National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Acute Myeloid Leukemia

Presented with support from NCCN FOUNDATION® Guiding Treatment. Changing Lives.

Available online at NCCN.org/patientguidelines

NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

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

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Acute Myeloid Leukemia Version 3.2026 — November 24, 2025.

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About AML

Acute myeloid leukemia (AML) is a type of blood cancer that starts in the stem cells of bone marrow. There are many subtypes of AML found in adults. This chapter will provide a general overview of AML.

What is acute myeloid leukemia?

In acute myeloid leukemia (AML), abnormal changes stop very immature white blood cells called myeloblasts, or blasts, from becoming mature blood cells. As a result, blasts build up in the bone marrow and blood. In turn, there aren't enough healthy mature red blood cells, platelets, and white blood cells. This causes serious health issues. For this reason, AML is fatal if left untreated. Although AML can progress quickly, many effective treatments are available, and outcomes continue to improve.

Subtypes of AML

There are many subtypes of AML. They are grouped and treated based on the presence or absence of certain gene mutations or abnormal chromosomes found within the leukemia cells and other factors. Some subtypes are defined by specific genetic changes that can be targeted with newer therapies. While many AML subtypes share similar treatment foundations, genetic differences increasingly guide therapy choices.

In addition to treatment for AML, this guide includes information about the following:

- **Acute promyelocytic leukemia (APL)** – In APL, the abnormal fusion gene *PML::RARA* is found.
- **Blastic plasmacytoid dendritic cell neoplasm (BPDCN)** – BPDCN can be found in blood, bone marrow, lymph nodes, and/or skin.

Read more to learn about the types of blood cells, how blood is made, and where AML starts.

What is blood?

There are 4 main components of blood—plasma, red blood cells, white blood cells, and platelets. Blood's function is to move oxygen and nutrients throughout your body and carry away waste. Blood also plays an important role for the immune system and in preventing bleeding.

Types of blood cells

Your blood contains different types of cells that float in plasma. Plasma is a clear, yellowish fluid made up of mostly water.

There are 3 types of blood cells:

- Red blood cells (erythrocytes) carry oxygen throughout the body.
- White blood cells (leukocytes) fight infections. White blood cells include granulocytes (or neutrophils), monocytes, and lymphocytes.
- Platelets (thrombocytes) help control bleeding.

How are blood cells formed?

Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are early blood-forming cells called blood (hematopoietic) stem cells. At any given time, the bone marrow contains cells in various stages of development, from very immature to nearly mature. Once a blood stem cell fully develops into a red blood cell, white blood cell, or platelet, it's released into the bloodstream as needed.

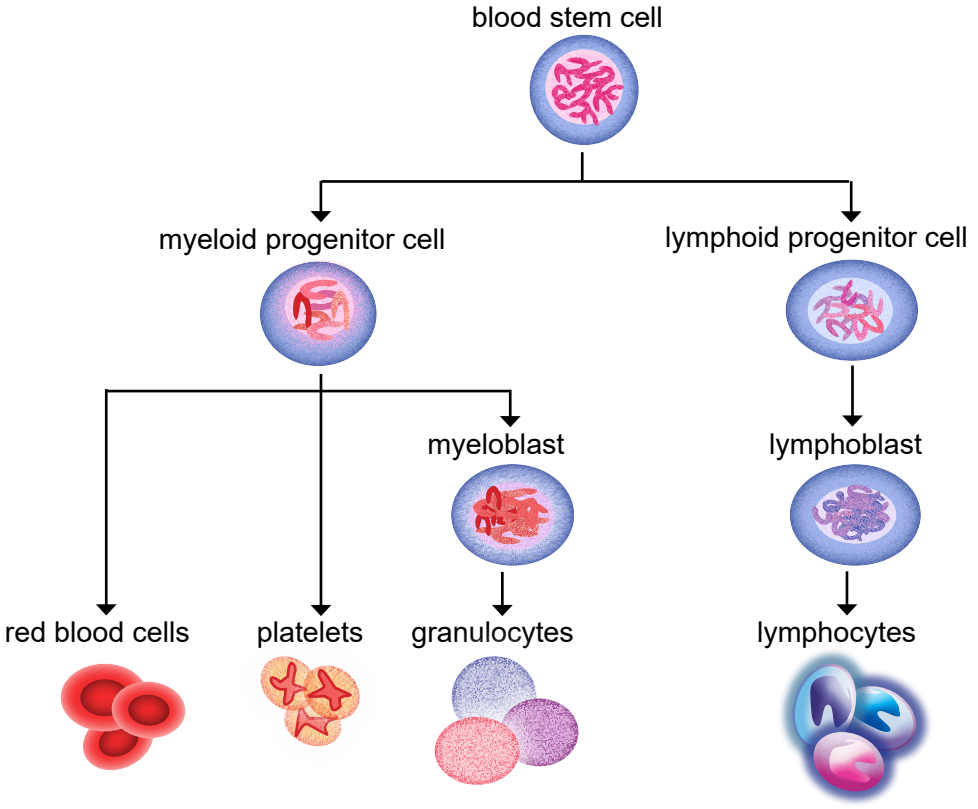
AML starts in the bone marrow when blood stem cells form abnormal myeloblasts, or leukemia cells. In AML, myeloblasts are often simply referred to as blasts.

What are blasts?

A blast is an immature white blood cell. Blasts are committed to becoming a type of blood cell. In AML, we're referring to a type of blast called a myeloblast. Myeloblasts mature into granulocytes, also known as neutrophils. Neutrophils are immune cells that help prevent and control infection. In AML, abnormal myeloblasts are found in the bone marrow or blood. The abnormal myeloblasts crowd out other normal blood cells, causing bone marrow or blood to not work as it should.

Blood cell formation

All blood cells start as blood stem cells. A blood stem cell has to mature or go through many stages to become a red blood cell, white blood cell, or platelet. AML affects the myeloid progenitor cells, which develop into red blood cells, granulocytes (a type of white blood cell), and platelets.



How is AML treated?

All types of AML are treated in phases. The goal of treatment is to put AML in remission. In remission, there's no sign of leukemia cells.

AML is usually treated with a combination of multiple drugs. Some treatments are designed to target specific genetic changes in leukemia cells. The type and combination of systemic drug therapy depend on the subtype of AML, your unique situation, and other factors.

This guide will discuss in greater detail how AML, APL, and BPDCN are diagnosed and treated. It will provide an overview of the types of tests and treatments and what to expect during testing and treatment. Some sections are educational, while others are more detailed for those who want to understand treatment decisions more deeply. It's okay to skip sections that feel overwhelming.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

2
Testing for AML

Accurate testing is needed to diagnose and treat acute myeloid leukemia (AML). This chapter presents an overview of possible tests you might receive and what to expect during testing.

Overview

Accurate testing is needed to diagnose and treat acute myeloid leukemia (AML). A diagnosis of AML is based on the presence of myeloid blasts in the bone marrow or blood. The number of blasts required to be diagnosed with AML can vary. In general, the number of blasts must be 20 percent (20%) or more of all white blood cells found in the bone marrow or blood. This means that at least 1 out of every 5 white blood cells are blasts. However, a diagnosis of AML is possible with any number of blasts, particularly if certain gene mutations or chromosome abnormalities are also present.

Unlike cancers of organs, like lung cancer or breast cancer, AML doesn't have stages. Many cancers spread from the location where they originate, and the extent or severity of cancer is determined by how far it has spread. AML arises from the bone marrow, which is present in nearly all of our bones. Because AML cells arise from multiple bones and flow in the blood all over the body, traditional staging isn't useful. Instead, AML testing looks for specific gene mutations or abnormal chromosomes, which can tell your care team how aggressive your leukemia might be.

Information on possible tests and procedures can be found in this chapter. It's okay to skip over information that doesn't interest you. AML treatment decisions depend on understanding the leukemia's biology, not just its appearance under the microscope—that's why there are so many possible tests and procedures listed in **Guide 1**.

Guide 1
Possible tests and procedures

Medical history and physical exam
Distress screening
Complete blood count, differential, comprehensive metabolic panel, uric acid, lactate dehydrogenase, B12, and folic acid
Blood clotting tests
Bone marrow aspirate and biopsy with AML biomarker and genetic testing
Referral to transplant center and/or human leukocyte antigen (HLA) typing
Brain CT without contrast, if central nervous system bleeding suspected
Brain MRI with contrast, if leukemic meningitis suspected
FDG-PET/CT, if leukemia outside the blood and bone marrow (extramedullary) suspected
Lumbar puncture
Heart tests
Fertility counseling
Palliative care information

General health tests

Some general health tests are described next.

Medical history

A medical history is a record of all health issues and treatments you've had in your life. It asks about past surgeries and current health conditions. Bring a list of old and new medicines and any over-the-counter medicines, herbals, or supplements you take. Some supplements interact with and affect medicines that your care team may prescribe. Also, tell your care team about any symptoms you have.

Physical exam

During a physical exam, your health care team may:

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

Family history

Your care team will ask about the health history of family members who are blood relatives. This information is called family history. Ask members on both sides of your family about their health issues, like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it's in multiple locations, and if they had genetic testing.

Distress screening

Dealing with a cancer diagnosis can be stressful and may cause further distress. Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt. You may also experience depression, anxiety, and sleep issues. Your treatment team will screen your level of distress. This is part of your cancer care.

Performance status

Performance status is a rating of a person's general level of fitness and ability to perform daily tasks. It includes whether you can walk, work, and take care of yourself. It's one factor taken into consideration when choosing a treatment plan.

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of blood, which is removed through a needle placed into a vein in your arm. Be prepared to have many blood tests during AML treatment and recovery to check treatment results, blood counts, and the health of organs like your liver and kidneys.

Some possible tests are described next. The list starts with more common tests.

Complete blood count and differential

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. A CBC is a key test that gives a picture of your overall health. AML often causes low counts of healthy blood cells, but a high number of abnormal white blood cells can also be found.

A differential counts the number of each type of white blood cell (neutrophils, lymphocytes, monocytes, eosinophils, and basophils). It also checks if the counts are in balance with each other. This test may show a high number of blasts in the blood.

Your care team will pay particular attention to the following CBC measurements:

- Hemoglobin measures the amount of oxygen-carrying protein in the blood and helps determine whether a red blood cell transfusion is needed.
- Platelets are cells that make the blood clot, thus preventing or stopping bleeding.
- An absolute neutrophil count measures cells that fight bacteria and protect us from infections.
- Blasts or leukemia cells can sometimes be detected in the blood and usually are reported as a percentage (%) of cells.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures substances in your blood. It provides important information about how well your kidneys and liver are working, among other things.

A CMP might measure the following:

- **Blood urea nitrogen (BUN)** is a waste product filtered out of the blood by the kidneys. A high level of BUN can be a sign of dehydration, or your kidneys aren't working well.
- **Creatinine** is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. Creatinine is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys aren't working as well as when someone has lower levels of creatinine, or it can be a sign of dehydration.
- **Electrolytes** help move nutrients into cells and help move waste out of cells. Electrolytes are ions or particles with electrical charges that help the nerves, muscles, heart, and brain work as they should. Your body needs electrolytes to function properly.

- **Liver function tests** look at the health of the liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver isn't working well, or the bile ducts might be blocked.
- **Phosphorus or phosphate** is found in every cell in the body. Your kidneys help get rid of extra phosphate, but too much phosphate in the blood can also damage the kidneys, making it harder to get the levels back down to normal.
- **Uric acid** is released by cells when DNA breaks down. It's a normal waste product that dissolves in your blood and is filtered by the kidneys where it leaves the body in urine. Too much uric acid in the body is called hyperuricemia. With AML, it can be caused by a fast turnover of white blood cells or as a side effect of treatment. Very high levels of uric acid in the blood can damage the kidneys.

