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NCCN GUIDELINES FOR PATIENTS®

2020

Acute Myeloid Leukemia

Presented with support from: NCCN FOUNDATION
NATIONAL COMPREHENSIVE CANCER NETWORK
Guiding Treatment. Changing Lives.

Available online at NCCN.org/patients

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- ✓ Step-by-step guides to the cancer care options likely to have the best results
- ✓ Based on treatment guidelines used by health care providers worldwide
- ✓ Designed to help you discuss cancer treatment with your doctors

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NCCN®

- ✓ An alliance of 28 leading cancer centers across the United States devoted to patient care, research, and education

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Guiding Treatment. Changing Lives.

These NCCN Guidelines for Patients® are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia (Version 3.2020, December 23, 2019).

NCCN Foundation® seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients®. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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Aplastic Anemia and MDS International Foundation (AAMDS)

An organization that strongly supports educating patients and physicians about bone marrow failure diseases like aplastic anemia, MDS, and PNH, as well as related diseases like AML, the Aplastic Anemia and MDS International Foundation is proud to support this comprehensive resource for patients and their families. aamds.org

Be The Match®

National Marrow Donor Program® (NMDP)/Be The Match® is the global leader in providing a possible cure to patients with life-threatening blood and marrow cancers, as well as other diseases. Our Be The Match Patient Support Center provides support, information and resources for patients, caregivers and families. We are here to help you get reliable, easy-to-understand information from diagnosis through recovery. Contact us for confidential, one-on-one support from caring experts. We'll listen and help you find answers. All of our programs and resources are free. Call 1-888-999-6743 or email: patientinfo@nmdp.org bethematch.org

National Bone Marrow Transplant Link (nbmtLINK)

Educating and informing people about their cancer diagnosis as well as the transplant process is an important part of the National Bone Marrow Transplant Link's mission and contributes to the psychosocial support of bone marrow/stem cell transplant and CAR T-cell therapy patients and their caregivers. For information and resources, please visit nbmtlink.org, call toll free at 800-LINK-BMT, or e-mail info@nbmtlink.org. The LINK is supportive of resources like the NCCN Guidelines for Patients. nbmtlink.org

The Leukemia & Lymphoma Society (LLS)

LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients. LLS.org/PatientSupport

To make a gift or learn more, please visit NCCNFoundation.org/donate or email PatientGuidelines@nccn.org


BLOOD
TEST

Contents

1
Leukemia basics

Acute myeloid leukemia (AML) is a fast-growing blood cancer that starts in the blood stem cells of bone marrow. There are many types of AML. Learn how AML starts in adults. This will help you prepare and plan for treatment.

Blood

Acute myeloid leukemia (AML) is a blood cancer. Blood is a tissue. A tissue is a group of cells that work together to perform a function. Blood's function is to move oxygen and nutrients throughout your body and carry away waste. Your blood contains different types of blood cells that float in plasma. Plasma is a clear, yellowish fluid made up of mostly water. More than half of your blood is plasma.

Blood cells

There are 3 types of blood cells:

- Red blood cells (erythrocytes)
- White blood cells (leukocytes)
- Platelets (thrombocytes)

Blood cells have important jobs. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help control bleeding.

Blood cells don't live forever. Many have a short lifespan. Some white blood cells live less than one day. Your blood cells are being replaced in your body all the time.

How blood cells are formed

Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are cells that make blood. These young or immature cells are called blood stem cells (hematopoietic stem cells). All types of 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. With each stage the blood stem cell changes and gets closer to what it is meant to be. After a blood cell develops into a red blood cell, white blood cell, or platelet, it is released in your bloodstream as needed.

Blood stem cells can do 2 things:

- Make exact copies of themselves
- Make new cells that have the potential to become red blood cells, white blood cells, or platelets

Blood stem cells can copy themselves or self-renew. These cells are rare.

