few days to help prepare the body. Then the CAR T cells are infused into a vein.

In most children who have had this treatment, the leukemia could no longer be detected within a few months of treatment, although it's not yet clear if this means that they have been cured.

#### **Possible side effects**

This treatment can have serious or even life-threatening side effects, which is why it needs to be given in a medical center that is specially trained 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 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.

## **Monoclonal antibodies**

Antibodies are proteins made by the body's immune system to help fight infections. Man-made versions of these proteins, called **monoclonal antibodies**, 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 known as a **bispecific T-cell** 

**engager (BiTE)**. 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 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 leukemia cells and immune cells together, which helps the immune system attack the leukemia cells.

types of B-cell ALL.

These medicines are described in more detail in Targeted Therapy Drugs for Childhood Leukemia.

Other types of immunotherapy are also being studied for use against leukemia.

# 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><sup>2</sup>.

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

# Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-</u> reactions.html
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

## References

Horton TM, Steuber CP. Overview of the treatment of acute lymphoblastic leukemia in children and adolescents. UpToDate. 2018. Accessed at www.uptodate.com/contents/overview-of-the-treatment-of-acute-lymphoblastic-leukemia-in-children-and-adolescents on December 29, 2018.

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National Cancer Institute. Childhood Acute Myeloid Leukemia/Other Myeloid Malignancies Treatment (PDQ®)–Health Professional Version. Accessed at https://www.cancer.gov/types/leukemia/hp/child-aml-treatment-pdq on December 29, 2018.

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# High-dose Chemotherapy and Stem Cell Transplant for Childhood Leukemia

· More information about stem cell transplant

A stem cell transplant (SCT) (also known as a **bone marrow transplant**) can sometimes be used to help improve the chances of curing childhood leukemia. SCT lets doctors use even higher doses of chemotherapy than a child could normally tolerate.

High-dose chemotherapy destroys the bone marrow, which is where leukemia starts, but it's also where new blood cells are formed. This could lead to life-threatening infections, bleeding, and other problems caused by low blood cell counts. A stem cell transplant is given after the chemo to restore the blood-forming stem cells in the bone marrow.

The blood-forming stem cells used for a transplant can come either from the blood or from the bone marrow. Sometimes stem cells from a baby's umbilical cord blood are used.

## Allogeneic stem cell transplant

For childhood leukemias, the type of transplant used is known as an allogeneic stem cell transplant. In this type of transplant, the blood-forming stem cells are donated from another person.

The donor's tissue type (also known as the **HLA type**) should match the patient's tissue type as closely as possible to help prevent the risk of major problems with the transplant. Tissue type is based on certain substances on the surface of cells in the body. The closer the tissue match between the donor and the recipient, the better the chance the transplanted cells will "take" and begin making new blood cells.

The donor is usually a brother or sister with the same tissue type as the patient. Rarely, it can be an HLA-matched, unrelated donor – a stranger who has volunteered to donate blood-forming stem cells. Sometimes umbilical cord stem cells are used. These stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut. (This blood is rich in stem cells.) Whatever their source, the stem cells are then frozen and stored until they are needed for the transplant.

To learn about how a stem cell transplant is done, see <u>Stem Cell Transplant for</u> <u>Cancer</u><sup>1</sup>.

#### When a stem cell transplant might be used

**Acute lymphocytic leukemia (ALL):** In ALL, SCT might be used in children in some <u>high-risk groups</u><sup>2</sup>, whose leukemia is more likely to come back after the initial (induction) chemo. In this case, the transplant is done after the induction chemo puts the leukemia into remission.

SCT might also be an option if the leukemia doesn't respond well to initial treatment, or if it relapses (comes back) soon after going into remission. It's less clear if SCT should be used for children whose ALL relapses later (such as more than 6 months or a year) after finishing the initial chemo. These children will often do well with another round of standard dose chemo.