Lactate dehydrogenase

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

B12 and folic acid

Vitamin B12 and folic acid (folate) help the body make new proteins. They are needed for normal red blood cell and white blood cell formation. B12 and folic acid levels will be monitored. You may be given vitamin supplements, if needed.

Iron

Iron is important in maintaining body functions, such as producing hemoglobin, the molecule in your blood that carries oxygen. You might be monitored for low levels of iron called iron deficiency. You may also be given an oral or IV (intravenous) iron supplement, if needed. It's possible to have too much iron in the body called overload. Therefore, only take what is prescribed by your doctor.

AML testing takes time. It might take weeks for all of your test results to come in. Please wait to discuss the results with your care team.

During treatment, you might have blood tests every day.

Blood clotting tests

Your body stops bleeding by turning blood into a gel-like form. The gel-like blood forms into a solid mass called a blood clot. Clotting is a process or series of events. Proteins, called coagulation factors, are needed for clotting. They are made by the liver. These tests are known together as a coagulation panel or disseminated intravascular coagulation panel.

An impaired clotting process is common in leukemia. This is called coagulopathy. You may have bleeding and bruises or blood clots.

HLA typing

Human leukocyte antigen (HLA) is a protein found on the surface of most cells. It plays an important role in your body's immune response. HLAs mark your body's cells. Your body detects these markers to tell which cells are yours. In other words, all of your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

HLA typing is a test that detects a person's HLA type. This test is done before a donor (allogeneic) hematopoietic cell transplant (HCT). To find a donor match, your proteins will be compared to the donor's proteins to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood samples from you and your blood relatives will be tested first.

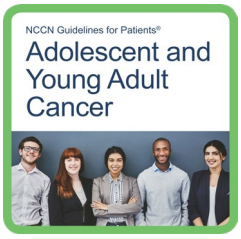
This test is only done if a transplant may be an option.

Fertility (all genders)

Treatment with targeted therapy and other forms of systemic therapy can affect your fertility, or the ability to have children. If you think you want children in the future, ask your care team how cancer and cancer treatment might affect your fertility.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren't sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation can be found at *NCCN Guidelines for Patients: Adolescent and Young Adult Cancer* NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Preventing pregnancy during treatment

Preventing pregnancy during treatment is important. Cancer treatment can affect the ovaries, damage sperm, and hurt a developing baby. Therefore, becoming pregnant or having one's partner become pregnant during treatment should be avoided. If you are pregnant or breastfeeding at the time of your cancer diagnosis, treatments may need to be adjusted.

Bone marrow tests

Leukemia starts in the bone marrow. To diagnose AML, samples of bone marrow are removed and tested before any treatment is started. Your bone marrow sample should be reviewed by a pathologist who's an expert in diagnosis of AML. This review is often referred to as histology, histopathology, or hematopathology review. The pathologist will note the overall appearance and size, shape, and type of your cells. Tests will be done on the biopsied cells.

There are 2 types of bone marrow tests that are often done at the same time:

- Bone marrow aspirate
- Bone marrow biopsy

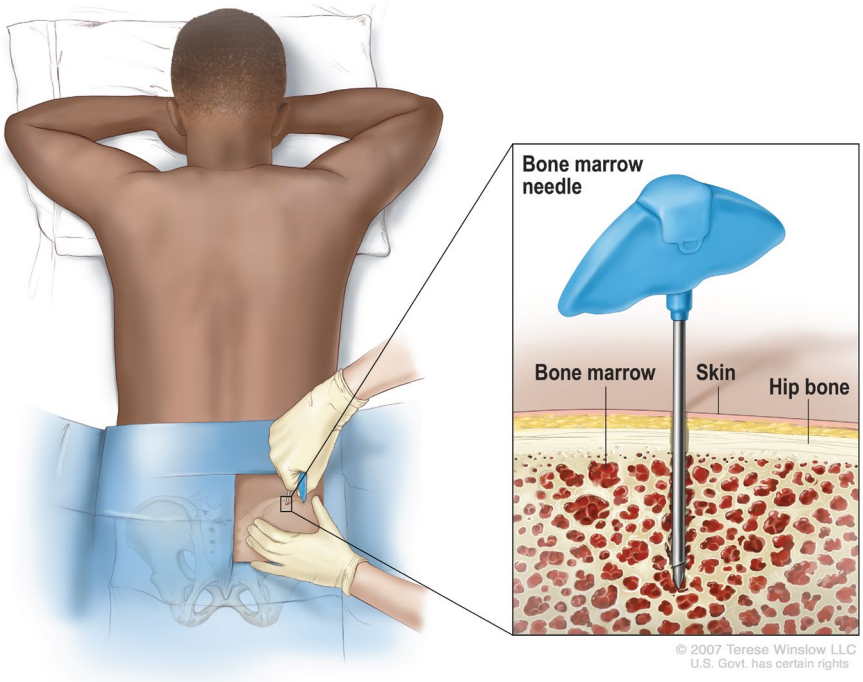
Your bone marrow is like a sponge holding liquid and cells. An aspirate withdraws some of the liquid and cells out of the sponge, and a biopsy removes a piece of the sponge.

A bone marrow aspirate and biopsy are bedside procedures. They aren't surgeries and don't require an operating room. Your care team will try to make you as comfortable as possible during the procedures.

The samples are usually taken from the back of the hip bone (pelvis). You'll likely lie on your belly or side. For an aspirate, a hollow needle will be pushed through your skin and into the bone marrow. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be used to remove a small piece of bone marrow. You may feel bone pain at your hip for a few days. Your skin may bruise.

Bone marrow aspirate and biopsy

Samples of bone and liquid bone marrow are removed in a biopsy.



- If the blastic plasmacytoid dendritic cell neoplasm (BPDCN) is suspected, you might also have a lymph node biopsy or a skin lesion biopsy.

Flow cytometry

Flow cytometry is a laboratory method used to detect, identify, and count specific cells. Flow cytometry involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine measures the number of cells, as well as things like the size and shape of the cells.

Flow cytometry may be used on cells from circulating (peripheral) blood or from a bone marrow aspirate. A blood test can count the number of white blood cells, but it can't detect the subtle differences between different types of blood cancers. Flow cytometry can detect these subtle differences. The most common use of flow cytometry is in the identification of markers on cells, particularly in the immune system (called immunophenotyping).

Immunophenotyping

Immunophenotyping is a process that uses antibodies to detect the presence or absence of white blood cell antigens called biomarkers. These antigens are proteins that can be found on the surface of or inside white blood cells. Certain biomarkers are targeted in AML treatment.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cells. The cells are then studied using a microscope. IHC looks for the immunophenotype of cells from a biopsy or tissue sample.

AML biomarker and genetic testing

Biomarker and genetic tests are used to learn more about your subtype of AML, to target treatment, and to determine the likely path the cancer will take, called a prognosis. This genetic testing is different from family history genetic testing or genetic cancer risk testing. This testing looks for changes only in the leukemia cells that have developed over time, and not changes in the rest of the body's cells. It's sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing.

Inside our cells are DNA (deoxyribonucleic acid) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes are coded instructions for the proteins your cells make. A mutation is when something goes wrong in the genetic code. Proteins are given names such as FLT3. Genes are identified in italics like this: *FLT3*.

AML cells sometimes have changes in genes and chromosomes that can be seen under a microscope or found with various other tests.

- Testing your leukemia cells can gather specific information about your leukemia to help guide treatment.
- Some results take days to weeks, but treatment may start before all results return.

AML genetic changes

AML cells can have changes in genes and chromosomes. Mutation testing looks for these changes or abnormalities that are unique to AML cells. Examples of such changes are called deletion, insertion, inversion, amplification, translocation (rearrangement), and point mutation.

- ✓ **Amplification** – When a part or whole chromosome or gene is increased (for example, duplicated)
- ✓ **Deletion** – When part of a chromosome or gene is missing, such as del(5q)
- ✓ **Insertion** – When a new part of a chromosome or gene is included
- ✓ **Inversion** – Switching of parts within one chromosome, such as inv(16) and inv(3)
- ✓ **Point mutation** – When part of a gene is changed
- ✓ **Chromosome translocation and gene rearrangement** – Switching of parts between 2 chromosomes. When described at the chromosome level, it's called translocation. When described at the gene level, it's called rearrangement. For example, the chromosome translocation is written as t(8;21)(q22;q22.1) and its gene rearrangement is written as *RUNX1::RUNX1T1*.

Leukemia predisposition syndromes

A family history of leukemia can affect treatment. A skin punch biopsy is used to learn more about the genetic changes you were born with. In this procedure, a small piece of skin and connective tissue are removed to get DNA that hasn't been altered by AML. The sample will be used to see if you inherited genes that increase your risk of leukemia. Blood and saliva can be used when AML cells disappear in remission.

Leukemia predisposition syndrome can affect how your body responds to treatment. Biological family members (blood relatives) who are possible hematopoietic cell donors might be tested for leukemia predisposition syndrome.

- Testing cells not affected by leukemia (like your skin) can help tell if you have a leukemia predisposition syndrome.
- Most people with AML don't have an inherited leukemia syndrome.

AML mutation testing

Mutation testing using methods such as karyotype, fluorescence in situ hybridization (FISH), next-generation sequencing (NGS), and polymerase chain reaction (PCR) look for changes or abnormalities that are unique to AML cells (genes and chromosomes). A sample of your blood or bone marrow will be used to see if the AML cancer cells have any specific mutations. Some genetic changes allow doctors to use targeted therapies, which can be more effective and less toxic than traditional chemotherapy.

FISH

Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. FISH can look for changes (abnormalities) that are too small to be seen with other methods. It can only be used for known changes. Since this test doesn't need growing cells, it can be performed on either a bone marrow or blood sample. Sometimes, a bone marrow sample is needed to get all of the information the care team needs to help plan your treatment.

Karyotype

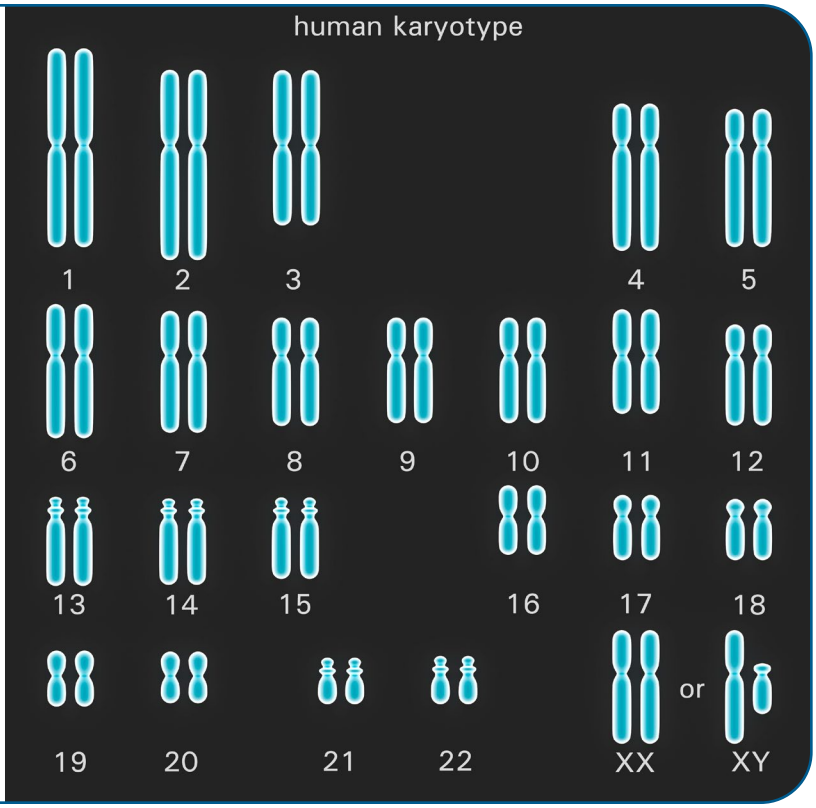
A karyotype is a picture of chromosomes. Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. A karyotype will show extra, missing, rearranged, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow or blood must be used.