Blood stem cells can make new cells that are committed to being a certain type of blood cell. These are called progenitor cells and are much more common than blood stem cells. Progenitor cells can become red blood cells, white blood cells, or platelets.

There are 2 types of blood progenitor cells:

- Lymphoid
- Myeloid

Both lymphoid and myeloid progenitor cells form into blast cells. There are different types of blasts. Myeloid blasts or myeloblasts are committed to becoming a type of white blood cell.

Lymphoid progenitor cells

Lymphoid progenitor cells develop into a type of white blood cell called lymphocytes. Lymphocytes are released from bone marrow into the bloodstream.

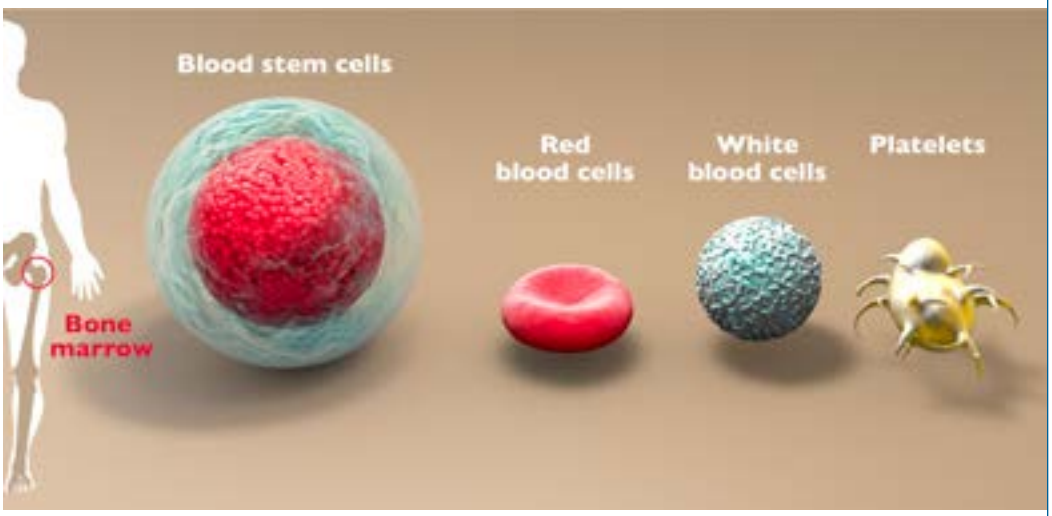
Myeloid progenitor cells

Myeloid progenitor cells develop into white blood cells, red blood cells, and platelets. Myeloid progenitor cells that become white blood cells are called granulocytes. These are different than the white blood cells produced by lymphoid progenitor cells. Granulocytes include neutrophils, eosinophils, and basophils. Red blood cells, platelets, and granulocytes are released from bone marrow into the bloodstream.

AML starts in myeloid progenitor cells. To be diagnosed with AML, 20 percent (20%) or more myeloblasts must be present in the marrow or blood. This means that at least 2 out of every 10 marrow cells are blasts. In certain cases, a diagnosis of AML is possible with less than 20% blasts.

Blood stem cells

Bone marrow contains stem cells. A blood stem cell is an immature cell that can develop into a red blood cell, white blood cell, or platelet.



Acute myeloid leukemia

Cancer is a disease that starts in the cells of your body. Leukemia is cancer of the white blood cells.

