Treating Acute Myeloid Leukemia (AML)

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

How is acute myeloid leukemia treated?

The main treatment for most types of AML is chemotherapy, sometimes along with a targeted therapy drug. This might be followed by a stem cell transplant. Other drugs (besides standard chemotherapy drugs) may be used to treat people with acute promyelocytic leukemia (APL). Surgery and radiation therapy are not major treatments for AML, but they may be used in special circumstances.

- Chemotherapy for Acute Myeloid Leukemia (AML)
- Targeted Therapy Drugs for Acute Myeloid Leukemia (AML)
- Non-Chemo Drugs for Acute Promyelocytic Leukemia (APL)
- Surgery for Acute Myeloid Leukemia (AML)
- Radiation Therapy for Acute Myeloid Leukemia (AML)
- Stem Cell Transplant for Acute Myeloid Leukemia (AML)

Common treatment approaches

The typical treatment approach for AML is different from the treatment approach for acute promyelocytic leukemia (APL). The response rates for treatment can vary based on the subtype of AML, as well as other factors. Treatment options might be different if the AML doesn't respond to the initial treatment or if it comes back later on.

The treatment approach for children with AML can be slightly different from that used for adults. It's discussed separately in Treatment of Children With Acute Myeloid Leukemia.
Typical Treatment of Acute Myeloid Leukemia (Except APL)
Treatment of Acute Promyelocytic Leukemia (APL)
Treatment Response Rates for Acute Myeloid Leukemia (AML)
If Acute Myeloid Leukemia (AML) Doesn’t Respond or Comes Back After Treatment

Who treats AML?

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 AML you have
  - The likelihood that treatment will cure you (or help in some other way)
  - Your feelings about the possible side effects from treatment

In most cases AML can progress quickly if not treated, so it's important to start treatment as soon as possible after the diagnosis is made. But it’s also very important to ask questions if there is anything you’re not sure about.

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.
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-of-the-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.

- Clinical Trials

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.

- Complementary and Alternative Medicine

Help getting through cancer treatment

Your 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 are 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 trained specialists.

- **Find Support Programs and Services in Your Area**

## 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 and 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**
- **Palliative or Supportive Care**

*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 him or her questions about your treatment options.*

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## Chemotherapy for Acute Myeloid Leukemia (AML)

Chemotherapy (chemo) is the use of anti-cancer drugs that are injected into a vein, under the skin, or into the cerebrospinal fluid (CSF), or drugs that are taken by mouth to
destroy or control cancer cells. Except when given into the CSF, these drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancers such as leukemia that spread throughout the body.

Chemotherapy is the main treatment for most people with acute myeloid leukemia (AML). Chemo is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemo.

How is chemo given?

Treatment of AML is usually divided into phases:

- **Induction** is the first phase of treatment. It is short and intensive, typically lasting about a week. The goal is to clear the blood of leukemia cells (blasts) and to reduce the number of blasts in the bone marrow to normal.

- **Consolidation** is chemo given after the patient has recovered from induction. It is meant to kill the small number of leukemia cells that are still around but can’t be seen (because there are so few of them). For consolidation, chemo is given in cycles, with each period of treatment followed by a rest period to allow the body time to recover.

A third phase called **maintenance** (or **post-consolidation**) involves giving a low dose of chemo for months or years after consolidation is finished. This is often used to treat **acute promyelocytic leukemia (APL)**, but it is rarely used for other types of AML.

Most chemo drugs used to treat AML are typically given into a vein in the arm (IV). If there are signs that the leukemia has reached the brain or spinal cord (which is not common with AML), chemo might also be given into the CSF (known as **intrathecal chemo**). This can be done with a small catheter that is put in through a small hole in the skull (such as an Ommaya reservoir), or during a lumbar puncture (spinal tap).

The chemo regimens used to treat AML are intensive and can cause serious side effects, so treatment is typically given in the hospital.

Which chemo drugs are used to treat AML?

The chemo drugs used most often to treat AML are a combination of:

- Cytarabine (cytosine arabinoside or ara-C)
• An anthracycline drug, such as daunorubicin (daunomycin) or idarubicin

Other chemo drugs that may be used to treat AML include:

• Cladribine (Leustatin, 2-CdA)
• Fludarabine (Fludara)
• Mitoxantrone
• Etoposide (VP-16)
• 6-thioguanine (6-TG)
• Hydroxyurea
• Corticosteroid drugs, such as prednisone or dexamethasone
• Methotrexate (MTX)
• 6-mercaptopurine (6-MP)
• Azacitidine (Vidaza)
• Decitabine (Dacogen)

For more on how chemo is used to treat AML, see Typical Treatment of Most Types of Acute Myeloid Leukemia (AML), Except APL.

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 how long they are taken. 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 these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask 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.

If your white blood cell counts are very low during treatment, you can help lower your risk of infection by carefully avoiding exposure to germs. During this time, your doctor or nurse may tell you to:

- Wash your hands often.
- Avoid fresh, uncooked fruits and vegetables and other foods that might carry germs.
- Avoid fresh flowers and plants because they may carry mold.
- Make sure other people wash their hands before they come in contact with you.
- Avoid large crowds and people who are sick.

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

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.