Next-generation sequencing

Next-generation sequencing (NGS) is a method used to determine a portion of a person's DNA sequence. It shows if a gene has any mutations that might affect how the gene works. NGS looks at the gene in a more detailed way than other methods and can find mutations that other methods might miss.

Karyotype

A karyotype is a picture of your chromosomes. The study of chromosomes is called cytogenetics.



PCR

A polymerase chain reaction (PCR) is a technique that can make millions or billions of copies of your DNA or RNA (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for NGS. A PCR is important when testing for treatment response or remission.

A special type of PCR, called real-time or reverse transcriptase (RT) PCR, is used to look for gene rearrangements, such as *PML::RARA*. This aids in diagnosis and monitoring response to targeted therapies.

Imaging tests

In some cases, imaging tests may be performed. This is based on your individual situation. Imaging tests take pictures of the inside of the body to look for sites with leukemia outside the bone marrow. Leukemia can spread outside the bloodstream to lymph nodes, liver, spleen, and skin. It rarely spreads to the lining of the brain and spinal cord. Imaging tests can also show areas of infection or bleeding that may impact your care.

A radiologist, a medical expert in interpreting imaging tests, will interpret the test and send a report to your care team.

The following information is in alphabetical order.

Contrast material

Contrast material is a substance used to improve the quality of imaging tests such as CT and MRI scans. It's used to make the pictures clearer. Not all imaging tests require contrast, but many do.

Contrast might be taken by mouth (oral) or given through a vein (intravenously or IV). The types of contrast vary and are different for CT and MRI.

Tell your care team if you've had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

CT scan of the brain

A CT scan of the brain is used to look for bleeding.

A CT or CAT scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All of the images are combined to make one detailed picture. Contrast may or may not be used.

MRI scan of the brain

An MRI can show if the outer layer of the brain is swollen from leukemia (called leukemic meningitis).

An MRI scan uses radio waves and powerful magnets to take pictures of the inside of the body. It doesn't use x-rays, which means there's no radiation delivered to your body during the test. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal or a pacemaker in your body. During the test, you'll likely be asked to hold your breath for 10 to 20 seconds as the technician collects the images.

MRI scans take longer to perform than CT scans. A closed MRI has a capsule-like design where the magnet surrounds you. The space is small and enclosed. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a fear of enclosed spaces), be sure to tell your care team about it.

PET scan

A PET scan might be used to look for leukemia outside of the bone marrow and blood (called extramedullary disease).

A PET scan uses a radioactive substance called a tracer. A tracer is injected into a vein to see where cancer cells are in the body and how much sugar is being taken up by the cancer cells. This gives an idea about how fast the cancer cells are growing. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots found on the PET scan are cancer. It's normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot.

When a PET scan is combined with CT, it's called a PET/CT scan. An FDG-PET/CT uses a radiotracer called fluorodeoxyglucose.

"Leukemia impacts every part of us—physical, emotional, mental, and spiritual. It takes support in all areas to get through the journey. Don't be afraid to ask for help."

Heart tests

Heart, or cardiac, tests are used to see how well the heart works. These tests might be used to monitor treatment side effects or to measure your heart function before you start treatment. You might be referred to a heart specialist called a cardiologist.

Electrocardiogram

An electrocardiogram (ECG or EKG) shows electrical activity in your heart. It reveals information about your heart rate and rhythm. A prolonged corrected QT interval (QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Certain treatments can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

Echocardiogram

An echocardiogram (or echo) uses sound waves to make pictures. It's a type of ultrasound. For this test, small patches will be placed on your chest to track your heartbeat. Next, a wand with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen on a screen. The pictures will be recorded for future viewing.

An echocardiogram shows the structure (valves and muscle thickness) and function of your heart (or ejection fraction). Ejection fraction is the amount of blood pumped out of the left side of your heart every time it beats. If the amount of blood pumping from the left side of the heart is lower than normal, this indicates decreased heart function.

Lumbar puncture

Leukemia can travel to the fluid that surrounds the spine or brain. This may cause symptoms such as headaches, neck pain, and sensitivity to light. A test may be needed to know if leukemia cells are in your spinal fluid. A lumbar puncture is a procedure that removes spinal fluid by inserting a needle into the middle of the lower back. It's also called a spinal tap.

Key points

- In acute myeloid leukemia (AML), abnormal changes stop very immature white blood cells, called myeloid blasts or myeloblasts, from becoming mature blood cells. As a result, blasts build up in the bone marrow and blood, making it hard for blood to do its work.
- An aspirate or biopsy is the removal of a sample of tissue or group of cells for testing. A diagnosis of AML is confirmed using a bone marrow aspirate and bone marrow biopsy.
- In general, to be diagnosed with AML, 20 percent (20%) or more myeloblasts must be present in the bone marrow or blood. This means that at least 1 out of every 5 cells are blasts.
- In certain cases, a diagnosis of AML is possible with any number of blasts, particularly if specific gene mutations or abnormal chromosomes are also present.
- Genetic and biomarker tests are used to learn more about your subtype of AML, to target treatment, and to determine the likely course the cancer will take called a prognosis.

Questions to ask

- What subtype of AML do I have? What does this mean in terms of prognosis and treatment options?
- Is there a cancer center or hospital nearby that specializes in AML?
- What tests will I have? How often will they be repeated?
- Will my insurance pay for these tests?
- Who will talk with me about the next steps? When?

What's next?

The next chapter provides information on the types of treatment, what to expect from treatment, and some possible side effects of treatment.

3
Types of treatment

Treatment for all types of acute myeloid leukemia (AML) will be in phases. The goal of treatment is to put AML in remission. This chapter presents an overview of the possible types of treatment and what to expect. Together, you and your care team will choose a treatment plan that's best for your subtype of AML.

Results from blood tests, bone marrow aspirate and biopsy, and imaging studies will be used to guide your treatment plan. It's important to have regular talks with your care team about your goals for treatment and your treatment plan.

Your care team

Treating cancer takes a team approach. Treatment decisions should involve a multidisciplinary team of health care and psychosocial care professionals from different backgrounds who have knowledge and experience in your type of cancer. This team is united in planning and implementing your treatment. Ask who will coordinate your care.

Your team might include the following specialists:

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers and treats these conditions.
- **A medical oncologist** treats cancer using systemic (drug) therapy.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed

"I was so fortunate to find an expert oncologist and health care team that I could talk to openly and honestly during and after my treatment. This shared decision-making made me feel like I had a say about my care."

during a biopsy and provides cancer diagnosis and information about biomarker testing.

Systemic therapy

AML is treated with systemic therapy. Systemic therapy is drug therapy that works throughout the body. It includes chemotherapy and targeted therapy, such as venetoclax. Because AML affects the bone marrow throughout the body, treatment must reach all leukemia cells wherever they are.

You'll likely get either a catheter or a port to deliver systemic therapy, fluids, and blood products into your body. A catheter is a thin, long tube that's often placed in the upper arm. This goes into a large vein and stays there until treatment is complete. A port is a small, round disc that's usually placed in the chest. The type and location of the catheter or port will be tailored to your needs and treatment plans.

All systemic treatments listed in this guide are recommended and appropriate. When helpful, NCCN experts also assign a level of preference to their recommendations for systemic therapies:

- **Preferred therapies** have the most evidence they may work better and may be safer than other therapies.
- **Other recommended therapies** can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.
- **Therapies used in certain cases** work best for individuals with specific cancer features or health circumstances.

Chemotherapy

Chemotherapy is the standard of care for treating AML. Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and normal cells.

Chemotherapy is most often a liquid that's slowly injected into a vein with a needle. In most cases, chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which chemotherapy is used. You might spend time in the hospital during treatment.

Types of chemotherapy

There are many types of chemotherapy used to treat AML. Often chemotherapies are combined. This is called multi-agent chemotherapy or a multi-agent regimen. Each chemotherapy works in a different way and causes different side effects. Specific drug combinations and doses vary widely. Your care team will explain why certain drugs are chosen for you, when you'll get them, and what side effects to expect.

Antimetabolites

Antimetabolites prevent the building blocks of DNA from being used. Examples include:

- Cladribine (Mavenclad)
- Clofarabine (Clolar)
- Cytarabine (Ara-C)
- Fludarabine
- Hydroxyurea (Hydrea)
- Methotrexate

Anthracyclines

Anthracyclines damage and disrupt the making of DNA, causing the death of both cancerous and non-cancerous cells. Some anthracyclines can cause heart issues and may not be an option for you. There's a limit to how much you can receive in your lifetime. Anthracycline examples include daunorubicin, idarubicin (Idamycin PFS), and mitoxantrone (Novantrone). Dual-drug liposome of cytarabine and daunorubicin (CPX-351, or Vyxeos) includes an antimetabolite and an anthracycline.

Hypomethylating agents

Methyl groups are molecules found in DNA. Leukemia cells often have too many methyl groups. These extra groups can block genes from being turned on and off. Hypomethylating agents (HMAs) block methyl groups from binding to DNA. They turn silenced genes back on, which allows leukemic blasts to mature into normal cells. Azacitidine (Vidaza) and decitabine (Dacogen) are HMAs.

Targeted therapy

Targeted therapy focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive.

Targeted therapies aren't always less intense than chemotherapy, and many are used together. Examples of targeted therapies that might be used to treat AML can be found in **Guide 2**.

Guide 2
Targeted therapy examples

Listed in alphabetical order
Enasidenib (Idhifa)
Gemtuzumab ozogamicin (Mylotarg)
Gilteritinib (Xospata)
Glasdegib (Daurismo)
Ivosidenib (Tibsovo)
Midostaurin (Rydapt)
Olutasidenib (Rezlidhia)
Quizartinib (Vanflyta)
Revumenib (Revuforj)
Sorafenib (Nexavar)
Venetoclax (Venclexta)
Ziftomenib (Komzifti)

People with AML should seek treatment at cancer centers experienced in this type of cancer.

The following explains how targeted therapy might be used to treat AML. Some of these drugs are used as part of combination therapy rather than alone.

CD33 protein

Gemtuzumab ozogamicin is a type of targeted therapy that's linked to a chemotherapy drug. It attaches to a cell surface protein called CD33, then enters the cell. Once inside, chemotherapy is released. Many leukemic blasts have CD33 proteins. Mature blood cells don't have CD33 and are not affected. Gemtuzumab ozogamicin may delay blood count recovery and cause liver issues.

Core binding factor

Core binding factor (CBF) AML refers to leukemia with specific chromosome changes that often respond well to certain treatments. Gemtuzumab ozogamicin might be used in combination with daunorubicin and cytarabine to treat AML with CBF or other genetic abnormalities.

FLT3 mutation

Gilteritinib, quizartinib, midostaurin, or sorafenib is used to treat AML with certain *FLT3* mutations such as *FLT3-ITD* and *FLT3-TKD*. Sorafenib or quizartinib is used to treat AML with an *FLT3-ITD* mutation.

IDH1 and *IDH2* mutations

Ivosidenib and olutasidenib are used to treat AML with an *IDH1* mutation. Enasidenib is used to treat AML with an *IDH2* mutation.

KMT2A rearrangement

Revumenib is used to treat AML with a *KMT2A* rearrangement.

Standard of care is the best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment that's considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.

NPM1 mutation

Revumenib or ziftomenib might be used to treat AML with an *NPM1* mutation.

Venetoclax

Venetoclax targets the BCL-2 protein to kill cancer cells. Venetoclax combined with azacitidine or decitabine is a common first treatment for people who can't tolerate intensive chemotherapy.

Clinical trials

You may also be able to receive treatment through a clinical trial. A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of treating cancer need to be studied in people.