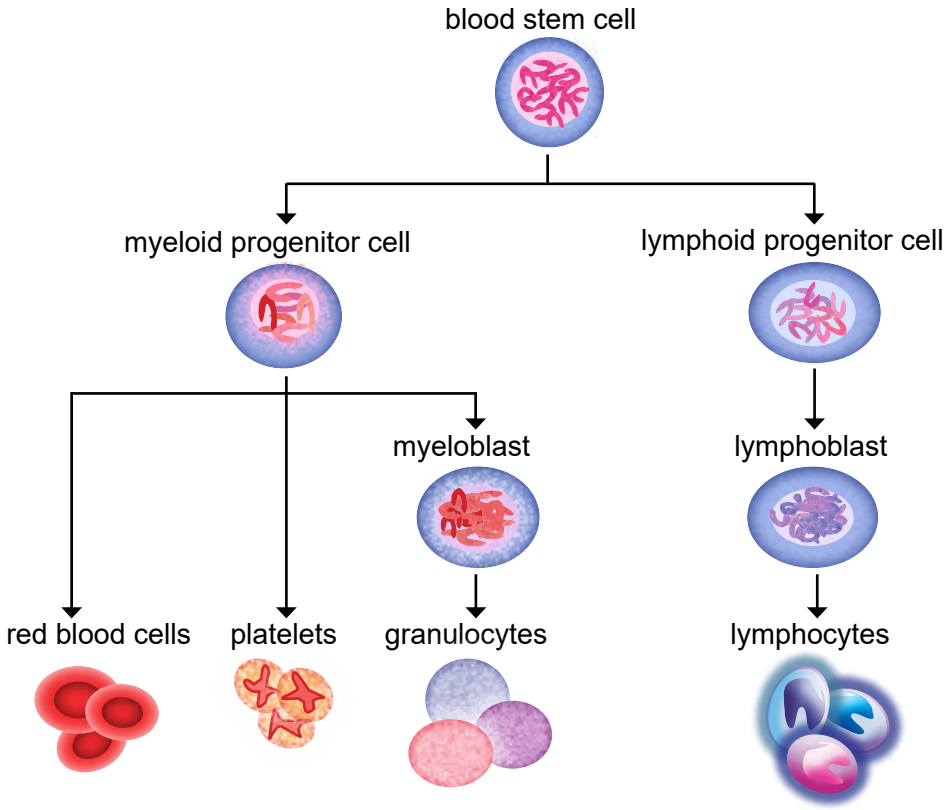
There are different types of leukemia, which include:

- Acute lymphocytic leukemia (ALL)
- Acute myeloid leukemia (AML)
- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)

AML is a fast-growing cancer of myeloid progenitor cells. Changes in these cells stop myeloid blasts (or myeloblasts) from becoming mature blood cells. As a result, there is a buildup of blasts in the marrow and blood. In turn, there are not enough red blood cells, platelets, and mature granulocytes. This causes serious health problems. If untreated, AML is fatal.

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.



Abnormal cell changes

Cells in your body contain chromosomes. Chromosomes are long strands of genetic information called DNA (deoxyribonucleic acid). Your DNA uses coded instructions to tell your cells what to do. These instructions are called genes.

Cancer starts when something goes wrong in the DNA of a cell. Often, there are abnormal changes in the genes of cancer cells. These abnormal changes are called mutations. Mutations are often found in AML.

Types of AML

AML is a group of diseases. There are many types of AML. They are grouped and treated based on gene mutations and other features. Genetic testing is very important to identify the AML subtype. It is a standard part of testing at diagnosis. You will learn more about this in the next chapter.