SCT may also be recommended for children with some less common forms of ALL, such as those whose leukemias have the Philadelphia chromosome or those with T-cell ALL that don't respond well to initial treatment.

Acute myelogenous leukemia (AML): Because AML relapses more often than ALL, SCT might be recommended right after the AML has gone into remission (after the initial chemo treatment), if the child has a brother or sister with the same tissue type who can donate stem cells for the transplant. This is especially true if there is a very high risk of relapse (as with some subtypes of AML or when there are certain gene or chromosome changes in the leukemia cells). There is still some debate about which children with AML need this type of intensive treatment.

If a child with AML relapses after their first round of standard chemo, most doctors will recommend SCT as soon as the child goes into remission again.

In either case, it is important that the leukemia is in remission before getting a stem cell transplant. Otherwise, the leukemia is more likely to return.

Other leukemias: SCT might also offer the best chance to cure some less common

types of childhood leukemia, such as juvenile myelomonocytic leukemia (JMML)

Children with Philadelphia chromosome-positive ALL may be given a targeted drug such as imatinib (Gleevec) as well. (See below.)

**Intrathecal chemotherapy:** All children also get chemo into the cerebrospinal fluid (CSF) to kill any leukemia cells that might have spread to the brain and spinal cord. This treatment, known as intrathecal chemotherapy, is given through a <u>lumbar puncture</u> (<u>spinal tap</u>)<sup>3</sup>. It is usually given twice (or more if the leukemia is high risk or leukemia cells have been found in the CSF) during the first month and several times during the next 1 or 2 months. It is then repeated less often during the rest of treatment.

Usually, methotrexate is the drug used for intrathecal chemo. Hydrocortisone (a steroid) and cytarabine (ara-C) may be added, particularly in high-risk children.

Along with intrathecal chemo, some high-risk patients (for example, those with T-cell ALL) and those with many leukemia cells in their CSF when the leukemia is diagnosed may be given radiation therapy to the brain. This was more common in the past, but recent studies have found that many children even with high-risk ALL may not need radiation therapy if they are given more intensive chemo. Doctors try to avoid giving radiation to the brain if possible, especially in younger children, because no matter how low the dose is kept, it can cause problems with thinking, growth, and development.

A possible side effect of intrathecal chemo is seizures during treatment, which happen in a small percentage of children. Children who develop seizures are treated with drugs to prevent them.

# **Consolidation (intensification)**

The next, and usually more intense, consolidation phase of chemo starts once the leukemia is in remission and typically lasts for several months. This phase further reduces the number of leukemia cells still in the body. Several chemo drugs are combined to help prevent the remaining leukemia cells from developing resistance. Intrathecal chemo (as described above) is continued at this time.

Children with standard-risk ALL are usually treated with drugs such as methotrexate, 6mercaptopurine (6-MP), vincristine, L-asparaginase, and/or prednisone, but regimens differ among cancer centers.

Children with high-risk leukemia (because of gene or chromosome changes in the leukemia cells, for example, or because there is still minimal residual disease after induction) generally get more intense chemo. Extra chemo drugs such as L-asparaginase, doxorubicin (Adriamycin), etoposide, cyclophosphamide, and cytarabine

(ara-C) are often used, and dexamethasone is substituted for prednisone.

There may be a second round of intense chemotherapy as part of consolidation. (This is known as **delayed intensification**.)

Children with Philadelphia chromosome-positive ALL may also get a targeted drug such as imatinib (Gleevec). (See below.)

For some children with B-cell ALL, the immunotherapy drug blinatumomab (Blincyto) might be part of the consolidation phase as well.

For some children in high-risk groups, a stem cell transplant might be an option at this time once the leukemia is in remission.

## Maintenance

If the leukemia remains in remission after induction and consolidation, maintenance

# **Treatment of recurrent ALL**

If the ALL recurs (comes back) during or after treatment, the child will most likely be treated again with chemotherapy. Much of the treatment strategy depends on how soon the leukemia returns after the first treatment. If the relapse occurs after a long time, the same drugs might still be effective, so the same or similar treatment may be used to try to get the leukemia into a second remission.