**Low platelet counts:** If your platelet counts are low, you may be given drugs or platelet transfusions to help prevent 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 his or her 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 have some specific possible side effects. For example:

- High doses of cytarabine can cause dryness in the eyes and effects on certain parts of the brain, which can lead to problems with coordination or balance. The drug dose may need to be reduced or stopped altogether if these side effects appear.
- Anthracyclines (such as daunorubicin or idarubicin) can damage the heart, so they might not be used in someone who already has heart problems.

Other organs that could be damaged by chemo drugs include the kidneys, liver, testicles, ovaries, and lungs. Doctors and nurses carefully monitor treatment to limit 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 short time. Careful monitoring and adjustment of drug doses are important because some side effects can last a long time.

Tumor lysis syndrome: This side effect of chemo can occur in patients who have large numbers of leukemia cells in the body, mainly during the induction phase of 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. Excess amounts of certain minerals can also affect the heart and nervous system. This can 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.

For more about chemo and its side effects, see Chemotherapy.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy/chemotherapy-side-effects.html
2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html
References


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Targeted Therapy Drugs for Acute Myeloid Leukemia (AML)
In recent years, drugs that target specific parts of cancer cells have been developed. Targeted drugs work differently from standard chemotherapy (chemo) drugs and tend to have different side effects. They can sometimes be helpful even when chemo isn’t, or they can be used along with chemo to help it work better.

Some of these drugs can be useful in treating certain people with acute myeloid leukemia (AML).

**FLT3 inhibitors**

In some people with AML, the leukemia cells have a mutation in the \( \text{FLT3} \) gene. This gene helps the cells make a protein (also called FLT3) that helps the cells grow. Drugs that target the FLT3 protein can help treat some of these leukemias.

**Midostaurin (Rydapt)** is a drug that works by blocking FLT3 and several other proteins on cancer cells that can help the cells grow. This drug can be used along with certain chemotherapy drugs to treat newly diagnosed adults whose leukemia cells have a \( \text{FLT3} \) gene mutation. Your doctor can test your blood to see if you have this mutation.

Midostaurin is taken by mouth twice a day.

Common side effects can include low levels of white blood cells (with increased risk of infection), fever, nausea, vomiting, redness or sores in the mouth, headache, muscle or bone pain, bruising, nosebleeds, high blood sugar levels, and upper respiratory infections.

Less often, this drug can cause serious lung problems, which might show up as a cough, chest pain, or shortness of breath. Tell someone on your cancer care team right away if you have any of these symptoms.

**Gilteritinib (Xospata)** is another drug that works by blocking FLT3 and other proteins on cancer cells that can help the cells grow. This drug can treat adults whose leukemia cells have a \( \text{FLT3} \) gene mutation and whose AML has not gotten better on previous treatments or has recurred (come back). Your doctor can test your blood to see if you have this mutation.

Gilteritinib is taken by mouth once a day.

Common side effects can include fever, shortness of breath, diarrhea, swelling, redness or sores in the mouth, muscle or bone pain, fatigue, abnormal liver tests, and pneumonia (lung infection).
Less often, this drug may cause serious heart problems, which might show up as an abnormal electrocardiogram (ECG), or neurological problems which may show up as seizures or confusion. Tell someone on your cancer care team right away if you have any of these symptoms.

**IDH inhibitors**

In some people with AML, the leukemia cells have a mutation in the *IDH1* or *IDH2* gene. These genes help the cells make certain proteins, which are also called IDH1 and IDH2. Mutations in one of these genes can stop blood cells from maturing the way they normally would.

Targeted drugs called *IDH inhibitors* can block these IDH proteins. These drugs seem to work by helping the leukemia cells mature (differentiate) into more normal cells. Because of this, they are sometimes referred to as differentiation agents.

These drugs can be used to treat AML with an *IDH1* or *IDH2* mutation. Your doctor can test your blood or bone marrow to see if your leukemia cells have one of these mutations.

- **Ivosidenib (Tibsovo)** is an IDH1 inhibitor. It can be used to treat AML with an *IDH1* mutation that comes back after treatment or is no longer responding to other treatments.
- **Enasidenib (Idhifa)** is an IDH2 inhibitor. It can be used to treat AML with an *IDH2* mutation that comes back after treatment or is no longer responding to other treatments.

These drugs are taken by mouth, once a day.

Common side effects can include nausea, vomiting, diarrhea, fatigue, joint pain, shortness of breath, increased levels of bilirubin (a substance found in bile), and loss of appetite.

An important possible side effect of these drugs is known as **differentiation syndrome**. This occurs when the leukemia cells release certain chemicals into the blood. It most often occurs during the first treatment cycle. Symptoms can include fever, breathing problems from fluid buildup in the lungs and around the heart, low blood pressure, liver or kidney damage, and severe fluid buildup elsewhere in the body. It can often be treated by stopping the drugs for a while and giving a steroid such as dexamethasone.
Gemtuzumab ozogamicin (Mylotarg)

This targeted therapy consists of a monoclonal antibody (a man-made immune protein) linked to a chemotherapy drug. The antibody attaches to a protein called CD33, which is found on most AML cells. The antibody acts like a homing signal, bringing the chemotherapy drug to the leukemia cells, where it enters the cells and kills them when they try to divide into new cells.

This drug can be used along with chemotherapy as part of the initial treatment of AML that has the CD33 protein. It can also be used by itself, either as the first treatment (especially in people who might not be healthy enough for intense chemo), or if other treatments are no longer working. It is given as an infusion into a vein (IV).