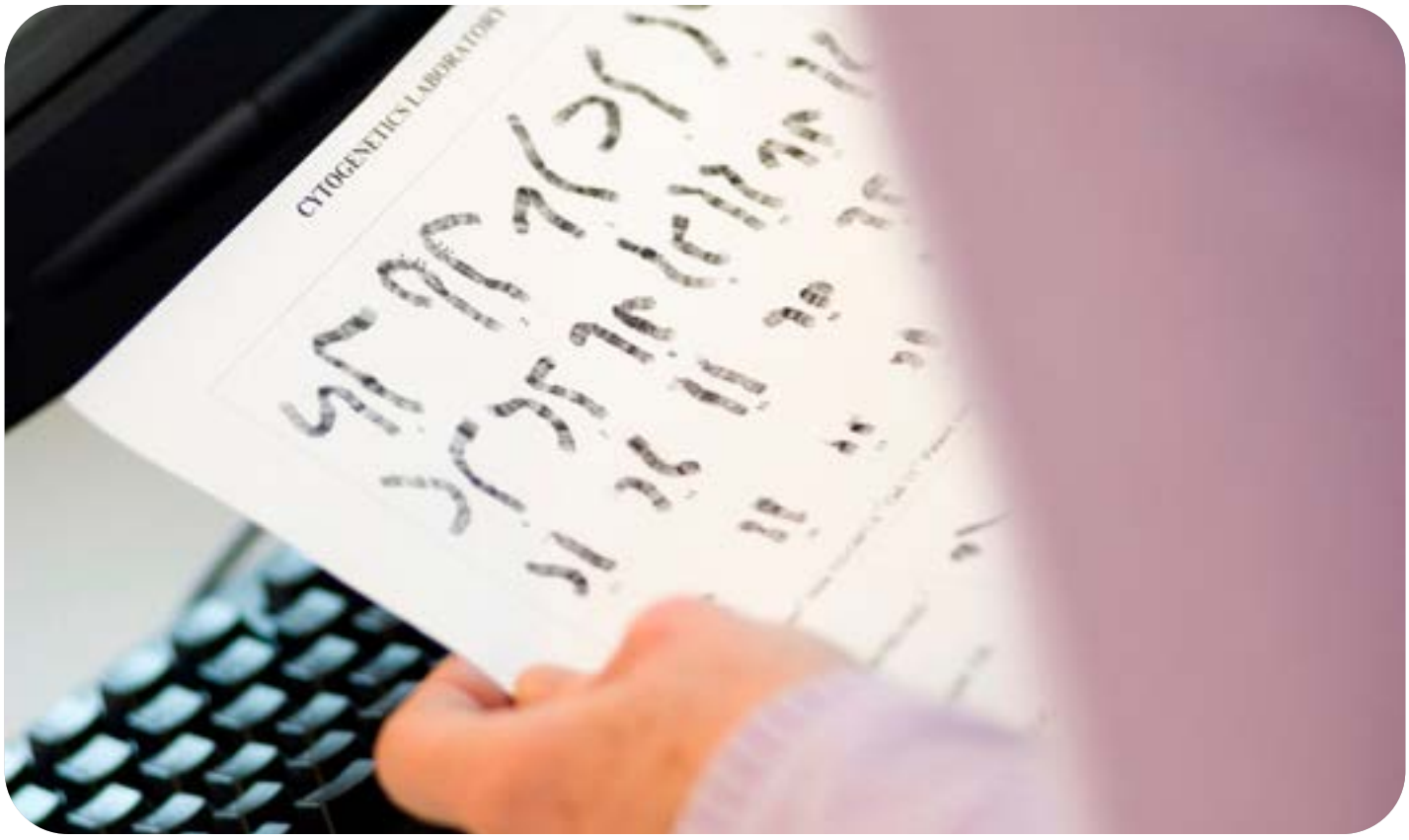
Treatment chapters in this book are divided into:

- Acute promyelocytic leukemia (APL)
- Acute myeloid leukemia (AML)
- Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Review

- There are 3 types of blood cells: red blood cells (erythrocytes) carry oxygen, white blood cells (leukocytes) fight infection, and platelets (thrombocytes) help blood to clot.
- Acute myeloid leukemia (AML) is a blood cancer of the myeloid progenitor cells. Changes in these cells stop myeloid blasts from becoming mature blood cells. As a result, there is a buildup of blasts in the marrow and blood making it hard for blood to do its work.
- Myeloid progenitor cells develop into red blood cells, granulocytes (a type of white blood cell), and platelets.
- To be diagnosed with AML, 20 percent (20%) or more myeloid blasts must be present in the marrow or blood. This means that at least 2 out of every 10 marrow cells are blasts. In certain cases, a diagnosis of AML is possible with less than 20% blasts.
- There are many subtypes of AML. They are grouped and treated based on gene mutations.
- Genetic testing is very important to identify the AML subtype.