If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. FDA.

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a research team. This group of experts will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It's common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you'll continue to receive standard cancer care. This care is often covered by insurance.

The goal of an HCT is for the new immune system to recognize what remains of the leukemia as foreign, destroy it, and provide you with new, healthy bone marrow.

Hematopoietic cell transplant

A hematopoietic cell transplant (HCT), or stem cell transplant, is a cancer treatment that replaces a person's bone marrow and immune system with donor cells to form new bone marrow and to fight the leukemia. An HCT replaces hematopoietic stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy as part of the transplant process. A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. HCTs are performed in specialized centers.

- Many people with AML don't need an HCT.

There are 2 types of HCTs:

- **Autologous** – stem cells come from you.
- **Allogeneic** – stem cells come from a donor who may or may not be related to you. Compared to an autologous HCT, an allogeneic HCT introduces new immune cells from the donor, which may be able to detect and eliminate cancer cells better than your immune system was able to (known as graft-versus-leukemia effect). **An allogeneic HCT is preferred over an autologous HCT in AML**.

Allogeneic HCT

An allogeneic HCT uses healthy stem cells from a donor who may or may not be related to you. Before an HCT, treatment using chemotherapy is needed to destroy the bone marrow cells where the disease came from and create room for the transplanted healthy donor stem cells. It also weakens the immune system so your body will accept and won't kill the transplanted cells. This process is called conditioning. The dose of conditioning varies between people. Radiation therapy may also be given as part of conditioning treatment.

After conditioning, you'll receive a transfusion of healthy stem cells from a donor who's matched to you. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. Until then, you'll have little or no immune defense. While waiting for the cells to engraft, you'll likely feel tired and weak. HCT has very serious and life-threatening side effects. You may need to stay in a very clean room at the hospital and take certain precautions against infections. You may be given antibiotics to prevent or treat infection.

Transfusions of other blood products are often needed. A red blood cell transfusion is used to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding.

The goal of the transplant is for the new immune system to recognize what remains of the leukemia as foreign, destroy it, and provide you with new, healthy bone marrow.

Possible side effects

Every treatment has side effects. You'll be monitored for infections, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack your normal, healthy tissue, such as your organs and skin. There are treatments for GVHD. Ask your care team about the possible side effects or complications of HCT and how this might affect your quality of life.

For more information, see the NCCN Guidelines for Patients: Graft-Versus-Host Disease, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Key points

- A treatment plan is based on your age and other factors, such as your overall health and performance status. Performance status is your general level of fitness.
- Systemic therapy works throughout the body. Acute myeloid leukemia (AML) is treated with systemic therapy.
- A hematopoietic cell transplant (HCT) aims to restore the body's ability to produce normal blood cells by replacing cancerous bone marrow stem cells with healthy stem cells.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.

Questions to ask

- Which treatment(s) do you recommend and why?
- What can I expect from treatment?
- Are there resources to help pay for treatment or other care I may need?
- What clinical trial options are available?
- Am I a candidate for a hematopoietic cell transplant?

What's next?

Now that you've read about the different types of treatment and what to expect, the next chapter talks about some general side effects of treatment and what might be done to manage those effects.

4
Supportive care

Supportive care helps manage the symptoms of cancer and the side effects of treatment. This chapter discusses possible side effects.

What is supportive care?

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life. It's also known as palliative care.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advanced care and end of life

Supportive (palliative) care is provided alongside leukemia treatment and doesn't mean stopping cancer therapy. To learn more about the types of support you may receive, read *NCCN Guidelines for Patients: Palliative Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

General side effects

Cancer treatment can cause unwanted health issues called side effects. Some side effects may be unpleasant. Others may be harmful to one's health. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person.

You'll be monitored throughout treatment for side effects or other unwanted (adverse) reactions. Some potential, more general side effects are described next. They are not listed in order of importance.

Information on supportive care specific to acute myeloid leukemia (AML), acute **promyelocytic leukemia (**APL), and blastic plasmacytoid dendritic cell neoplasm (BPDCN) treatment can be found in Chapters 5, 6, and 7.

Blood clots

Cancer treatment can cause blood clots to form. This can block blood flow and oxygen delivery to parts of the body. Blood clots can break loose and travel to other parts of the

body causing breathing problems, strokes, or other problems.

Diarrhea or constipation

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. When it occurs, it's important to drink lots of fluids.

Constipation is also common, especially if taking certain pain medicines, including narcotic pain medication and some anti-nausea medications. Constipation means having less frequent and more difficult bowel movements. Drinking fluids, staying active, and taking medicines for constipation are often recommended.

Emotional distress

Depression, anxiety, and sleeping issues are common during a cancer diagnosis. Talk to your care team and those with whom you feel most comfortable about how you're feeling. There are services, people, and medicine that may be recommended to help relieve your distress

Fatigue

Fatigue is a state of physical or mental tiredness that can feel like lack of energy, motivation, or stamina. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue. It's important to try to stay active.

Tell your care team about all side effects, including new or worsening symptoms, so they can be managed.

Infection

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

Neutropenia, a low number of white blood cells that often occurs during treatment, can lead to frequent or severe infections. When someone with neutropenia develops a fever, it's called febrile neutropenia (FN). A fever is a temperature of over 100.4º F. With FN, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections. Sometimes the infection can be from bacteria entering the bloodstream, which is very dangerous. FN is a side effect of some types of systemic therapy. Ask your care team how to prevent FN, what to look for, and what to do in an emergency.

Loss of appetite

The side effects from cancer or its treatment and the stress of having cancer might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth or difficulty swallowing.

Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who's an expert in nutrition and food can help.

Low blood cell counts

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body doesn't have enough healthy red blood cells, resulting in less oxygen being carried to your organs. You might tire easily if you're anemic.
- **Neutropenia** is a decrease in neutrophils, a type of white blood cell. This puts you at risk for infection.
- **Thrombocytopenia** is a condition where there aren't enough platelets found in the blood. This puts you at risk for bleeding.

Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You may be given medicine to prevent nausea and vomiting.

Neuropathy and neurotoxicity

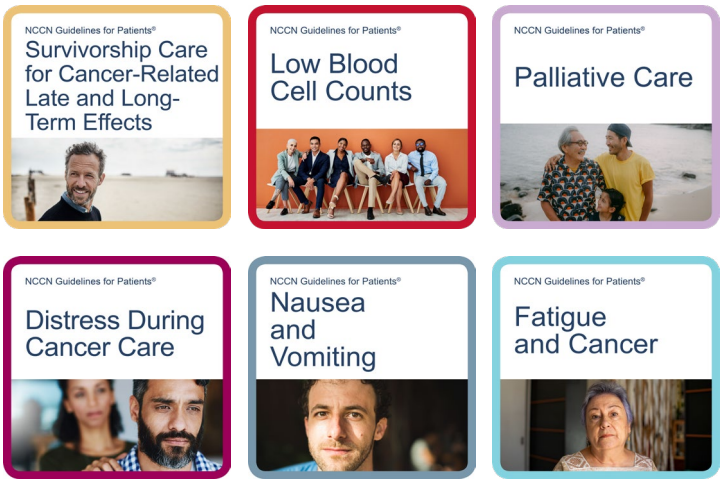
Some treatments can damage the nervous system (neurotoxicity), causing neuropathy and problems with concentration, memory, and thinking. Neuropathy is a nerve end problem that causes pain, numbness, tingling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse with additional cycles of treatment. Most of the time, neuropathy improves gradually and may eventually go away after treatment.

Pain

Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

Supportive care resources

More information on supportive care is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Palliative care

Palliative care is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. It focuses on physical, emotional, social, and spiritual needs that affect quality of life.

Transfusions

Blood transfusions may be needed during AML treatment. A transfusion is a slow infusion of blood products, such as red blood cells or platelets, into a vein. Over time, the body may begin to reject blood transfusions if your immune system develops antibodies against the blood cells from other donors.

Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social health issues, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. After treatment, your health will be monitored for side effects of treatment and the return of cancer. This is part of a survivorship care plan. It's important to keep any follow-up doctor visits and imaging test appointments. Find out who will coordinate your follow-up care.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.
NCCN.org/patients/response

Key points

- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.
- All cancer treatments can cause unwanted health issues called side effects. It's important for you to tell your care team about all of your side effects so they can be managed.
- Some side effects are very rare. Ask your care team what to expect.
- Tell your care team about any new or worsening symptoms.
- A person is a cancer survivor from the time of diagnosis until the end of life. After treatment, your health will be monitored for side effects of treatment and the return of cancer.

Questions to ask

- What side effects can I expect from treatment?
- How are these side effects treated?
- What should I do if I notice changes in my condition?
- What should I do if I notice side effects on weekends and other non-office hours?
- Will my care team be able to communicate with the emergency department or urgent care team?

What's next?

Now that you've read about the different types of treatment and what to expect, the next chapter explains specific treatment options for people with AML.

5
Treating AML

There are many subtypes of acute myeloid leukemia (AML). Most subtypes are treated with an intensive combination of chemotherapy. AML with a specific mutation may be treated with targeted therapy. Treatment aims to put leukemia in remission so your bone marrow can make normal blood cells again.

Overview

In AML, abnormal changes stop very immature white blood cells called myeloblasts from becoming mature blood cells.

AML subtypes

There are many subtypes of AML. They are grouped and treated based on the presence or absence of certain gene mutations and abnormal chromosomes found within the leukemia cells and other factors. Most subtypes of AML are treated alike.

How is AML diagnosed?

To be diagnosed with AML, myeloblasts must be present in the bone marrow or blood. At diagnosis, most people will have a bone marrow aspirate and biopsy. Some may have a lumbar puncture if there are signs and symptoms of central nervous system leukemia.

What causes AML?

AML can happen for certain known reasons, but most often there's no clear cause that can be determined. Some treatments for other cancers, such as radiation therapy or a specific type of chemotherapy, can later cause AML. Myelodysplastic syndrome (MDS) and other chronic bone marrow cancers can become AML. MDS is a type of cancer that occurs when the bone marrow stops making enough healthy blood cells and abnormal cells are found. AML can also run in certain families, although this is uncommon.

Treatment phases

The goal of the induction phase of treatment is to put AML into complete remission. In complete remission, the leukemia blasts are suppressed, allowing normal bone marrow function to resume. However, undetected leukemia cells may persist and sometimes return, causing cancer relapse. Following the induction phase, consolidation therapy may be given to deepen remission. Some people are offered maintenance therapy to prolong remission.

"Be your own advocate. Talk to someone who has gone through the same thing as you. Ask a lot of questions, even the ones you are afraid to ask. You have to protect yourself and ensure you make the best decisions for you, and get the best care for your particular situation."

It's important to note that some drug therapies don't have stages of treatment. In this case, therapy will be ongoing and without interruption.

Treatment responses

There are different types of treatment responses. When there are no signs of cancer, it's called a complete response or complete remission (CR). This doesn't always mean that AML has been cured—there can still be undetectable leukemia cells. Remission can be short-term (temporary) or long-lasting (permanent). Partial remission (PR) and a complete remission with partial hematologic (CRh) or incomplete (CRi) blood recovery are also possible. Ask your care team what these terms might mean for your type of AML.

It takes time for bone marrow to make normal blood cells again. This is called recovery. When bone marrow is starting to recover but hasn't fully recoved yet, it's called hypoplasia.

In complete remission:

- Leukemia isn't detectable, but additional treatment is often needed to keep it from returning.
- Your blood counts have returned to normal.
- You have less than 5 percent (5%) blasts in your bone marrow (or fewer than 5 blasts out of every 100 blood cells).

Treatment for AML can occur over years. The several phases are described next.