The most common side effects are fever, nausea and vomiting, low levels of blood cells (with increased risks of infection, bleeding, and fatigue), swelling and sores in the mouth, constipation, rash, and headaches.

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

Venetoclax (Venclexta)

Venetoclax targets BCL-2, a protein in cancer cells that helps them live longer than they should. This drug can be used with chemotherapy in people with newly diagnosed AML who are 75 years or older and are not healthy enough to tolerate strong chemotherapy. It’s taken by mouth once a day.

Side effects can include low levels of certain white blood cells (neutropenia), low red blood cell counts (anemia), diarrhea, nausea, bleeding, low platelet counts (thrombocytopenia), and feeling tired. Less common but more serious side effects can include pneumonia and other serious infections.
Tumor lysis syndrome (TLS) is another possible side effect of this drug. It's more common in patients who have large numbers of leukemia cells in their body when treatment starts. When the leukemia cells are killed, they break open and release their contents into the bloodstream. This can overwhelm the kidneys to the point that they get rid of all of these substances quickly. This can lead to the build-up of too many minerals in the blood and even kidney failure. The excess minerals can also cause problems with the heart and nervous system. To help keep this from happening, you may start at a very low dose and then slowly increase it over time. Sometimes, other medicines may be given to help drop your white blood cell count below a certain level before starting this drug. Your treatment team will do blood tests and also watch for signs of TLS.

Hedgehog pathway inhibitor

AML cells can have mutations (changes) in genes that are part of a cell signaling pathway called hedgehog. The hedgehog pathway is crucial for the development of the embryo and fetus and is important in some adult cells, but it can be overactive in leukemia cells.

Glasdegib (Daurismo) is a drug that targets a protein in this pathway. It can be used with chemotherapy in people with newly diagnosed AML who are 75 years or older and are not healthy enough to tolerate strong chemotherapy. In this group, it has been shown to help people live longer.

This drug is taken by mouth once a day.

Side effects can include muscle and bone pain, fatigue, low white blood cell counts (neutropenia), low red blood cell counts (anemia), bleeding, nausea, low platelet counts (thrombocytopenia), and redness or sores in the mouth.

Because the hedgehog pathway affects fetal development, these drugs should not be taken by women who are pregnant or could become pregnant. It is not known if they could harm the fetus if taken by a male partner. Anyone taking these drugs should use reliable birth control during and for some time after treatment.

To learn more about targeted therapy drugs as a treatment for cancer, see Targeted Cancer Therapy¹.

Hyperlinks

Non-Chemo Drugs for Acute Promyelocytic Leukemia (APL)

Chemotherapy is the main treatment for most types of acute myeloid leukemia (AML). But acute promyelocytic leukemia (APL) is different from other types of AML in some important ways.

The leukemia cells in APL (called blasts) aren’t able to mature into normal white blood cells, and they can grow and divide very quickly. These cells contain proteins that when released into the bloodstream can cause out-of-control blood clotting. This can lead to problems not only with blood clots, but also with severe bleeding. In the past, when regular chemotherapy (chemo) drugs were used alone to kill these cells, these proteins were released into the bloodstream. Patients sometimes died from clotting or bleeding complications.

Researchers have found that the leukemia cells in APL have a specific gene change that makes them sensitive to certain drugs that aren’t like regular chemo drugs. These drugs help the blasts mature into normal white blood cells. This process is known as differentiation, and these drugs are called differentiation agents. Since the blasts don’t die, they don’t release the harmful proteins into the blood, which helps keep the clotting process from getting out of control. But these drugs can also have side effects of their own.
Two of these drugs can be used to treat APL:

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

For more on how these drugs are used for APL, see Treatment of Acute Promyelocytic Leukemia (APL).

**ATRA**

ATRA is a form of vitamin A that is typically part of the initial (induction) treatment of APL. It is given either along with chemo, or along with arsenic trioxide for the initial treatment of APL. It is also often used for some time after as part of the consolidation phase of treatment to help keep the leukemia from coming back. For this phase of treatment, it may be used with chemo or with arsenic trioxide (or possibly with both). For longer-term maintenance, ATRA might be used by itself or with chemo.

ATRA can have side effects similar to those seen if you take too much vitamin A. Symptoms can include headache, fever, dry skin and mouth, skin rash, swollen feet, sores in the mouth or throat, itching, and irritated eyes. It can also cause blood lipid levels (like cholesterol and triglycerides) to go up. Often blood liver test results become abnormal. These side effects often go away when the drug is stopped.

**Arsenic trioxide (ATO)**

Arsenic trioxide (ATO) is a form of arsenic, which can be a poison if given in high doses. But doctors found that it can act in a way similar to ATRA in patients with APL. It can be given with ATRA in the induction and consolidation phases of treatment, but it is also helpful in treating patients whose APL comes back after treatment with ATRA plus chemo. In these patients, ATO might be given along with the targeted drug gemtuzumab ozogamicin (Mylotarg).

Most side effects of ATO are mild and can include fatigue (tiredness), nausea, vomiting, diarrhea, abdominal (belly) pain, and nerve damage (called neuropathy) leading to numbness and tingling in the hands and feet. ATO can also cause problems with heart rhythm, which can be serious. Your doctor may check your heart rhythm with an EKG often (even daily) while you are getting this drug.