2
Testing for AML



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

A diagnosis of AML is based on the presence of 20 percent (20%) or more myeloid blasts in the marrow or blood. This means that at least 2 out of every 10 marrow cells are blasts. However, in some cases a diagnosis of AML is possible with less than 20% blasts. Accurate testing is needed to diagnose and treat AML. See Guide 1.

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbs, or supplements you take. Tell your doctor about any symptoms you have. A medical history will help determine which treatment is best for you.

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Physical exam

A physical exam is a study of your body. A doctor will check your body for signs of disease.

A health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you
- 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. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell the doctor if you have felt any lumps or have any pain.
- Look for skin lesions on your body

Doctors should perform a thorough physical exam along with a complete health history.

Bring a list of any medications, vitamins, over-the-counter drugs, herbs, or supplements you take.

Guide 1 Testing for AML
Medical history and physical exam
CBC, platelets, differential, comprehensive metabolic panel (CMP), uric acid, and lactic acid
Blood clotting tests: PT, PTT, and fibrinogen
Bone marrow biopsy, bone marrow aspirate, immunophenotyping, and cytochemistry
Cytogenetic analysis (karyotype and FISH)
Molecular analysis of at least: *c-KIT*, *FLT3* (ITD and TKD), *NPM1*, *CEBPA*, *IDH1*, *and IDH2*
Comprehensive pathology report with cytogenetics, blast count, and more
HLA typing for blood stem cell transplant (HCT) candidates and/or referral to transplant center
Brain CT without contrast, if central nervous system (CNS) bleed suspected
Brain MRI with contrast, if leukemic meningitis suspected
PET/CT if extramedullary disease suspected
Lumbar puncture
Heart tests such as electrocardiogram, echocardiogram, or MUGA scan

Blood tests

Blood tests check for signs of disease, how well organs are working, and treatment results. They require a sample of your blood, which is removed through a needle placed into your vein.

Be prepared to have a lot of blood tests. You might have blood tests as often as every 6 to 48 hours during AML treatment and recovery.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Remember, all of these cells are made in your bone marrow. A CBC is a key test that gives a picture of your overall health. AML often causes low counts of healthy blood cells.

There are several types of white blood cells. A CBC with differential counts the number of each type of white blood cell. It also checks if the counts are in balance with each other. This test may show a high number of blasts in the blood.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) is a test that measures 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things. A CMP includes some of the following tests.

Electrolytes

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. Phosphate (PO4) is important for strong bones and teeth. Too much phosphate in blood can be a sign your kidneys aren't working well.

Blood urea nitrogen

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 your kidneys aren't working well.

Creatinine

Creatinine is a waste produced in the muscles. It is filtered out of the blood by the kidneys and tells how well the kidneys are working.

Liver function tests

Liver function tests look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well.

Lactic acid

Lactate dehydrogenase (LDH) or lactic acid is a protein found in most cells. Dying cells release LDH into blood. Fast-growing cells also release LDH. High levels of LDH can be a sign of AML.

Uric acid

Uric acid is released by cells when DNA breaks down. It is a normal waste product that dissolves in your blood and is filtered by the kidneys where it leaves the body as 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. High uric acid might be a side effect of chemotherapy or radiation therapy.

Be prepared to have a lot of blood tests. You might have blood tests as often as every 6 to 48 hours during AML treatment and recovery.

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.

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

There are 3 tests that look for coagulopathy:

- **Prothrombin time (PT)** - measures how long it takes blood to clot
- **Partial thromboplastin time (PTT)** – measures how long it takes blood to clot
- **Fibrinogen activity** - measures how much fibrinogen, a blood protein, is being made by the liver

It is standard to screen for clotting problems.

Tissue tests

A biopsy is the removal of a sample of tissue or group of cells for testing. If the blastic plasmacytoid dendritic cell neoplasm (BPDCN) subtype of AML is suspected, you might have a lymph node biopsy or a skin lesion biopsy. This would be in addition to the standard bone marrow tests described next.