If it comes back after a shorter time interval, more aggressive chemo with other drugs may be needed. The most commonly used chemo drugs are vincristine, L-asparaginase, anthracyclines (doxorubicin, daunorubicin, or mitoxantrone), cyclophosphamide, cytarabine (ara-C), and either etoposide or teniposide. The child will also receive a steroid (prednisone or dexamethasone). Intrathecal chemo will also be given.

For children whose leukemia comes back sooner after starting treatment, or for children with T-cell ALL who relapse, a stem cell transplant may be considered, especially if the child has a brother or sister who is a good tissue type match. Stem cell transplants may also be used for children who relapse after a second course of chemotherapy.

Some children have an **extramedullary relapse**, meaning that leukemia cells are found in one part of the body (such as the cerebrospinal fluid [CSF] or the testicles) but are not detectable in the bone marrow. In addition to intensive chemotherapy as described above, children with spread to the CSF may get more intense intrathecal chemotherapy, sometimes with radiation to the brain and spinal cord (if that area had not been already treated with radiation). Boys with relapse in a testicle may get radiation to the area.

If ALL doesn't go away completely or if it comes back after a stem cell transplant, newer types of immunotherapy, such as CAR T-cell therapy or blinatumomab (Blincyto), or the antibody-drug conjugate inotuzumab ozogamicin (Besponsa) might be options.

# Philadelphia chromosome-type ALL

For children with certain types of ALL, such as those with the Philadelphia chromosome, standard chemotherapy for ALL (as outlined above) might not be as effective. A stem cell transplant may be advised if induction treatment puts the leukemia in remission and a suitable stem cell donor is available.

Newer, targeted drugs such as imatinib (Gleevec) and dasatinib (Sprycel) are designed to kill leukemia cells that have the Philadelphia chromosome. These drugs are taken as pills. Adding these drugs to chemotherapy throughout treatment seems to help improve

outcomes, according to studies done so far.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children/detection-diagnosis-</u> staging/prognostic-factors.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
- 3. <u>www.cancer.org/cancer/types/leukemia-in-children/detection-diagnosis-</u> staging/how-diagnosed.html
- 4. <u>www.cancer.org/cancer/types/leukemia-in-children/detection-diagnosis-</u> staging/how-diagnosed.html

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# **Treatment of Children With Acute Myeloid Leukemia (AML)**

Treatment of most children with acute myeloid leukemia (AML) is divided into 2 main phases of chemotherapy:

- Induction
- Consolidation (intensification)

Because of the intensity of treatment and the risk of serious complications, children with AML need to be treated in <u>cancer centers</u><sup>1</sup> or hospitals that have experience with this disease.

#### Induction

The chemo drugs most often used to treat AML are daunorubicin (daunomycin) and cytarabine (ara-C), which are each given for several days in a row. The treatment

schedule may be repeated in 10 days or 2 weeks, depending on how intense doctors

dose of this drug will likely be given during this phase of treatment as well.

Intrathecal chemo (into the CSF) is usually given every 1 to 2 months for as long as intensification continues.

Maintenance chemo is not needed for children with AML (other than those with APL).

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- 1. <u>www.cancer.org/cancer/survivorship/children-with-cancer/finding-</u> treatment/pediatric-cancer-centers.html
- 2. <u>www.cancer.org/cancer/types/leukemia-in-children/detection-diagnosis-</u> staging/prognostic-factors.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
- 4. <u>www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>

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# Treatment of Children with Acute Promyelocytic Leukemia (APL)

Treatment of acute promyelocytic leukemia (APL), a subtype of acute myeloid leukemia (AML), differs from the usual AML treatment. This leukemia usually responds well to treatment, which is given in 3 phases:

Induction

- Consolidation (also called intensification)
- Maintenance

#### Induction

Many children with APL have bleeding and blood-clotting issues when APL is diagnosed, which can cause serious problems during early treatment. Because of this, children with APL must be treated carefully and are often given an anticoagulant ("blood thinner") to help prevent or treat these problems.