**Differentiation syndrome**

The most important side effect of either of these drugs is known as differentiation
syndrome (previously called retinoic acid syndrome). This occurs when the leukemia cells release certain chemicals into the blood. It is most often seen during the first couple of weeks of treatment, and in patients with a high white blood cell count.

Symptoms can include fever, breathing problems due to fluid buildup in the lungs and around the heart, low blood pressure, kidney damage, and severe fluid buildup elsewhere in the body. While differentiation syndrome can be serious, it can often be treated by stopping the drugs for a while and giving a steroid such as dexamethasone.

References


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Surgery for Acute Myeloid Leukemia (AML)

Surgery has a very limited role in the treatment of acute myeloid leukemia (AML). Because leukemia cells are spread widely throughout the bone marrow and blood, it’s not possible to cure this type of cancer with surgery. Surgery rarely has any role even in the diagnosis of AML, since this can usually be done with a bone marrow aspirate and biopsy. On rare occasions, an isolated tumor of leukemia cells (known as a myeloid sarcoma, granulocytic sarcoma, or chloroma) may be treated with surgery.
Placement of a central venous catheter

Often before chemotherapy starts, a minor type of surgery is done to place a small flexible tube, called a central venous catheter (CVC)\(^2\) (also known as a central line or venous access device), into a large vein in the chest. This may be done by a surgeon in the operating room, or by a special type of radiologist. The end of the tube stays just under the skin or sticks out in the chest area or upper arm. The CVC can be left in place during treatment (often for several months) to give intravenous (IV) drugs, such as chemotherapy, and to take blood samples for tests. This lowers the number of needle sticks needed during treatment. If you have a CVC, it is very important to learn how to care for it to keep it from getting infected.

Hyperlinks


References


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Radiation Therapy for Acute Myeloid Leukemia (AML)
Radiation therapy uses high-energy radiation to kill cancer cells. It is usually not part of the main treatment for people with acute myeloid leukemia (AML), but there are a few instances in which it may be used:

- Radiation is sometimes used to treat leukemia that has spread outside of the bone marrow and blood, such as to the brain and spinal fluid, or to the testicles.
- Radiation to the whole body is often an important part of treatment before a stem cell transplant. See Stem Cell Transplant for Acute Myeloid Leukemia (AML).
- It is used (rarely) to help shrink a tumor (myeloid sarcoma) if it is pressing on the trachea (windpipe) and causing breathing problems. But chemotherapy is often used instead, as it often works more quickly.
- Radiation can be used to reduce pain in an area of bone that is invaded by leukemia, if chemotherapy hasn’t helped.

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 imaging tests such as CT or MRI scans.

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

The possible sideeffects of radiation therapy depend on where the radiation is aimed. Sunburn-like skin changes and hair loss in the treated area are possible. Radiation to the head and neck area can lead to mouth sores and trouble swallowing. Radiation to the abdomen can cause nausea, vomiting, or diarrhea. Radiation can lower blood counts, leading to fatigue (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).

To learn more, see Radiation Therapy².

Hyperlinks

1. /content/cancer/en/treatment/treatments-and-side-effects/treatment-types/radiation/radiation-therapy-guide/common-side-effects.html
Stem Cell Transplant for Acute Myeloid Leukemia (AML)

The doses of chemotherapy drugs that doctors can give to treat acute myeloid leukemia (AML) are limited by the serious side effects they can cause. Even though higher doses of these drugs might kill more cancer cells, 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 caused by low blood cell counts.

Doctors can sometimes use a stem cell transplant (SCT), also called a bone marrow transplant, to give higher doses of chemotherapy than could normally be given. (Sometimes radiation therapy is given as well.) After the treatment is finished, the patient gets an infusion of blood-forming stem cells to restore their bone marrow.

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

Types of SCT used for AML

Stem cell transplants differ based on whom the blood-forming stem cells come from.
Allogeneic stem cell transplant

This is the most common type of SCT used to treat AML. In an allogeneic SCT, the stem cells come from someone other than the patient – usually a donor whose tissue type (also known as the HLA type) closely matches the patient’s. Tissue type is based on certain substances on the surface of cells in the body. Differences in HLA types between the stem cell donor and recipient can cause the body’s immune system to react against the cells. Therefore, the closer a tissue “match” is between the donor and the recipient, the better the chance the transplanted cells will “take” and begin making new blood cells.

The best donor is often a close relative, such as a brother or sister, if they are a good match. If no close relatives match, stem cells might be available from a matched unrelated donor (MUD), an unrelated volunteer whose tissue type matches that of the patient. But the use of stem cells from a MUD is linked to more complications. 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.

For most patients with AML, especially those at higher risk of having the leukemia return after treatment, using an allogeneic SCT is preferred over an autologous SCT (see below). Leukemia is a disease of the blood and bone marrow, so giving the patient his or her own cells back after treatment may mean giving them back some leukemia cells as well. Donor cells are also helpful 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 autologous stem cell transplants.

Allogeneic transplants can have serious risks and side effects, so patients typically need to be younger and relatively healthy to be good candidates. Another challenge is that it can sometimes be difficult to find a matched donor.

One of the most serious complications of allogeneic SCTs is known as graft-versus-host disease (GVHD). It happens when the patient’s immune system is taken over by that of the donor. When this happens, the donor immune system may see the patient’s own body tissues as foreign and attack them.