Bone marrow tests

Leukemia starts in the bone marrow. To diagnose AML, samples of bone marrow must be removed. Lab results will be used to confirm the disease. Your bone marrow will also be tested to see how well treatment is working.

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

- Bone marrow aspiration
- Bone marrow biopsy

The samples are usually taken from the back of the hip bone (pelvis). Ask your doctor about the type of bone marrow test you might have, where the sample will be taken, and what you will be given to help you relax.

A hematologist is a doctor who specializes in the study of blood diseases and cancers. A hematopathologist is a doctor who specializes in blood diseases by looking at cells under a microscope. The hematopathologist will study the results of various blood and bone marrow tests and write a report that will be sent to your doctor.

Aspiration and biopsy

A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a core sample of bone.

You will likely lie on your belly or side. Your doctor will first clean and numb your skin. The outer surface of your bone will be numbed, too.

For aspiration, a hollow needle will be pushed through your skin and into the bone. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be used to remove a core sample. The samples will be sent to a lab for testing. You may feel bone pain at your hip for a few days. Your skin may bruise.

Testing takes time. It might take days or weeks for all test results to come in.

Immunophenotyping

Immunophenotyping (said immuno-fee-no-typing) uses antibodies to detect the presence or absence of white blood cell antigens. These antigens are proteins that can be found on the surface of or inside white blood cells. They are called markers or biomarkers. Certain biomarkers are targeted in AML treatment.

A complete blood test can count the number of white blood cells, but it cannot detect the subtle differences between different types of blood cancers. Immunophenotyping can detect these subtle differences.

There are 2 testing methods:

- Flow cytometry
- Immunohistochemistry

Flow cytometry

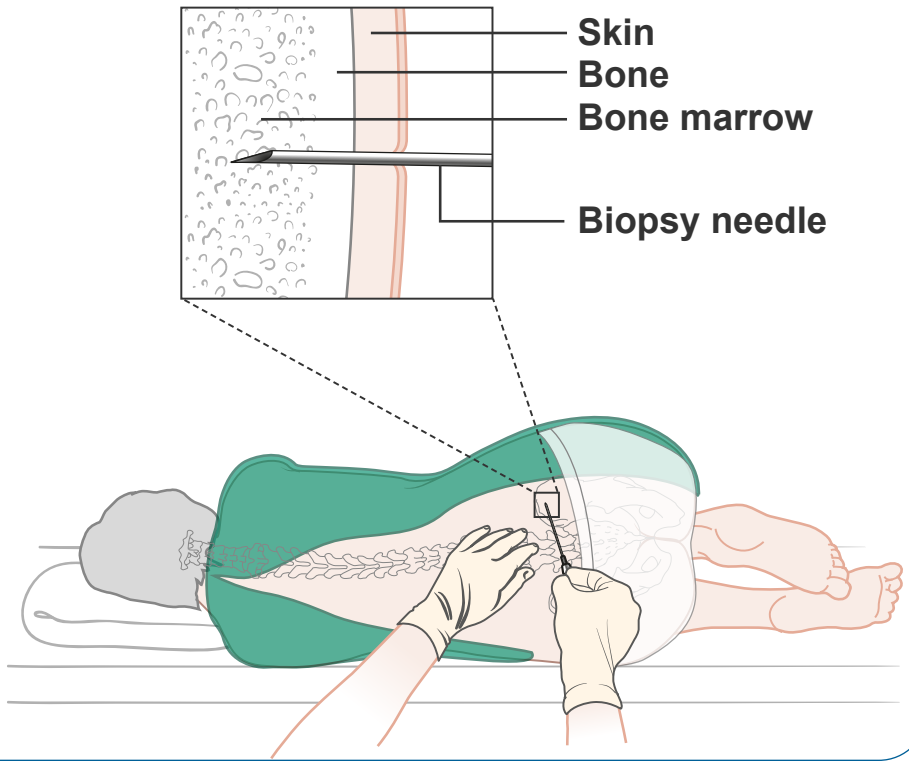
This method involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine measures the number of cells, things like the size and shape of the cells, and proteins on the surface of thousands of cells.

