

TREATMENT UPDATE:

Acute Myeloid Leukemia (AML)

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Treatment Update: Acute Myeloid Leukemia (AML)

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Each year in the United States, over 20,000 people are diagnosed with acute myeloid leukemia (AML), a cancer of the blood and bone marrow.

Bone marrow is the spongy tissue inside bones where blood cells are made. It produces “blast” cells that normally mature into fully functional cells and are released into the bloodstream, along with other mature blood cells. These include white blood cells that fight infection, red blood cells that carry oxygen and platelets that help with blood clotting. In cases of AML, these blast cells do not mature and their numbers increase in the marrow and often in the bloodstream. Along with the increase in blast cells, people with AML also have a reduced number of white blood cells, red blood cells and platelets.

Symptoms of AML typically develop suddenly and without warning, and can include fatigue, fever, loss of appetite, pale skin, recurrent infections and bleeding problems. There is currently no screening test for early detection of AML.

AML is a cancer most often seen in older people, although about 20 percent of cases occur in people under the age of 45. In the vast majority of cases, susceptibility to AML does not run in families.

Treatment Options

Treatment options for AML depend on several factors, including its type, the results of lab tests and the person's overall health. Once AML is diagnosed, you and your doctor will discuss the approach that is right for you, based on your individual circumstances.

No matter what treatment approach is chosen, it is essential that people being treated for AML receive attentive supportive care. This care typically includes antibiotics to prevent or treat infections, which can occur due to the decrease in white blood cells seen in cases of AML. Supportive care also involves regular transfusions of red blood cells and platelets. In some cases, transfusions include clotting factors such as “fresh frozen plasma” (FFP) or cryoprecipitate. The specific nature and schedule of the transfusion support is guided by the person's bleeding history and results of blood tests. In addition to helping the blood to clot, transfusions can help reduce fatigue.

Blood counts are routinely measured during AML therapy. The frequency and method of testing depends on the type of therapy being administered and other factors specific to the person's situation.

Chemotherapy

Chemotherapy is a mainstay of AML treatment, as it is a highly effective approach. It typically begins with “induction” chemotherapy, in which a combination of drugs is used to destroy the majority of the leukemia cells and bring blood counts to normal levels. For some people, a second course of induction chemotherapy is needed to normalize blood counts.

After induction therapy, “consolidation” chemotherapy (ongoing treatment) is given for a period of time to destroy any remaining leukemia cells in the blood and bone marrow and prevent a return of signs and symptoms of disease.

Some cases of AML are treated with high-intensity chemotherapy. The most frequently used high-intensity chemotherapies are:

- **Cytarabine.** Cytarabine (Cytosar-U, Ara-C) is an “antimetabolite”; it prevents cancer cells from dividing.
- **Anthracyclines.** Daunorubicin (Cerubidine) and idarubicin (Idamycin and others) are used to treat many types of cancer; they are designed to damage the DNA in cancer cells, causing those cells to die.
- **Mitoxantrone.** While chemically different from anthracyclines, mitoxantrone (Novantrone) can be used interchangeably with anthracyclines in the treatment of AML.



A common high-intensity chemotherapy regimen for AML is called “7 + 3.” This regimen consists of cytarabine given daily for 7 days, followed by an anthracycline given daily for 3 days. This treatment is administered intravenously (into a vein), in an in-patient hospital setting.

In 2017, the Food and Drug Administration (FDA) approved CPX-351 (Vyxeos), a combination of cytarabine and daunorubicin, for treatment of newly-diagnosed therapy-related AML (t-AML), and for the treatment of AML with myelodysplasia-related changes. Those changes cause the body to stop making enough healthy red blood cells and platelets.

Some people are not good candidates for “7 + 3” or CPX-351, as they are intensive treatments. For those people, other options are often used, such as targeted therapies (as detailed in the next section) or low doses of cytarabine. Some people may receive azacitidine or decitabine, treatments approved for myelodysplastic syndromes, which are less-aggressive conditions related to AML. These lower-intensity drugs generally have less severe side effects, but they may take longer to work, and still require significant transfusion support and frequent visits to the doctor.