Symptoms can include severe skin rashes, itching, mouth sores (which can affect eating), nausea, and severe diarrhea. Liver damage can cause yellowing of the skin and eyes (jaundice). The lungs can also be damaged. The patient may also become easily fatigued and develop muscle aches. Sometimes GVHD can become disabling, and if it’s severe enough, it can be life-threatening. Drugs that affect the immune system may be
given to try to control it.

**Non-myeloablative transplant (mini-transplant):** Many older people can’t tolerate a standard allogeneic transplant that uses high doses of chemo. Some may still be able to get a non-myeloablative transplant (also known as a mini-transplant or reduced-intensity transplant), where they get lower doses of chemo and radiation that don't completely destroy the cells in their bone marrow. They then get the allogeneic (donor) stem cells. These cells enter the body and establish a new immune system, which sees the leukemia cells as foreign and attacks them (a graft-versus-leukemia effect).

A non-myeloablative transplant can still sometimes work with much less toxicity. In fact, a patient can get the transplant as an outpatient. The major complication is graft-versus-host disease.

Many doctors still consider this an experimental procedure for AML, and it is being studied to determine how useful it may be.

**Autologous stem cell transplant**

In an autologous transplant, a patient’s own stem cells are removed from his or her bone marrow or blood. They are frozen and stored while the person gets treatment (high-dose chemotherapy and/or radiation). In the lab, a process called purging may be used 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.

Autologous transplants are sometimes used for people with AML who are in remission after initial treatment and who don’t have a matched donor for an allogeneic transplant. Some doctors feel that it is better than standard “consolidation” chemotherapy (see Typical Treatment of Acute Myeloid Leukemia (AML)) for these people, but not all doctors agree with this.

Autologous transplants are generally easier for patients to tolerate than allogeneic transplants, because they are getting their own cells back, which lowers the risk of some complications. But the high-dose chemo can still cause major side effects. This type of transplant can be done in any otherwise healthy person, although patients who are very old or have other health problems might not be suitable.

One problem with autologous transplants is that it's hard to separate normal stem cells from leukemia cells in the bone marrow or blood samples. Even after purging (treating the stem cells in the lab to try to kill or remove any remaining leukemia cells), there is the risk of returning some leukemia cells with the stem cell transplant.
To learn more about the details of stem cell transplants, including how they're done and the possible risks and side effects, see Stem Cell Transplant for Cancer³.

**Hyperlinks**


**References**


**Typical Treatment of Acute Myeloid Leukemia (Except APL)**

Treatment of most patients with acute myeloid leukemia (AML) is typically divided into 2 chemotherapy (chemo) phases:

- **Remission induction** (often just called induction)
- **Consolidation** (post-remission therapy)
The acute promyelocytic leukemia (APL) subtype of AML is treated differently.

Treatment for AML usually needs to start as quickly as possible after it is diagnosed because it can progress very quickly. Sometimes another type of treatment needs to be started even before the chemo has had a chance to work.

**Treating leukostasis**

Some people with AML have very high numbers of leukemia cells in their blood when they are first diagnosed, which can cause problems with normal blood circulation. This is called leukostasis. Chemo can take a few days to lower the number of leukemia cells in the blood. In the meantime, leukapheresis (sometimes just called pheresis) might be used before chemo.

In leukapheresis, the patient’s blood is passed through a special machine that removes white blood cells (including leukemia cells) and returns the rest of the blood to the patient. Two intravenous (IV) lines are required – the blood is removed through one IV, goes through the machine, and then is returned to the patient through the other IV. Sometimes, a single large catheter is placed in a vein in the neck or under the collar bone for the pheresis, instead of using IV lines in both arms. This type of catheter is called a central venous catheter (CVC) or central line and has both IVs built in.

This treatment lowers blood counts right away. The effect is only for a short time, but it may help until the chemo has a chance to work.

**Induction**

This first phase of treatment is aimed at quickly getting rid of as many leukemia cells as possible. How intense the treatment is can depend on a person’s age and health. Doctors often give the most intensive chemo to people under the age of 60, but some older patients in good health may benefit from similar or slightly less intensive treatment.

People who are much older or are in poor health might not do well with intensive chemo. Treatment for these patients is discussed below.

Age, health, and other factors clearly need to be taken into account when considering treatment options. For example, people whose leukemia cells have certain gene or chromosome changes are more likely to benefit from certain types of treatment.

In younger patients, such as those under 60, induction often involves treatment with 2...
chemo drugs:

- Cytarabine (ara-C)
- An anthracycline drug such as daunorubicin (daunomycin) or idarubicin

This is sometimes called a **7 + 3 regimen**, because it consists of getting cytarabine continuously for 7 days, along with short infusions of an anthracycline on each of the first 3 days.

In some situations, a third drug might be added as well to try to improve the chances of remission:

- For patients whose leukemia cells have an *FLT3* gene mutation, the targeted therapy drug *midostaurin (Rydapt)* might be given along with chemo. This drug is taken twice daily as a pill.
- For patients whose leukemia cells have the CD33 protein, the targeted drug *gemtuzumab ozogamicin (Mylotarg)* might be added to chemo.
- Adding the chemo drug *cladribine* might be another option for some people.

Patients with poor heart function might not be able to be treated with anthracyclines, so they may be treated with another chemo drug, such as fludarabine (Fludara) or etoposide.