Immunohistochemistry

Immunohistochemistry (said immuno-histo-chemistry or IHC) is a special staining process that involves adding a chemical marker to cells. The cells are then studied using a microscope.

Bone marrow biopsy

Samples of bone and marrow are removed in a biopsy.



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Genetic tests

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome.

Normal human cells contain 23 pairs of chromosomes. Each chromosome contains thousands of genes. Genes tell cells what to do and what to become. Most genes contain information about a specific protein. Genes can be turned on and off.

AML cells sometimes have chromosome changes that can be seen under a microscope or found with other tests.

Cytogenetic testing

Cytogenetics is the study of chromosomes, which contain most of the genetic information in a cell. Cytogenetics involves testing samples of blood, tissue, and bone marrow to look for broken, missing, re-arranged, or extra chromosomes. Chromosomes are often abnormal in AML cells. Testing looks for common defects. Results help confirm AML and predict the path it will take. This is called a prognosis. The type of AML will also be identified for treatment planning.

Cytogenetic testing uses a microscope to look for abnormalities. Not all chromosome changes can be seen under a microscope. Other lab tests can help find these changes.

There are 2 types of cytogenetic tests used in AML:

- Karyotype
- FISH

Karyotype

A karyotype is a picture of chromosomes. Doctors look for whether 23 pairs of chromosomes are present. They also look for missing or abnormal pieces of chromosomes.

FISH

A fluorescence in situ hybridization (FISH) is a method that involves special dyes, called probes, which attach to pieces of DNA. Doctors can then look for defects such as translocation or inversion that are too small to be seen with other methods.

- A translocation is the switching of parts between two chromosomes. Possible translocations in AML are written as t(15;17), t(8;21), and t(16;16).
- An inversion is a switching of parts within one chromosome. A type of inversion in AML is inv(16).

Molecular testing

Molecular testing is very important to identify the AML subtype and is a standard part of testing at diagnosis. Molecular testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might affect treatment. Proteins are written like this: CD33. Genes are written like this: *FLT3.*

Molecular test results are used to predict the outcome of AML called a prognosis. An actionable mutation is one that is likely to directly impact treatment. The presence of these actionable mutations will also affect treatment: *CBF*, *FLT3* (ITD and TKD), *NPM1*, *IDH1*, and *IDH2*.

You might see specific treatment options in this book for:

- CD33
- *FLT3* (ITD and TKD)
- *IDH1*
- *IDH2*

Other genes that may be tested in AML include: *TP53*, *KIT*, *DNMT3A*, *RUNX1*, and *ASXL1*.

Molecular testing can also detect fusion genes made by translocations. An example of two fused genes is *PML-RARA* and *RARA-PML*. *RARA-PML* is found in those with acute promyelocytic leukemia (APL).