Targeted Therapy

Traditional chemotherapy drugs attack cancer cells, but can also cause significant injury to healthy cells. Based on what researchers have learned in recent years about how cancer cells grow, targeted therapies are designed to focus only on cancer cells and the associated mechanisms that fuel their survival and growth, sparing healthy cells and tissues.

There are a number of targeted therapies approved by the FDA as treatments for AML:

- **Midostaurin (Rydapt).** The FLT3 gene makes a protein that encourages cell growth. Approximately 30 percent of people with AML have a mutation in this gene, resulting in the increased growth of cancer cells. Midostaurin works by targeting (blocking) the action of the FLT3 protein; it is most effective when given in combination with chemotherapy. The presence of the FLT3 mutation can be determined from a bone marrow biopsy, or sometimes by a blood test.
- **Enasidenib (Idhifa).** Some people with AML have a mutation in the IDH2 gene that stops cells from maturing in the way they should. This mutation can be detected by a blood test. Approved by the FDA in 2017 for the treatment of relapsed (recurred) or refractory (not responding to treatment) AML, enasidenib works by helping leukemia cells mature into normal cells.
- **Ivosidenib (Tibsovo).** This targeted therapy can treat mutations in the IDH1 gene that, like IDH2 gene mutations, stops cell maturation. Ivosidenib was approved by the FDA in 2018 as a frontline (initial) treatment and for treatment of relapsed or refractory AML.
- **Gemtuzumab ozogamicin (Mylotarg).** A monoclonal antibody (manmade immune protein) linked to a chemotherapy drug, gemtuzumab ozogamicin was approved by the FDA in 2017 for the treatment of newly-diagnosed or relapsed AML. Gemtuzumab ozogamicin attaches to the CD33 protein found on most AML cells, delivering targeted chemotherapy to those cells.

In November 2018, the FDA approved two additional targeted therapies for the treatment of newly-diagnosed AML in people age 75 years or older who have medical conditions that preclude induction chemotherapy:

- **Glasdegib (Daurismo).** Glasdegib, which is given in combination with low-dose cytarabine, works by inhibiting a specific pathway (called the hedgehog signaling pathway) that can activate the growth of cancer cells.
- **Venetoclax (Venclexta).** Many people with AML have a mutation of the BCL2 gene that prevents the death of cancer cells and is associated with a resistance to chemotherapy. Venetoclax, a BCL2 inhibitor, is designed to correct this mutation. It is given in combination with low-dose cytarabine or other chemotherapies.

In November 2018, the FDA also granted approval to the targeted therapy gilteritinib (Xospata) for the treatment of adult patients with AML that has relapsed or is refractory and has a mutation of the FLT3 gene.

Stem Cell Transplant

A stem cell transplant is a procedure in which diseased bone marrow is replaced with healthy bone marrow. In an allogeneic stem cell transplant, stem cells (blood cells that divide to make new blood cells within the bone marrow) are taken from a donor. Donors are often a close relative such as a brother or sister, but sometimes can be an unrelated volunteer who has compatible bone marrow.

The person is given high doses of chemotherapy to destroy as many leukemia cells as possible. The stem cells are then transplanted into the body, where they travel to the bones and begin rebuilding bone marrow. To prevent the rejection of donor cells and to ensure the transplanted cells do not cause an autoimmune disease such as graft-versus-host disease (GVHD), immunosuppressive drugs, such as cyclosporine or tacrolimus, are typically given for a period of time after the transplant.

An allogeneic stem cell transplant is an important treatment option for many people with AML. To determine if stem cell transplant is the right treatment approach, doctors weigh a number of factors, including the risk of recurrence if a transplant is not performed, and how well the AML has responded to prior treatment approaches. A patient's age and general physical health are also taken into consideration.

Many older people (and those with other chronic illnesses) are not able to safely tolerate the high doses of chemotherapy that are used in stem cell transplants. In this case, a “reduced-intensity” transplant may be performed. In this procedure, which is also called a mini-transplant, lower doses of chemotherapy are given, potentially with radiation. The patient then receives allogeneic stem cells.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It is important that you report any side effects you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but it can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Have something in your stomach when you take medication to help ease nausea.



Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade, which provide electrolytes.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary and after having a discussion with a member of your health care team.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow).
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, granola bars, liquid nutritional supplements, nuts and canned tuna.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective.

If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.



Managing Pain

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating With Your Health Care Team

As you manage your AML, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. They may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you have a mobile device, ask if you can use it to take notes or record the discussion, which will help you review the information later.

CancerCare's Free Support Services and Programs

Receiving a diagnosis of AML can be very difficult, and adjusting to the necessary changes in your life can be challenging.

CancerCare can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store or ask a friend who's a good listener to come over for a chat.



Frequently Asked Questions

Q: Am I more susceptible to infections when being treated for AML?

A: People with AML have an increased risk of infection, both from the disease itself and its treatment. When white blood cells are abnormally low (a condition called neutropenia), an infection may progress rapidly and become serious. For this reason, it's important that people being treated for AML immediately report fevers or other signs of infection to their health care team as treatments are available to prevent the infection from becoming severe.

During treatment, patients should avoid contact with those who have symptoms of a cold and should stay away from crowded places during cold and flu season. Frequent handwashing with soap or alcohol-based sanitizer is another important preventative activity.

The risk of foodborne infection can be reduced by avoiding foods that easily spoil or become moldy without an obvious change in smell or appearance. This includes berries that grow out of the ground and soft fruits that lack a thick peel. Undercooked ground beef, poultry, and eggs should be avoided during treatment, as should buffets and salad bars.

Q: If I am being treated for AML during flu season, should I get a flu shot?

A: Flu shots are generally considered safe for people undergoing treatment for AML but their effectiveness is greatly reduced for those receiving chemotherapy. There are other measures that can reduce the risk of a viral illness, such as frequent hand-washing and avoiding people who have (or are just getting over) a cold.

It is also important that family members and close companions of those receiving any type of cancer treatment get flu shots, to prevent catching and passing on the flu.

On a related note, ask your doctor or a member of your health care team if you should continue to receive the vaccines recommended for your age and specific situation, such as those for pneumonia, shingles and herpes zoster.

Q: I heard that mouth care is important during treatment for AML. What advice can you give me?

A: To minimize the risk of bleeding gums, using an extra-soft toothbrush and avoiding flossing is recommended until platelet counts return to normal levels after therapy. Dry mouth is common in AML chemotherapy treatments and can be a risk factor for mouth ulcers and inflammation. To avoid dry mouth, rinse with salt water after every meal and at bedtime or more frequently if dryness worsens, use artificial saliva and avoid drugs that contribute to dryness, such as antihistamines and mouthwashes containing alcohol.

Q: Should I have genetic testing?

A: Genetic testing (also called molecular testing) of leukemia cells is advised for people newly diagnosed with AML, as nearly all cases develop due to the existence of genetic mutations in those cells. The treatment approach may be determined by the presence of certain mutations (such as mutations of the FLT3, IDH1 or IDH2 genes). On a related note, very few of the mutations that cause leukemia are inherited, and genetic testing of family members to determine their risk of leukemia is rarely necessary.



Resources

CancerCare®

800-813-HOPE (800-813-4673)
www.cancercares.org

American Cancer Society

800-227-2345
www.cancer.org

Be the Match® Patient Services

800-627-7692
www.bethematch.org

**Blood & Marrow Transplant
Information Network**

888-597-7674
www.bmtinfonet.org

The Bone Marrow Foundation

800-365-1336
www.bonemarrow.org

Cancer.Net

Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

**National Bone Marrow
Transplant Link**

800-546-5268
www.nbmtlink.org

National Cancer Institute

800-422-6237
www.cancer.gov

The Leukemia & Lymphoma Society

800-955-4572
www.lls.org

Leukemia Research Foundation

847-424-0600
www.allbloodcancers.org

CLINICAL TRIALS WEBSITES**Coalition of Cancer Cooperative Groups**

www.cancertrialshelp.org

National Cancer Institute

www.cancer.gov

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