In rare cases where the leukemia has spread to the brain or spinal cord, chemo may also be given into the cerebrospinal fluid (CSF). Radiation therapy might be used as well.

Patients typically need to stay in the hospital during induction (and possibly for some time afterward). Induction destroys most of the normal bone marrow cells as well as the leukemia cells, so most patients develop dangerously low blood counts, and may be very ill. Most patients need antibiotics and blood product transfusions. Drugs to raise white blood cell counts (called growth factors) may also be used. Blood counts tend to stay low for a few weeks.

About a week after chemo is done, the doctor will do a **bone marrow biopsy**. It should show few bone marrow cells (hypocellular bone marrow) and only a small portion of blasts (making up no more than 5% of the bone marrow) for the leukemia to be considered in remission. Most people with leukemia go into remission after the first round of chemo. But if the biopsy shows that there are still leukemia cells in the bone marrow, another round of chemo may be given, either with the same drugs or with
another regimen. Sometimes a stem cell transplant is recommended at this point. If it isn’t clear on the bone marrow biopsy whether the leukemia is still there, another bone marrow biopsy may be done again in about a week.

Over the next few weeks, normal bone marrow cells will return and start making new blood cells. The doctor may do other bone marrow biopsies during this time. When the blood cell counts recover, the doctor will again check cells in a bone marrow sample to see if the leukemia is in remission.

Remission induction usually does not destroy all the leukemia cells, and a small number often remain. Without post-remission therapy (consolidation), the leukemia is likely to return within several months.

Consolidation (post-remission therapy)

Induction is considered successful if remission is achieved. Further treatment (called consolidation) is then given to try to destroy any remaining leukemia cells and help prevent a relapse.

Consolidation for younger patients

For younger patients (typically those under 60), the main options for consolidation therapy are:

- Several cycles of chemo with high-dose cytarabine (ara-C) (sometimes known as HiDAC)
- Allogeneic (donor) stem cell transplant
- Autologous stem cell transplant

The best option for each person depends on the risk of the leukemia coming back after treatment, as well as other factors.

For HiDAC, cytarabine is given at very high doses, typically over 5 days. This is repeated about every 4 weeks, usually for a total of 3 or 4 cycles. For people who got the targeted drug midostaurin (Rydapt) during induction, this is typically continued during consolidation. Again, each round of treatment is typically given in the hospital because of the risk of serious side effects.

For patients who got chemo plus the targeted drug gemtuzumab ozogamicin (Mylotarg) for their induction therapy, a similar regimen might be used for consolidation.
Another approach after induction therapy is to give very high doses of chemo followed by either an allogeneic (from a donor) or autologous (patient’s own) stem cell transplant. Stem cell transplants have been found to reduce the risk of leukemia coming back more than standard chemo, but they are also more likely to have serious complications, including an increased risk of death from treatment.

Consolidation for patients who are older or have other health problems

Older patients or those in poor health may not be able to tolerate intensive consolidation treatment. Often, giving them more intensive therapy raises the risk of serious side effects (including treatment-related death) without providing much more of a benefit. These patients may be treated with:

- Higher-dose cytarabine (usually not quite as high as in younger patients)
- Standard-dose cytarabine, possibly along with idarubicin, daunorubicin, or mitoxantrone (For people who got the targeted drug midostaurin (Rydapt) during induction, this is typically continued during consolidation as well.)
- Non-myeloablative stem cell transplant (mini-transplant)

Factors affecting choice of consolidation treatment

It’s not always clear which treatment option is best for consolidation. Each has pros and cons. Doctors look at several factors when recommending what type of therapy a patient should get. These include:

- **How many courses (cycles) of chemo it took to bring about a remission.** If it took more than one, some doctors recommend that the patient get a more intensive program, which might include a stem cell transplant.
- **The availability of a brother, sister, or an unrelated donor who matches the patient’s tissue type.** If a close enough tissue match is found, an allogeneic (donor) stem cell transplant may be an option, especially for younger patients.
- **The possibility of collecting leukemia-free bone marrow cells from the patient.** If lab tests show that a patient is in remission, collecting stem cells from the patient’s bone marrow or blood for an autologous stem cell transplant may be an option. Stem cells collected from the patient would be purged (treated in the lab to try to remove or kill any remaining leukemia cells) to lower the chances of relapse.
- **The presence of one or more adverse prognostic factors**, such as certain gene
or chromosome changes, a very high initial white blood cell count, AML that develops from a previous blood disorder or after treatment for an earlier cancer, or spread of AML to the central nervous system. These factors might lead doctors to recommend more aggressive therapy, such as a stem cell transplant. On the other hand, for people with good prognostic factors, such as favorable gene or chromosome changes, many doctors might advise holding off on a stem cell transplant unless the disease recurs.

- **The patient’s age and overall health.** Older patients or those with other health problems might not be able to tolerate some of the severe side effects that can occur with high-dose chemo or stem cell transplants.

- **The patient’s wishes.** There are many issues relating to quality of life that need to be considered. An important issue is the higher chance of death from high-dose chemo or a stem cell transplant. This and other issues must be discussed between the patient and the doctor.