Induction

Induction is the first phase of treatment. It's also called remission induction. The goal is to reduce the number of blasts and put AML in remission. As the number of blasts decreases, other cells produced by the bone marrow, like red blood cells and platelets, will also decrease. Your bone marrow will need time to recover, about 4 to 6 weeks, so blood cells can return to normal levels. Treatment attempts to restore the process of making normal blood cells. When blood counts are normal, bone marrow tests will be repeated to see if the leukemia is in remission.

If treatment doesn't reduce the number of blasts, you may receive more treatment, called re-induction. If blasts persist after re-induction, treatment options can be found in *Relapsed and refractory disease* on page 46.

Measurable or minimal residual disease

In measurable or minimal residual disease (MRD), very sensitive lab tests, such as PCR, find leukemia cells in your bone marrow. When testing finds MRD, it's called a positive MRD result or MRD positive (MRD+). MRD positivity doesn't mean treatment wasn't successful, but it may guide next steps.

MRD results may influence decisions about hematopoietic cell transplant (HCT) or additional therapy. Ask your care team what the next steps will be.

Consolidation

Your blood will be given time to recover before starting consolidation. Consolidation is the second phase of treatment. It's also called post-remission therapy. Consolidation treats blasts that may have survived induction. Consolidation may be done to prevent relapse while waiting for hematopoietic cell transplant (HCT).

Monitoring

You'll have frequent blood tests during induction and consolidation. Bone marrow tests are possible.

Maintenance

For some people, maintenance is the final phase of treatment. The goal is to prolong remission, and the treatment may continue for months to years.

Surveillance

Surveillance watches for any changes in your condition after remission or an HCT. You'll have tests during surveillance to check for relapse.

Treatment overview

AML isn't treated the same for everyone. As the body ages, it can have difficulty tolerating higher doses or more intense cancer treatments. In addition to age, your overall health, general level of fitness (performance status), and genetic risk play a role in treatment decisions. Some cancers like AML are treated more aggressively than others. An intensive therapy might have more side effects or be of a higher dose than a less intensive therapy. Intensive therapy isn't necessarily better. Remission or a complete response is still possible with lower-intensity treatments.

All treatments have risk. Talk with your care team about these risks and why a certain treatment might be better for you. Find out how treatment might affect your quality and length of life. Your preferences about treatment are also important.

Risk groups

ELN refers to the system developed by the European LeukemiaNet specifically for AML. This system categorizes people with AML into different risk groups based on various factors, such as age, cytogenetics (chromosomal abnormalities), molecular genetics (gene mutations), and response to initial treatment. The purpose of this risk classification is to help health care professionals predict the likely course of the disease (prognosis) and tailor treatment strategies accordingly.

- The ELN 2022 risk classification system is used to identify people receiving intensive induction therapy who may benefit from more aggressive therapies.
- The ELN 2024 risk classification system is used to predict treatment response in those receiving less intensive induction.

Risk groups describe the leukemia's behavior, not the person's strength or ability to respond to treatment. Risk groups are used to make decisions about treatment and to gain information about the likely course your cancer will take. This is called a prognosis. Risk groups will be used in addition to other factors, such as your age and overall health, to plan treatment. See **Guide 3**.

Some treatments are based on risk groups, while others are specific to an AML subtype such as:

- Therapy-related AML (AML caused by an earlier treatment for a different cancer)
- People who had myelodysplastic syndrome (MDS) or chronic myelomonocytic leukemia (CMML) (previously called antecedent MDS or antecedent CMML)
- AML with chromosome changes consistent with MDS. This used to be called AML with myelodysplasia-related changes (AML-MRC)

Guide 3
ELN risk groups for AML

Favorable risk	Includes any of the following abnormal genes: • t(8;21)(q22;q22.1)/*RUNX1::RUNX1T1* • inv(16)(p13.1q22) or t(16;16)(p13.1q22)/*CBFB::MYH11* • Mutated *NPM1* without *FLT3*-ITD • bZIP in-frame mutated *CEBPA*
Intermediate risk	Includes any of the following abnormal genes: • Mutated *NPM1* with *FLT3*-ITD • Wild-type *NPM1* with *FLT3*-ITD (without adverse-risk genetic lesions) • t(9;11)(p21.3;q23.3)/*MLLT3::KMT2A* • Other abnormalities not classified as favorable or adverse
Poor risk	Includes any of the following abnormal genes: • t(6;9)(p23;q34.1)/*DEK::NUP214* • t(v;11q23.3)/*KMT2A*-rearranged • t(9;22)(q34.1;q11.2)/*BCR::ABL1* • t(8;16)(p11.2;p13.3)/*KAT6A::CREBBP* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2, MECOME(EVI1)* • *t(3q26.2;v)/MECOM(EVI1)*-rearranged • -5 or del(5q); -7; -17/abn(17p) • Complex karyotype, monosomal karyotype • Mutated A*SXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1*, and/or *ZRSR2* • Mutated *TP53*

Intensive induction

Favorable and intermediate risk

Intensive induction options for favorable- and intermediate-risk groups can be found in **Guide 4**.

Poor risk

Induction options for poor-risk groups can be found in **Guide 5**.

Guide 4
Favorable- and intermediate-risk groups: Intensive induction options

Favorable-risk core binding factor (CBF) AML	Preferred therapy: • Standard 7+3 (7 days of Cytarabine plus 3 days of Daunorubicin or Idarubicin) plus Gemtuzumab ozogamicin if CD33 positive
	Other recommended therapies: • Standard 7+3 • FLAG-IDA plus Gemtuzumab ozogamicin if CD33 positive. FLAG-IDA includes Fludarabine, Cytarabine, Granulocyte colony-stimulating factor (G-CSF), and Idarubicin
	Therapy used in certain cases: • FLAG plus Gemtuzumab ozogamicin if CD33 positive
Favorable-risk AML or intermediate-risk AML based on ELN	Preferred therapy: • Standard 7+3
	Other recommended therapies: • Standard 7+3 plus Gemtuzumab ozogamicin if CD33 positive • FLAG-IDA • FLAG-IDA plus Gemtuzumab ozogamicin if CD33 positive • CLAG-M (Cladribine plus Cytarabine, G-CSF, and Mitoxantrone)
AML with *FLT3*-ITD mutation	• Standard 7+3 plus Midostaurin or Quizartinib
AML with *FLT3*-TKD mutation	• Standard 7+3 plus Midostaurin

Less intensive induction

Not everyone wants or can tolerate intensive induction treatment. Age, overall health, and disease features play an important role. Less intensive induction therapy can still cause a complete response. Many people achieve long remissions with lower-intensity treatment. Typically, less intensive chemotherapy will continue indefinitely, as long as it controls the disease and there isn't excess toxicity.

Guide 5
Poor-risk groups: Induction options

Therapy-related AML (not CBF-AML), antecedent MDS or CMML, or AML with chromosome changes consistent with MDS	Preferred therapies: • CPX-351/dual-drug Liposomal Cytarabine and Daunorubicin (preferred for those 60 years of age and over) • Standard 7+3 (preferred for those 60 years of age and under)
	Other recommended therapies: • CPX-351/dual-drug Liposomal Cytarabine and Daunorubicin (for those under 60 years of age) • Standard 7+3 (for those 60 years of age and over) • Decitabine plus Venetoclax • Azacitidine plus Venetoclax • CLIA (Cladribine, Idarubicin, and Cytarabine) • FLAG-IDA (Fludarabine, Cytarabine, G-CSF, and Idarubicin) plus Venetoclax
Poor-risk AML	Clinical trial is recommended
	Other recommended therapies: • Standard 7+3 • CPX-351/dual-drug Liposomal Cytarabine and Daunorubicin • FLAG-IDA • Decitabine plus Venetoclax • Azacitidine plus Venetoclax • CLAG-M (Cladribine with Cytarabine, G-CSF, and Mitoxantrone) • CLIA plus Venetoclax • FLAG-IDA plus Venetoclax
Poor-risk AML with *TP53* mutation or del(17p) abnormality	• Clinical trial

Venetoclax combined with azacitidine or decitabine is a common first treatment for people who can't tolerate intensive chemotherapy.

Treatment options are based on the presence or absence of certain actionable gene mutations. An actionable mutation is one that's likely to respond to a targeted therapy. Actionable mutations include *IDH1*, *IDH2*, and *FLT3*. Treatment options can be found in **Guide 6**.

Guide 6
Less intensive induction options

AML with *IDH1* mutation	Preferred therapies: • Azacitidine or Decitabine plus Venetoclax • Azacitidine plus Ivosidenib
	Other recommended therapy: • Ivosidenib
	Therapies used in certain cases: • Low-dose Cytarabine (LDAC) plus Venetoclax • Azacitidine or Decitabine • Olutasidenib
AML without *IDH1* mutation	Preferred therapy: • Azacitidine or Decitabine plus Venetoclax
	Other recommended therapy: • Cladribine plus LDAC plus Venetoclax
	Other recommended therapies: • LDAC plus Venetoclax • Azacitidine or Decitabine • LDAC plus Glasdegib • LDAC • Gilteritinib with or without Azacitidine (*FLT3*-ITD or TKD mutation) • Enasidenib with or without Azacitidine (*IDH2* mutation) • Gemtuzumab ozogamicin if CD33 positive

After induction

Your next round of induction will be based on which therapy you had first and how AML responded to treatment. Treatment options are based on the amount of cancer, or blasts, that remains after induction, called measurable or minimal residual disease. In hypoplasia, bone marrow is starting to recover but hasn't fully recovered yet. Further treatment is based on if there was a complete response or less than a complete response to induction.

- **If there was a complete response** (remission), then treatment might be a cytarabine-based therapy, a continuation of a previous therapy, or a hematopoietic cell transplant (HCT). A clinical trial is also an option, if available and it's what you want.
- **If there was less than a complete response** or cancer progressed, then options include chemotherapy, targeted therapy, a clinical trial, an HCT, or best supportive care. Best supportive care is treatment to improve quality of life and relieve discomfort.

A lumbar puncture might be done in people who don't have symptoms, but who are at risk of developing leukemia around the brain. There are special criteria to determine who's at risk.

Maintenance

Not everyone who had intensive induction will receive maintenance therapy. If given, it will likely be azacitidine, a chemotherapy.

People who started with lower-intensity therapy and achieve a response typically continue with the same therapy.

For people with a history of *FLT3* mutation, maintenance might be a targeted therapy.

For people who had an HCT, maintenance will be based on your specific situation.

Surveillance

Surveillance is a period of testing that begins after remission to monitor for relapse, or the return of cancer. During surveillance, you'll have a complete blood count (CBC) every 1 to 3 months for 2 years. After that, a CBC should be repeated every 3 to 6 months for up to 5 years. A bone marrow aspirate and biopsy may be needed.

Relapsed and refractory disease

When leukemia returns, it's called a relapse. The goal of treatment is to achieve remission again. You may receive treatment to prevent the blasts from spreading to your brain and spine. A search for an HCT donor should begin at first relapse, if this is an option being considered.

Guide 7
Targeted therapy based on mutation

AML with *FLT3*-ITD mutation
- Gilteritinib
- Hypomethylating agents (HMAs), such as Azacitidine or Decitabine plus Sorafenib
- Quizartinib

AML with *FLT3*-TKD mutation
- Gilteritinib

AML with *IDH1* mutation
- Ivosidenib
- Olutasidenib

AML with *IDH2* mutation
- Enasidenib

AML with *KMT2A* rearrangement
- Revumenib

AML with *NPM1* mutation
- Revumenib
- Ziftomenib

CD33-positive AML
- Gemtuzumab ozogamicin

When leukemia doesn't respond to treatment or worsens during treatment, it's called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment. New therapies and clinical trials continue to expand options for relapsed AML.

Biomarker testing (including *NPM1*, *IDH1*, *IDH2*, and *FLT3* mutations) should be done or repeated at each relapse or progression to determine treatment options.