Children with APL get a non-chemotherapy drug similar to vitamin A called **all-trans retinoic acid (ATRA)**. ATRA alone can often put APL into remission, but combining it with chemotherapy (usually daunorubicin and cytarabine) gives better long-term results. APL rarely spreads to the brain or spinal cord, so intrathecal chemotherapy is usually not needed.

In adults, ATRA is often combined with **arsenic trioxide (ATO)**, another **non-chemo** drug, instead of chemo, as the initial treatment of APL. The results seem to be at least as good, and without some of the side effects of chemo. The combination of ATRA and ATO is now being studied in children as well.

## **Consolidation (intensification)**

This is usually similar to induction, using both ATRA and chemotherapy (daunorubicin, sometimes along with cytarabine). Because of the success of this treatment, a stem cell transplant is not usually advised as long as the leukemia stays in remission.

ATRA plus ATO is also being studied as an option for consolidation therapy.

#### Maintenance

Children with APL may get maintenance therapy with ATRA (often with the chemo drugs methotrexate and 6-mercaptopurine) for about a year.

#### **Relapsed APL**

If the leukemia comes back after treatment, most often it can be put into a second remission. Arsenic trioxide is a drug that is very effective in this setting. ATRA plus chemo may be another option. A stem cell transplant may be considered once a second

remission is achieved.

#### References

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# Treatment of Children with Juvenile Myelomonocytic Leukemia (JMML)

Juvenile myelomonocytic leukemia (JMML) is fairly rare, so it has been hard to study which treatment might be best. There is no clear single best chemotherapy treatment for this leukemia. A stem cell transplant is the treatment of choice when possible, as it offers the best chance to cure JMML. About half of the children with JMML who get a stem cell transplant are still free of leukemia after several years. Sometimes, even if the leukemia recurs, a second stem cell transplant can be helpful.

Because JMML is hard to treat with current chemo drugs, taking part in a <u>clinical trial</u><sup>1</sup> looking at newer drugs may be a good option for children who can't get aq2gi g 1/GS1/244 gsqr/61 72

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Caywood EH, Kolb EA. Juvenile myelomonocytic leukemia. UpToDate. 2018. Accessed at www.uptodate.com/contents/juvenile-myelomonocytic-leukemia on November 29, 2018.

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# Treatment of Children with Chronic Myeloid Leukemia (CML)

Chronic myeloid (myelogenous) leukemia (CML) is rare in children, but it does occur. Treatment in children is similar to what is used for adults.

Targeted drugs called tyrosine kinase inhibitors (TKIs), such as **imatinib (Gleevec)**, dasatinib (Sprycel), nilotinib (Tasigna), and bosutinib (Bosulif), attack cells with the Philadelphia chromosome, which is the key gene abnormality in CML cells. These drugs are usually very good at controlling CML, often for long periods of time and with less severe side effects than chemotherapy drugs. However, it's not yet clear if these drugs can cure CML when used alone, and they must be taken every day.

Imatinib is usually the drug tried first. If it doesn't work or if it becomes less effective over time, another drug may be tried.

If targeted drugs are no longer helpful, high-dose chemotherapy with a stem cell transplant offers the best chance for a cure. Doctors are now studying whether adding targeted drugs to stem cell transplant regimens can help increase cure rates.

For more information on CML and its treatment, see Chronic Myeloid Leukemia.<sup>1</sup>

# **Hyperlinks**

1. www.cancer.org/cancer/types/chronic-myeloid-leukemia.html

#### References

National Cancer Institute. Childhood Acute Myeloid Leukemia/Other Myeloid Malignancies Treatment (PDQ®)–Health Professional Version. Accessed at https://www.cancer.gov/types/leukemia/hp/child-aml-treatment-pdq on December 29, 2018.

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