Stem cell transplants are intensive treatments with real risks of serious complications, including death, and their exact role in treating AML is not always clear. Some doctors feel that if the patient is healthy enough to withstand an allogeneic transplant and a compatible donor is available, this option offers the best chance for long-term survival. Others feel that studies have not yet shown this conclusively, and that in some cases a transplant should be reserved in case the leukemia comes back after standard treatment. Still others feel that stem cell transplants should be given if the leukemia is likely to come back based on certain gene or chromosome changes. Research in this area continues to study which AML patients get the most benefit from stem cell transplant and which type of transplant is best in each situation.

**Treating frail, older adults**

Treatment of AML in people under 60 is fairly standard. It involves cycles of intensive chemo, sometimes along with a stem cell transplant (as discussed above). Many patients older than 60 are healthy enough to be treated in the same way, although sometimes the chemo may be less intense.

People who are much older or are in poor health may not be able to tolerate this intense treatment. In fact, intense chemo could actually shorten their lives. Treatment of these patients is often not divided into induction and consolidation phases, but it may be given every so often as long as it seems helpful.

In some cases, doctors may recommend low-intensity chemo with a low dose of
cytarabine given in cycles. Sometimes, these patients may be treated with other chemo
drugs like azacitidine (Vidaza) or decitabine (Dacogen). These drugs aren’t approved to
treat AML, but still may be helpful. In some cases, this may induce remission. In others,
it may control the leukemia for a time. These chemo drugs can also be given along with
the targeted agents venetoclax (Venclexta) or glasdegib (Daurismo). Another option
might be the targeted drug gemtuzumab ozogamicin (Mylotarg) without chemotherapy.

Some people might decide against chemo and other drugs and instead choose
supportive care. This focuses on treating any symptoms or complications that arise and
keeping the person as comfortable as possible.

Hyperlinks


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Treatment of Acute Promyelocytic Leukemia (APL)

Prompt diagnosis and treatment of acute promyelocytic leukemia (APL), the M3 subtype of acute myeloid leukemia (AML), is very important because patients with APL can quickly develop life-threatening blood-clotting or bleeding problems if not treated. In fact, treatment might need to be started even if the diagnosis of APL is suspected but hasn’t been confirmed yet by lab tests.

The treatment of APL typically differs from the treatment of most other types of AML. The most important drugs for treating APL are non-chemo drugs called differentiating agents, like all-trans-retinoic acid (ATRA). Other treatments might include chemotherapy (chemo) and transfusions of platelets or other blood products¹.

Treatment is typically divided into 3 phases:

- Induction (remission induction)
- Consolidation (post-remission therapy)
- Maintenance

Induction

The goal of induction, the first part of treatment, is to get the number of leukemia cells to very low levels, putting the APL into remission. The most important drug in the initial
treatment of APL is **all-trans-retinoic acid (ATRA)**. This is usually combined with one of these:

- **Arsenic trioxide (ATO)**, another non-chemo drug. For some people at higher risk of APL coming back after treatment, the targeted drug **gemtuzumab ozogamicin (Mylotarg)** might be added as well.
- **Chemotherapy** with an anthracycline drug (daunorubicin or idarubicin). For some people at high risk of their APL coming back after treatment, the chemo drug cytarabine (ara-c) might be added as well.
- **Chemotherapy** (an anthracycline) plus ATO

ATRA plus ATO is often the preferred treatment in people at lower risk of the leukemia coming back, as it tends to have fewer side effects. Chemo or Mylotarg is more likely to be included in treatment if this risk is higher.

A **bone marrow biopsy** is usually done about a month after starting treatment, to see if the leukemia is in remission. Induction is typically continued until the APL is in remission, which might take up to 2 months.

### Consolidation (post-remission therapy)

Once APL is in remission, consolidation is needed to keep it in remission and try to get rid of the remaining leukemia cells. Which drugs are used depends on what was given for induction, as well as other factors. Patients typically get some of the same drugs they got during remission, although the doses and timing of treatment might be different. Some of the options include:

- ATRA plus ATO (If Mylotarg was part of induction, it might be continued here as well.)
- ATRA plus chemo (typically with an anthracycline such as idarubicin or daunorubicin)
- ATO plus chemo (typically with an anthracycline such as idarubicin or daunorubicin)
- Chemo alone (typically with an anthracycline plus cytarabine)

Consolidation typically lasts for at least several months, depending on the drugs being used.

### Maintenance
For some patients, especially those at higher risk of the APL coming back, consolidation may be followed by maintenance therapy, which uses lower doses of drugs over a longer period of time. People who have a lower risk of the leukemia coming back and who have a good response to ATRA plus ATO might not need maintenance therapy, although this is still being studied.

The most common options for maintenance therapy are ATRA alone, or ATRA along with chemo (6-mercaptopurine (6-MP) and/or methotrexate). Maintenance therapy is typically given for about a year.

**Treating APL that doesn't go away or comes back**

Treatment for APL that doesn't go away or that comes back after initial treatment is discussed in If Acute Myeloid Leukemia (AML) Doesn't Respond or Comes Back After Treatment.

**Hyperlinks**


**References**


National Comprehensive Cancer Network. NCCN Practice Guidelines in Oncology:
Treatment Response Rates for Acute Myeloid Leukemia (AML)

The goal of treatment for acute myeloid leukemia (AML) is to put the leukemia into complete remission (the bone marrow and blood cell counts return to normal), preferably a complete molecular remission (no signs of leukemia in the bone marrow, even using sensitive lab tests), and to keep it that way.