For relapsed AML or AML that stops responding to treatment after consolidation, options include:

- Clinical trial (strongly preferred)
- Targeted therapy or chemotherapy followed by an HCT
- Best supportive care
- Standard treatment approaches that you didn't have before

Targeted therapy options based on mutation for relapsed or refractory disease can be found in **Guide 7**.

Chemotherapy options for relapsed or refractory disease can be found in **Guide 8**.

AML supportive care

Supportive care aims to improve your quality of life. It includes care for health issues caused by cancer or cancer treatment. It's sometimes called palliative care.

Some types of supportive care are described next. Ask your care team for more information.

Blood transfusions

A blood transfusion replaces blood or blood components, such as red blood cells or platelets. During treatment, you may need blood transfusions. A blood transfusion is a routine procedure where donated blood is given through a vein in your arm. A blood transfusion typically takes 1 to 4 hours, depending on how much is needed and what part of the blood you need.

In people with AML receiving a blood transfusion, most of the white blood cells will be removed from donor blood. If treatment will suppress your immune system, then donor blood will also be treated with radiation. These steps help prevent donor blood from attacking your body. They also help prevent infections.

If you don't want blood transfusions

Treatment without blood transfusions is sometimes referred to as bloodless or transfusion-free care. Treatment of AML requires the use of blood and blood products for supportive care. If you don't wish to receive transfusions or certain blood products, please make your wishes known.

Guide 8
Chemotherapy options: Relapsed and refractory disease

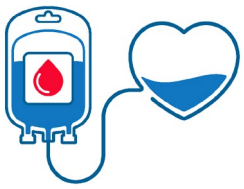
Intensive therapy	• Cladribine plus Cytarabine, Granulocyte colony-stimulating factor (G-CSF). Mitoxantrone or Idarubicin might be added. • Cytarabine. Daunorubicin, Idarubicin, or Mitoxantrone might be added. • Fludarabine plus Cytarabine and G-CSF. Idarubicin, Venetoclax, or both might be added. • Etoposide plus Cytarabine. Mitoxantrone might be added. • Clofarabine. Cytarabine, Idarubicin, or both might be added. • CLIA (Cladribine, Idarubicin, and Cytarabine) plus Venetoclax
Less intensive therapy	• Azacitidine or Decitabine • Azacitidine or Decitabine plus Venetoclax • Low-dose Cytarabine plus Venetoclax

If you don't want blood transfusions, your care team will:

- Minimize blood loss and the risk of bleeding
- Discuss goals of care and complications without transfusion
- Ask if certain blood products can be used under certain circumstances
- Discuss if stem cells (from you or a donor who may or may not be related to you) will be acceptable
- Avoid medicines or procedures that can increase the risk of bleeding or myelosuppression. In myelosuppression, bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets.

If you don't want blood transfusions, your care team might recommend:

- Vitamin K or other options for people at risk of bleeding or to manage bleeding
- Iron, folate, and vitamin B12 supplementation. Iron supplementation may be avoided in someone with excess iron levels.
- An erythropoiesis-stimulating agent, granulocyte colony-stimulating factor, and thrombopoietin after a thorough discussion of potential risks, benefits, and uncertainties
- Bed rest and supplemental oxygen in people with severe anemia



Transfusions

A transfusion is a common procedure to replace blood or blood components (red blood cells or platelets). It's given through an IV (intravenous) line, a tiny tube that is inserted into a vein with a small needle.

- The whole process can take about 1 to 4 hours, depending on how much blood is needed.
- Most transfusions use blood from a donor.
- Blood transfusions are usually very safe. Donated blood is carefully tested, handled, and stored.
- Most people's bodies handle blood transfusions very well. But, like any medical procedure, there are some risks. Speak with your care team for specific information about the risks.
- Systemic therapy can affect how bone marrow makes new blood cells. Some people getting treatment for cancer might need a transfusion of red blood cells or platelets.

Based on your disease, your care team might:

- Test for actionable mutations and consider use of targeted therapies instead of intensive chemotherapy
- Consider use of less myelosuppressive induction, including dose reduction of anthracyclines, and use of non-intensive chemotherapy
- Consider referring you to a center with experience in bloodless autologous (self) hematopoietic cell transplant (HCT)

Growth factors

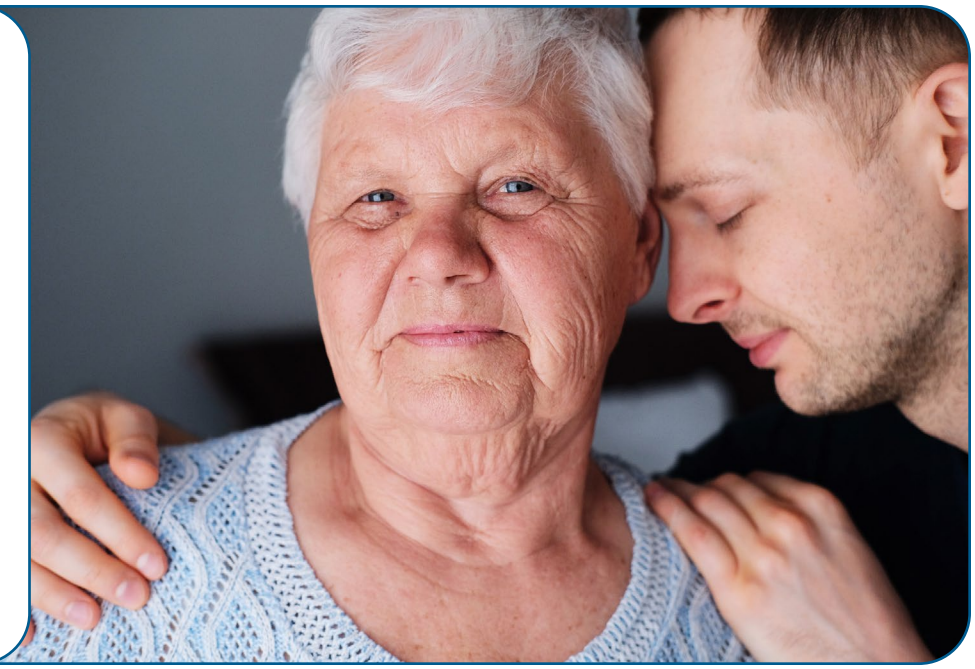
Growth factors, called granulocyte colony-stimulating factors (G-CSFs), trigger the bone marrow to make granulocytes (white blood cells). They are often given when white blood cell counts fall very low during treatment to increase the counts to help prevent infection. They are sometimes part of an aggressive chemotherapy regimen for relapsed or refractory cancer. Growth factors are an option for supportive care during consolidation if you have a life-threatening infection. Filgrastim (Neupogen) is a G-CSF.

A biosimilar or substitute might be used in place of filgrastim. A biosimilar is an almost identical drug made by another company. It's used in the same way and at the same dose as filgrastim.

High white blood cell count

Before treatment, your white blood cell count may be very high. A high count can cause severe health issues. Apheresis or hydroxyurea can quickly reduce the count. Apheresis is a procedure in which blood is collected, certain types of cells are removed, and your blood is returned to your body.

Palliative care is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. It focuses on physical, emotional, social, and spiritual needs that affect quality of life.



Infections

If not treated early, infections can be fatal. Infections can be caused by viruses, bacteria, or fungi. Antibiotics can treat bacterial infections. Antifungal medicines can treat fungal infections. You may be given drugs to prevent infections.

AML treatment side effects

All cancer treatments can cause unwanted health issues called side effects. Some side effects are very serious and rare. Some possible side effects or complications from treatment are described next.

Movement issues

Cytarabine can affect the part of the brain that coordinates movement. Symptoms include constant eye movement that can't be controlled. You may be unable to control the range of movement by your legs or arms. Your speech may become slurred.

Differentiation syndrome

Differentiation syndrome is a potentially serious side effect of certain anti-cancer drugs. It's caused by a large, fast release of cytokines (an immune protein) from leukemia cells that are responding to treatment.

- Symptoms include fever, swelling in limbs, and trouble breathing. You can also gain weight and get a skin rash.
- Signs include low blood pressure and a decrease in blood oxygen levels. Fluid can build up around your lungs or heart. Damage to your kidneys and liver may occur.

Treatment must start at the first signs or symptoms. Steroids are one effective option for treatment. If there's a rising white blood cell count with differentiation, then an antimetabolite called hydroxyurea (Hydrea) is also frequently used.

Eye issues

High-dose cytarabine may cause the white part of your eyes to become red. Your eyes may hurt and make more tears than usual. These issues may be prevented with saline or steroid eye drops.

Tumor lysis syndrome

In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. TLS can be life-threatening. Induction chemotherapy may cause TLS. TLS is more likely if your blast count is very high.

Key points

- Chemotherapy is a key part of acute myeloid leukemia (AML) treatment. Targeted therapy may be added if certain gene mutations are present.
- The goal of treatment is a complete response or remission.
- Measurable or minimal residual disease is AML that appears to be in remission, but very sensitive tests find leukemia cells in your bone marrow.
- Leukemia that returns after remission is called relapse.
- When leukemia doesn't respond to treatment or worsens during treatment, it's called refractory or resistant cancer.
- Supportive care can help to prevent or relieve side effects caused by AML or its treatment and improve quality of life
- Treatment of AML requires the use of blood and blood products for supportive care. If you don't want to receive transfusions or certain blood products, please make your wishes known.

Questions to ask

- How does my risk group affect the treatment options?
- Does the order of treatments matter?
- Which treatment do you recommend and why?
- Why are some treatment options preferred over others?
- Is there someone who can help me decide about treatment?

What's next?

The next chapter explains the diagnosis and treatment of acute promyelocytic leukemia (APL).

6
Treating APL

In acute promyelocytic leukemia (APL), pieces of chromosomes 15 and 17 break off and trade places, creating a fusion of 2 genes called *PML::RARA*. You'll be treated for APL if the *PML::RARA* gene is found.

Overview

Acute promyelocytic leukemia (APL) is a rare subtype of AML. About 1 out of every 10 people with AML have APL. Without treatment, APL can worsen quickly and be fatal. With treatment, APL is cured more often than other AML subtypes. APL is treated with all-trans retinoic acid (ATRA) in combination with another systemic therapy.

Diagnosis

The initial diagnosis of APL may be confirmed by tests such as fluorescence in situ hybridization (FISH) or polymerase chain reaction (PCR). APL can be diagnosed quickly, and treatment can be started within just a few hours.

APL usually occurs when parts of chromosome 15 and chromosome 17 break off and trade places, called translocation. This translocation is written as t(15;17). It makes 2 genes that are fused together. The fusion gene is called *PML::RARA*. You'll be treated for APL if the *PML::RARA* gene is found.

APL can cause bleeding and clotting that can be fatal. You'll start taking a retinoid (ATRA) right away if your doctor suspects APL. ATRA can stop the bleeding and clotting caused by APL. If tests find you don't have APL, then you'll stop taking ATRA.

What causes APL?

In most cases, the causes of APL are not known. Sometimes, certain treatments for other cancers can cause what is known as therapy-related APL.

Treatment phases

Treatment phases for APL include induction and consolidation. Treatment might take place over a period of years. Some types of treatment may be harmful to your heart. Before treatment, your doctor may test how well your heart is working. You may receive treatment for your heart, too.

Treatment response may be measured in the following ways:

- **A hematologic response** measures your blood cell counts.
- **A morphologic response** measures the number of blasts and abnormal cells.
- **A cytogenetic response** measures your chromosomes.
- **A molecular response** measures your molecules (genes).

Induction

Induction is the first phase of treatment. The goal is to reduce the number of blasts and put APL into remission. Treatment is sometimes called remission induction because the focus of induction is remission or a complete response.

In complete remission, there are no signs or symptoms of cancer. It might be more specifically described by the type of remission, such as morphologic or molecular remission. There are different types of complete response or remission. They are described next.

- **A morphologic complete response** occurs when less than 5 percent (5%) blasts are found. This means that fewer than 5 out of every 100 bone marrow cells are blasts. Induction usually causes a large drop in the number of blasts.
- **A cytogenetic complete response** happens when the translocation of chromosomes 15 and 17 or t(15;17) is no longer found, but the *PML::RARA* gene might still be found.
- **A molecular complete response** will likely follow a cytogenetic response. A molecular response is defined as the absence of the *PML::RARA* gene. This means the *PML::RARA* gene isn't found. Often, more treatment (consolidation) is needed to achieve a molecular response.

Treatment needs time to work. Your blood needs time to recover. Blood marrow samples will be taken before starting consolidation. Tests will look for blasts in the marrow. If blasts are absent, induction can be stopped to allow your marrow to make more blood cells.

Consolidation

Consolidation is the second phase of treatment. It treats blasts that may have survived induction. Often, consolidation uses the same drugs as before. Consolidation can cause a long-lasting molecular response. You may have a lumbar puncture before starting consolidation.

Treatment overview

Unlike other subtypes of AML, APL is treated with all-trans retinoic acid (ATRA). Often, ATRA is combined with arsenic trioxide. These treatments are specific to APL. Gemtuzumab ozogamicin, a targeted therapy, might be given. Chemotherapy may also be used.

ATRA

ATRA is made in the body from vitamin A, but it's also made in a lab to treat acne and APL. This drug is also called a retinoid. A retinoid forces APL blasts to mature and become normal cells.

A retinoid is an effective treatment for APL. Used by itself it can achieve a complete response (remission) in most people. However, this response is short-lived. Therefore, other treatments must be added to achieve better results.

Arsenic trioxide

Arsenic trioxide (Trisenox) causes the death of APL cells. When added to ATRA, arsenic trioxide improves treatment outcomes. This means more leukemia cells die, and relapse occurs in fewer people. Your heart and electrolytes will be monitored during treatment with arsenic trioxide.

Low-risk group

People with a white blood cell count of 10 x 10^9/L (10 billion) or less at diagnosis are placed into the low-risk group. For low risk, the preferred induction therapy option is ATRA with arsenic trioxide. Consolidation will include ATRA with arsenic trioxide.

If arsenic trioxide isn't an option, ATRA with idarubicin or gemtuzumab ozogamicin can be used for induction therapy. Consolidation will be a continuation of induction therapy and might include mitoxantrone.

It takes time for blood to recover. You might have a bone marrow biopsy and aspirate before starting consolidation.

High-risk group

People with a white blood cell count of more than 10 x 10^9/L (10 billion) at diagnosis are placed into the high-risk group.

Treatment for high risk is based on if you have:

- No heart issues or heart disease
- Heart issues, such as low ejection fraction or prolonged corrected QT interval (QTc)

In all high-risk groups, ATRA is used as part of induction therapy. After induction, a bone marrow aspirate and biopsy will be done to look for and confirm remission. A lumbar puncture might also be done.

No heart issues

For high risk without heart issues, the preferred induction therapy option is ATRA with arsenic trioxide and either idarubicin or gemtuzumab ozogamicin. Other options include ATRA with daunorubicin and cytarabine or ATRA with idarubicin. Consolidation will be a continuation of induction therapy and might include mitoxantrone.

High risk with heart issues

For high risk with heart issues, induction options are based on the type of heart issue. All induction options include ATRA. Other systemic therapies might be added. Consolidation will be a continuation of induction therapy. A lumbar puncture is possible.

There are 2 types of heart issues that affect treatment:

- **Low ejection fraction** is when the amount of blood pumping from the left side of the heart is lower than normal. This is measured using a multigated acquisition (MUGA) scan or echocardiogram.
- **Prolonged corrected QT interval (QTc)** occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an electrocardiogram (ECG).

Maintenance

Some people may be offered maintenance therapy. This decision is based on your unique situation.

Monitoring

After completing consolidation therapy, you'll enter a monitoring phase. Monitoring is a prolonged period of testing to look for signs that APL has returned, called relapse. PCR tests will be done. Bone marrow or blood samples might be used. You'll have no drug therapy during this time.

Relapse

APL can return after remission. A relapse is possible after either a morphologic or molecular response. In relapse after molecular response, the *PML::RARA* gene has returned. You'll have bone marrow and genetic tests to confirm you have relapsed APL and not AML caused by previous treatment (called therapy-related AML).

Treatment for first relapse will be based on the treatment you have before and if it's:

- **Early relapse** – less than 6 months after treatment
- **Late relapse** – 6 or more months after treatment

The goal of treatment is to achieve remission again. This isn't always possible.

Second therapy

After first relapse treatment is complete, your next therapy will be based on if remission was achieved.

- If remission, then the options are a hematopoietic cell transplant (HCT), arsenic trioxide, or a clinical trial.
- You may receive chemotherapy to prevent APL from spreading to your brain and spine (central nervous system or CNS).
- If no remission, then the options are clinical trial or HCT (matched sibling or another donor).

APL supportive care

Supportive care aims to improve your quality of life. It includes care for health issues caused by cancer or cancer treatment. It's sometimes called palliative care. Palliative care is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. It focuses on physical, emotional, social, and spiritual needs that affect quality of life. Tell your treatment team about any new or worsening symptoms.

Supportive care for APL is described next.

Arsenic trioxide monitoring

Arsenic trioxide can cause serious irregular heart rhythms (arrhythmias). You'll be monitored for a prolonged corrected QT interval (QTc). In prolonged QTc, the heart muscle takes longer than normal to recharge between beats. This electrical disturbance can be seen on an electrocardiogram.

Bleeding

APL can cause bleeding, or coagulopathy, that can be fatal. Your blood will be tested to see how well it clots. Bleeding can usually be managed with platelet transfusions, cryoprecipitate, and fresh frozen plasma. Cryoprecipitate comes from thawed frozen blood.

Differentiation syndrome

In differentiation syndrome, APL treatment causes a large release of cytokines (immune substances) from leukemia cells. Symptoms of differentiation syndrome include fever, swelling in limbs, and trouble breathing. Weight gain and a skin rash are possible. Signs of differentiation syndrome include low blood pressure and a decrease in blood oxygen. Fluid can build up around your lungs or heart. Damage to your kidneys and liver may occur. This syndrome can be fatal if not caught early.

Key points

- Acute promyelocytic leukemia (APL) is a rare subtype of acute myeloid leukemia (AML). With treatment, APL is cured more often than other AML subtypes.
- APL usually occurs when pieces of chromosomes 15 and 17 break off and trade places, creating a fusion gene called *PML::RARA*. You'll be treated for APL if the *PML::RARA* gene is found.
- APL can cause bleeding that can be fatal. You'll start taking a retinoid (all-trans retinoic acid or ATRA) right away if your doctor suspects APL.
- APL is treated with ATRA in combination with another systemic therapy.
- Treatment phases for APL include induction and consolidation. Treatment might take place over a period of years.
- Supportive care aims to improve quality of life and prevent life-threatening health issues caused by APL or its treatment.

Questions to ask

- Which treatment do you recommend and why?
- Does this treatment offer a cure? If not, how well can the treatment stop the cancer from growing?
- What side effects can I expect from this treatment?
- Does the order of treatments matter?
- Is a HCT or a clinical trial an option for me?

What's next?

The next chapter explains the diagnosis and treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN).

7
Treating BPDCN

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a very rare, aggressive blood cancer. It's somewhat like acute myeloid leukemia (AML), but is often misdiagnosed. BPDCN affects skin and lymph nodes. It can also affect the central nervous system, blood, and bone marrow.

Overview

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is cancer of another type of immune cell—immature plasmacytoid dendritic cells (blasts). These blood cells start in the bone marrow and travel to the lymphatic organs, such as the spleen and lymph nodes. Skin lesions are common. BPDCN can also affect the central nervous system.

BPDCN occurs in all races. It's often misdiagnosed because the symptoms and signs vary greatly, and the disease is rare. Therefore, ideally, your treatment team should include doctors from different fields of medicine who are experts in BPDCN.

You might have BPDCN if you have:

- Skin lesions that might be dark purple and large or small spots across the skin. It might look like a rash or bruises. Everyone is different.
- Enlarged lymph nodes
- Stomach pain caused by the disease in the spleen
- Fatigue caused by a decrease in normal blood cells

What causes BPDCN?

People with BPDCN might have had another blood cancer before or can have another blood cancer with BPDCN. These blood cancers include myelodysplastic syndrome (MDS), chronic myelomonocytic leukemia (CMML), and acute myeloid leukemia (AML). MDS is a type of cancer that occurs when bone marrow stops making enough healthy blood cells and abnormal cells are present. MDS starts in the blood stem cells of bone marrow. CMML is a slow-growing type of MDS or myeloproliferative neoplasm (MPN) in which there are too many myelomonocytes, a type of white blood cell, in the bone marrow.

Testing and diagnosis

BPDCN is very difficult to diagnose. It's very important for an expert hematopathologist to review a biopsy when there's concern for BPDCN. A hematopathologist is an expert in analyzing blood diseases and cancers using a microscope.

Almost everyone with BPDCN gets skin lesions. BPDCN is often found through a skin biopsy after a visit to the dermatologist (a skin doctor) for skin lesions. BPDCN may be diagnosed through a lymph node or bone marrow biopsy.

Biomarker and genetic testing will be done to confirm BPDCN and to look for any mutations. Some common gene mutations include *TET2*, *ASXL1*, *ZRSR2*, *SRSF2*, *TP53*, *NRAS*, *IDH2*, and *ETV6*.

For possible tests and procedures, see **Guide 9**.

Treatment overview

BPDCN is a difficult disease to treat. Treatment decisions should involve a team of doctors from different fields of medicine, including a dermatologist, who are experienced in treating BPDCN.

Treatment for BPDCN includes tagraxofusp-erzs (preferred) or high-dose chemotherapy followed by a hematopoietic cell transplant (HCT). Not everyone can tolerate this approach. A lower intensity treatment includes hypomethylating agents (azacitidine or decitabine) with venetoclax. BPDCN usually returns (relapses) soon after treatment.

Seek treatment at a cancer center that specializes in BPDCN.

Intrathecal (IT) chemotherapy will be given to people with central nervous system (CNS) disease at diagnosis or suspected CNS disease. IT chemotherapy might also be given to prevent CNS disease.

Guide 9
Possible tests and procedures: BPDCN

Medical history and physical exam
Complete blood count, platelets, differential, and comprehensive metabolic panel
Analysis of skin lesions (your doctor should work with a dermatologist), blood, bone marrow, and lymph nodes
Bone marrow aspirate and biopsy, lymph node biopsy
BPDCN biomarker and genetic testing
FDG-PET/CT, if leukemia suspected outside the blood and bone marrow (extramedullary) or in lymph nodes
Lumbar puncture with chemotherapy at the time of initial diagnosis, at disease relapse, or any other time when cancer might be in the fluid that surrounds the spine or brain

Intensive therapy

The goal of intensive therapy is to put BPDCN into remission (to achieve a complete response). Intensive therapy isn't for everyone. Treatment will be based on factors such as your overall health and your body's ability to tolerate drug therapies that could be toxic. Your wishes are also important. Talk with your care team about what to expect from treatment and what you want from treatment.

Tagraxofusp-erzs

Tagraxofusp-erzs (Elzonris) targets the CD123 protein marker found at high levels on BDPCN cancer cells. This leads to cancer cell death. You must be in good overall health to receive this treatment. Tagraxofusp-erzs can cause harmful side effects.

The first cycle of this drug should be given in a hospital where it's recommended you stay for at least 24 hours after the treatment is complete. This is to monitor for toxicity and to treat side effects. You'll probably spend more than one week in the hospital.