For most types of AML

About 2 out of 3 people with AML who get standard induction chemotherapy (chemo) go into remission. This usually means the bone marrow contains fewer than 5% blast cells, the blood cell counts return to within normal limits, and there are no signs or symptoms of the disease. The actual chance of remission depends to a large part on a person’s specific prognostic factors, such as their age and the presence of certain gene or chromosome changes in the leukemia cells.

For example, older people generally don’t do as well as those younger than 60. They often have trouble tolerating intensive treatment and often have chromosome changes in leukemia cells that are linked to a poorer outlook. About half of these patients go into remission after initial treatment.

If remission is achieved, patients typically get more chemo (consolidation) to try to get rid of any remaining leukemia cells. Up to half of patients who get consolidation go into long-term remission (and may be cured). But this number is also affected by prognostic factors, such as a person’s age and whether the leukemia cells have certain gene or chromosome changes. Using an allogeneic stem cell transplant as consolidation has a higher success rate, but it also has a higher risk of death as a complication.

For acute promyelocytic leukemia (APL)
The outlook for people with acute promyelocytic leukemia (APL) tends to be better than for those with other types of AML, although again prognostic factors can be important. About 9 out of 10 people with APL will go into remission with standard induction treatment. With consolidation and maintenance, about 8 or 9 out of 10 people with APL stay in long-term remission.

Hyperlinks


References


If Acute Myeloid Leukemia (AML) Doesn’t Respond or Comes Back After Treatment

Most often, acute myeloid leukemia (AML) will go into remission after the initial treatment. But sometimes it doesn't go away completely, or it comes back (relapses) after a period of remission. If this happens, other treatments can be tried, as long as a person is healthy enough for them.

Treatment for most types of AML

If AML doesn’t go away completely with induction treatment, sometimes a second, similar course of chemotherapy (chemo), often called reinduction, can be tried. If this isn't helpful, treatment with other chemo drugs or more intensive doses of chemo may be tried, if the person can tolerate them. A stem cell transplant may be an option for some people, as it can allow higher doses of chemo to be used. Clinical trials\(^1\) of new treatment approaches may also be an option.

If the leukemia went away and has now come back, the treatment options depend on the patient’s age and health, and on how long the leukemia was in remission. AML most often recurs in the bone marrow and blood. The brain or cerebrospinal fluid (CSF) is rarely the first place where it recurs, but if this happens, it is often treated with chemo given directly into the CSF.

If remission lasted at least a year, it's sometimes possible to put the leukemia into remission again with more chemo, although this is not likely to be long-lasting. For younger patients (generally those younger than 60), most doctors would then advise a stem cell transplant if a suitable donor can be found. Clinical trials of new treatment approaches might also be an option.

If AML comes back sooner than 12 months, most doctors will advise a stem cell transplant for younger patients, if possible. Taking part in a clinical trial is another option.
Another option for AML that doesn’t go away or comes back after treatment might be the targeted drug gemtuzumab ozogamicin (Mylotarg).

If the leukemia keeps coming back or doesn’t go away, further chemo treatment will probably not be very 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.

**For AML with a FLT3 gene mutation**

If the leukemia cells have the FLT3 gene mutation and the leukemia doesn’t go away or if it comes back later, one option might be treatment with the targeted drug gilteritinib (Xospata), a FLT3 inhibitor.

**For AML with an IDH1 or IDH2 gene mutation**

If the leukemia cells have an IDH1 or IDH2 gene mutation, one option if the leukemia doesn’t go away or if it comes back later might be treatment with a targeted drug called an IDH inhibitor, such as ivosidenib (Tibsovo) for AML with an IDH1 mutation, or enasidenib (Idhifa) for AML with an IDH2 mutation. Other options might include chemo or a stem cell transplant.

**Treatment for acute promyelocytic leukemia (APL)**

Treatment options for APL that doesn’t go away with initial treatment or that relapses depend on which treatments were used before, as well as other factors.

For patients whose initial treatment was with the non-chemo drugs all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) and who relapse early (usually within about 6 months), treatment will most likely be with some of the same chemo drugs used to treat other types of AML. If the remission lasts longer, ATO might be used again, possibly along with other treatments such as ATRA, chemo, and the targeted drug Mylotarg.

If the initial treatment was ATRA plus chemo, ATO is often very effective.

At some point, a stem cell transplant might be a good option if a person is healthy enough. Another option might be taking part in a clinical trial.

**Supportive treatment for leukemia that won’t go away**

If further treatment or a clinical trial is not an option, the focus of treatment may shift to
controlling symptoms caused by the leukemia, rather than trying to cure it. This is called palliative treatment⁴ or supportive care. For example, the doctor may advise less intensive chemo to try to keep the leukemia under control 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 therapy and appropriate pain-relieving medicines⁴. If medicines such as aspirin and ibuprofen don’t help with the pain, stronger opioid medicines such as morphine are likely to be helpful. Some people may worry about taking stronger drugs for fear of being sleepy all the time or becoming addicted to them. But many people get very effective pain relief from these medicines without serious side effects.

Other common symptoms from leukemia are low blood counts and fatigue. Medicines or blood transfusions⁵ may be needed to help correct these problems. Nausea and loss of appetite can be treated with medicines and high-calorie food supplements. Infections that occur may be treated with antibiotics.

It’s very important to let your cancer care team know if you are having pain or any other symptoms so that they can be treated.

Hyperlinks


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