Chemotherapy

There are 3 chemotherapy induction options:

- HyperCVAD
- Cytarabine with idarubicin or daunorubicin
- CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)

In hyperCVAD chemotherapy, treatment alternates between 2 groups of drugs. Hyper means chemotherapy is given in smaller doses and more often to minimize side effects. CVAD stands for the first group of drugs: cyclophosphamide, vincristine, doxorubicin (also known by its trade name, Adriamycin), and dexamethasone. The second group of drugs consists of methotrexate and cytarabine. Sometimes, other drugs are added.

Complete remission

After a complete response (also called complete remission), options are to continue tagraxofusp-erzs until disease progression or consider an HCT. After an HCT, you'll enter surveillance. Surveillance is a plan that closely watches your condition. You might hear it called watch and wait. During this time, you'll have tests on a regular basis to look for changes in your blood. You won't have any treatment during surveillance.

Surveillance includes a complete blood count every 1 to 3 months for 2 years, then every 3 to 6 months for up to 5 years. You might have a bone marrow aspirate and biopsy. You might also have an FDG-PET/CT if you had extramedullary disease before. Extramedullary disease is cancer that might be in the lymph nodes or other organs. Skin or other lesions might be biopsied.

Less than complete remission

If BPDCN doesn't seem to be responding to treatment or there's less than a complete response, then it will be treated as refractory disease. If the skin still shows microscopic disease, you might have more cycles (at least 4) of therapy before starting treatment for refractory disease.

No intensive therapy

If intensive therapy isn't an option, then treatment options are based on whether BPDCN is systemic or localized. In both cases, treatment is to palliate, or give relief.

Localized disease

If BPDCN is found only in the skin or isolated to a certain area of the body, then treatment will focus on those areas. It might include radiation therapy to the lesion(s) or surgery to remove lesions.

Systemic disease

Systemic means the cancer is throughout the body. Treatment includes venetoclax-based therapy, systemic steroids, and supportive care. Venetoclax-based therapy is a low-intensity targeted therapy that includes azacitidine or decitabine.

Relapsed and refractory disease

When leukemia returns, it's called a relapse. The goal of treatment is to achieve remission again. You may receive treatment to prevent the blasts from spreading to your brain and spine. Relapse is common in BPDCN. Not everyone's cancer responds to treatment in the same way.

When leukemia doesn't respond to treatment or progresses during treatment, it's called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment.

A clinical trial is the preferred treatment for relapsed and refractory BPDCN. Tagraxofusp-erzs is also a preferred option if it was not used before. Other options include systemic therapy or radiation therapy. See **Guide 10**.

Guide 10
Treatment options: Relapsed and refractory BPDCN

Evaluate central nervous system (CNS) for disease
Clinical trial (preferred)
Tagraxofusp-erzs (if not used before) with supportive care
Chemotherapy (if not used before)
Local radiation to isolated areas or specific lesions
Systemic steroids
Hypomethylating agents (Azacitidine or Decitabine) plus Venetoclax
Start a donor search at first relapse for those who are candidates for a hematopoietic cell transplant (HCT) with no sibling donor match

BPDCN supportive care

Supportive care is health care that relieves your symptoms caused by cancer and improves your quality of life. It's not cancer treatment. In BPDCN, supportive care might include radiation therapy or surgery to treat skin lesions. Everyone with BPDCN should have a dermatologist as part of their care team. A dermatologist is a doctor who's an expert in skin disorders. It's important to see an experienced dermatologist and that your doctors work together on your treatment.

Capillary leak syndrome

Tagraxofusp-erzs injection may cause a serious and life-threatening reaction called capillary leak syndrome. In capillary leak syndrome, fluid and proteins leak out of tiny blood vessels causing dangerously low blood pressure. This may lead to organ failure and death. You'll be monitored for capillary leak syndrome. You might be asked to weigh yourself every day while taking tagraxofusp-erzs. Sudden weight gain might be a sign of capillary leak syndrome.

Hypoalbuminemia

Hypoalbuminemia is a medical sign that protein levels of albumin are too low in the blood. It's most often the result of capillary leak syndrome.

Tagraxofusp-erzs

Tagraxofusp-erzs can have very serious side effects. You'll have blood tests to closely monitor your health. Capillary leak syndrome and hypoalbuminemia are serious and life-threatening conditions that can occur if you take tagraxofusp-erzs.

Key points

- Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is cancer of immature plasmacytoid dendritic cells.
- BPDCN affects skin and lymph nodes. It can also affect the central nervous system, blood, and bone marrow.
- BPDCN is often found through a skin biopsy after a visit to the dermatologist for skin lesions.
- BPDCN is treated with a biologic therapy called tagraxofusp-erzs or with a combination of chemotherapies. A hematopoietic cell transplant might follow treatment.
- Capillary leak syndrome and hypoalbuminemia are serious and life-threatening conditions that can occur if you take tagraxofusp-erzs.
- A clinical trial is the preferred treatment for relapsed and refractory BPDCN.

Questions to ask

- What can I expect from treatment and what are the risks?
- How can I find a dermatologist who specializes in BPDCN?
- What side effects should I look for and when should I contact my care team?
- How can I prepare for the possibility of relapse?
- Will the treatment I choose today affect my choices if cancer relapses or is refractory?

What's next?

The next chapter provides information about resources and where you can get support.

Take our survey and help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

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Other resources

Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- Finding an oncologist who's an expert in AML
- Making treatment decisions
- The details of treatment and possible side effects
- Getting financial help
- Coping with cancer treatment and other health challenges

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

AnCan Foundation
ancan.org

Blood & Marrow Transplant Information Network (BMT InfoNet)
bmtinfonet.org

Blood Cancer United
bloodcancerunited.org/patientsupport

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

GRACE
cancergrace.org

HealthTree Foundation
healthtree.org

Imerman Angels
imermanangels.org

Leukemia Research Foundation
leukemiarf.org

National Bone Marrow Transplant Link (nbmtLINK)
nbmtlink.org

NMDP
nmdp.org

PAN Foundation
panfoundation.org

Stupid Cancer
stupidcancer.org

Triage Cancer
triagecancer.org

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?
- What other services are available to me and my caregivers?
- How can I connect with others and build a support system?
- Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?

"Understand your cancer journey, seek out resources that can help you do this, and most of all keep a positive attitude!"

Words to know

acute myeloid leukemia (AML)
A fast-growing cancer of young white blood cells called myeloblasts.

acute promyelocytic leukemia (APL)
A fast-growing subtype of AML.

allogeneic
Donor who may or may not be related to you.

allogeneic hematopoietic cell transplant (HCT)
A treatment in which the patient receives healthy, immature blood-forming cells from another person to replace damaged or diseased cells in the bone marrow. Also called allogeneic stem cell transplant (SCT).

all-trans retinoic acid (ATRA)
ATRA is made in the body from vitamin A. ATRA made in a lab is used to treat APL.

anemia
A health condition in which the number of red blood cells is low.

antimetabolite
A drug that interferes with normal cell division and cell function.

arsenic trioxide
A drug used to treat APL that has the fusion gene *PML::RARA*.

best supportive care
Treatment to improve quality of life and relieve discomfort.

biomarker testing
A lab test of any molecule in your body that can be measured to assess your health. Also called molecular testing.

blast
An immature white blood cell. Also called a myeloblast.

blastic plasmacytoid dendritic cell neoplasm (BPDCN)
A rare, aggressive blood cancer that has features of leukemia, lymphoma, and skin cancer.

blood stem cell
A blood-forming cell from which all other types of blood cells are formed. Also called hematopoietic stem cell.

bone marrow
The sponge-like tissue in the center of most bones where blood cells are made.

bone marrow aspirate
The removal of a small amount of liquid bone marrow to test for a disease.

bone marrow biopsy
The removal of a small amount of solid bone and bone marrow to test for a disease.

chemotherapy
Drugs that kill fast-dividing cells, including cancer cells and normal cells.

chromosome
Long strands that contain bundles of coded instructions for making and controlling cells.

complete remission (CR)
An absence of all signs and symptoms of cancer after treatment. Also called complete response.

consolidation
A shorter and more intense treatment phase to further reduce the number of cancer cells. It's the second phase of treatment.

contrast
A substance put into your body to make clearer pictures during imaging tests.

core binding factor (CBF) AML
A form of AML that creates a shortage of all types of mature blood cells.

cytogenetic complete response
The absence of t(15;17) after treatment for acute promyelocytic leukemia (APL).

cytogenetics
The study of chromosomes using a microscope.

deoxyribonucleic acid (DNA)
Long strands of genetic information found inside cells.

differential
A lab test of the number of white blood cells for each type.

differentiation syndrome
A group of health signs and symptoms that's caused by leukemia or its treatments.

extramedullary
Outside of the bone marrow.

flow cytometry
A lab test of substances on the surface of cells to identify the type of cells present.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal chromosomes and genes.

fusion gene
A gene that's made when parts of 2 separate genes join.

gene
A set of coded instructions in cells for making new cells and controlling how cells behave.

graft-versus-host disease (GVHD)
A disease that occurs when transplanted blood stem cells attack a patient's normal cells.

hematologist
A doctor who's an expert in diseases of the blood.

hematopathologist
A doctor who specializes in the study of blood diseases and cancers using a microscope.

hematopoietic cell
An immature blood-forming cell from which all blood cells are formed. Also called blood stem cell.

hematopoietic cell transplant (HCT)
A treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

human leukocyte antigen (HLA)
Special proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

immunohistochemistry (IHC)
A lab test used to find specific cell traits.

immunophenotyping
A lab test that detects the type of cells present based on the cells' surface proteins.

induction
The first phase of treatment.

maintenance
Usually the last treatment phase given to prolong treatment results.

molecular complete response
The absence of the *PML::RARA* gene after treatment for acute promyelocytic leukemia (APL).

morphologic complete response
A large decrease in number or percent of blasts after treatment for acute myeloid leukemia (AML).

mutation
An abnormal change.

myeloid
Referring to a type of white blood cell called a granulocyte.

myelosuppression
A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets.

pathologist
A doctor who's an expert in testing cells and tissue to find disease.

peripheral blood
Blood that circulates throughout the body.

platelet
A type of blood cell that helps control bleeding. Also called thrombocyte.

polymerase chain reaction (PCR)
A lab process in which copies of a piece of DNA are made.

prognosis
The likely course and outcome of a disease.

progression
The growth or spread of cancer during or after treatment.

recovery
A period of time without treatment to allow blood cell counts to return to normal.

red blood cell (RBC)
A type of blood cell that carries oxygen from the lungs to the rest of the body. Also called an erythrocyte.

refractory
A cancer that doesn't improve with treatment.

regimen
A treatment plan that includes specific information about drug dose, when medicine is taken, and how long treatment will last.

relapse
The return or worsening of cancer after a period of improvement.

remission
Minor or no signs of a disease.

resistance
When cancer doesn't respond to a drug treatment.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

standard of care
The best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that's considered standard of care.

subtype
A smaller group within a type of cancer that's based on certain cell features.

supportive care
Health care that includes symptom relief but not cancer treatment. Also called palliative care or best supportive care.

surveillance
Testing that's done after treatment ends to check for the return of cancer.

systemic therapy
Treatment that works throughout the body.

targeted therapy
A drug treatment that targets and attacks specific cancer cells.

translocation
When pieces of 2 chromosomes (long strands of coded instructions for controlling cells) break off and switch with each other.

tumor lysis syndrome (TLS)
A condition caused when waste released by dead cells isn't quickly cleared out of your body.

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

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia, Version 3.2026. It was adapted, reviewed, and published with help from the following people:

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Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
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Duke Cancer Institute
Durham, North Carolina

Fox Chase Cancer Center
Philadelphia, Pennsylvania

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Madison, Wisconsin

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut

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Cancer care recommendations from leading experts at the
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Acute Myeloid Leukemia

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