PCR

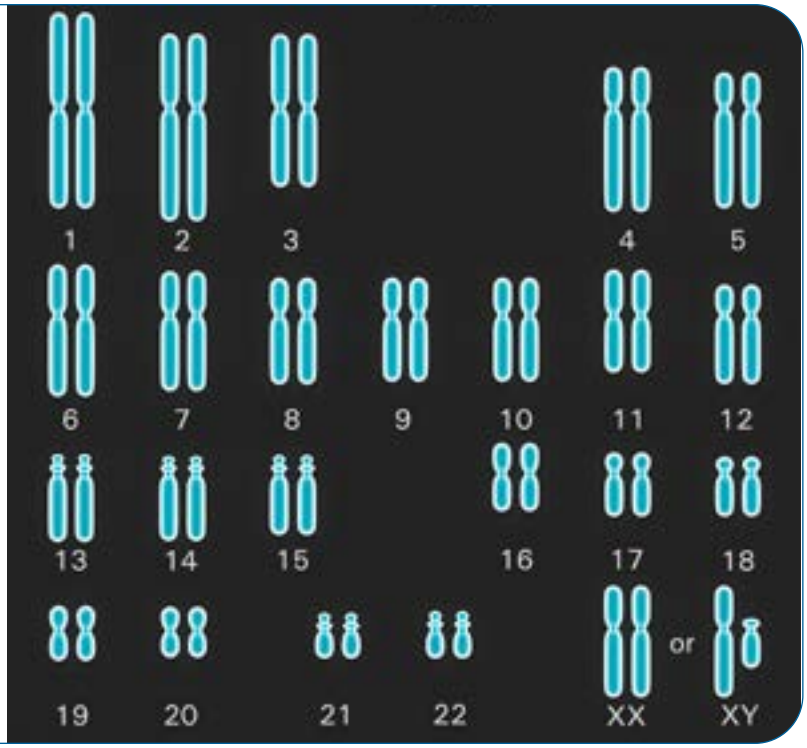
A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA in just a few hours, but test results can take days. PCR is very sensitive, more sensitive than cytogenetic tests. It can find 1 leukemia cell among more than 100,000 cells. This is important when testing for treatment response or remission. It is part of molecular testing.

Genetic testing recommendations

Genetic testing is recommended for everyone diagnosed with AML. Certain tests might not be available in your area. If this is the case, it is advised that an original sample be saved for future testing at an outside lab. Ask your doctor which molecular tests you will have and if there is a need to save a blood sample. Your doctor should consult a pathologist on how make the best use of the sample. Additional testing may also be recommended.

Karyotype

A karyotype is a picture of the chromosomes in cells. It is a test that shows abnormal changes in chromosomes.



HLA typing

A 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 are unique to each person. They mark your body's cells. Your body detects these markers to tell which cells are yours. In other words, all 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 blood stem cell transplant. Your proteins will be compared to the donor's white blood cells to see how many proteins are the same in order to find the best match. 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.

Who needs HLA typing?

HLA typing should be done in all patients with newly diagnosed AML for whom allogeneic (donor) blood stem cell transplant is an option. HLA typing of family members up to 80 years of age is recommended. Tissue typing should include searches for other possible donors.

Imaging tests

Leukemia can spread outside the bloodstream. It rarely spreads to the lining of the brain and spinal cord. It can spread to disease-fighting structures called lymph nodes. It can also spread to the liver, spleen, and skin.

Imaging tests take pictures of the insides of your body. These tests are used to show which sites have leukemia. They can also show sites of infection or bleeding. Such health problems may impact your care.

To prepare for these tests, you may need to stop taking some medicines. Also, you may be asked to stop eating and drinking for a few hours before the scan. Tell your doctor if you get nervous when in small spaces. You may be given a pill to help you relax.

Some imaging tests use contrast. Contrast is a substance used to improve the pictures inside the body. It helps certain areas of the body stand out. Tell your doctor if you've had bad reactions to contrast in the past. This is important. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

A radiologist, who is an expert that looks at test images, will review your images and write a report. The radiologist will send the report to your doctor who will discuss the results with you. Feel free to ask as many questions as you like.

Brain CT

A computed tomography (CT or CAT) scan uses hundreds of x-rays and computer technology to take pictures from many angles to create real-looking images of the inside your body. All of the images are combined to make one detailed picture. A CT of the brain is used to look for bleeding. Contrast should not be used.

Brain MRI

A magnetic resonance imaging (MRI) scan uses radio waves and strong magnets to make detailed pictures. It can show if the outer layer of the brain is swollen. Swelling caused by leukemia is called leukemic meningitis.

A device will be placed around your head that sends and receives radio waves. Contrast should be used.

PET/CT

A positron emission tomography uses a radioactive drug called a tracer. A tracer is a substance put into your body. Cancer cells show up as bright spots on PET scans.

Sometimes CT is combined with PET. This combined test is called a PET/CT scan. It may be done with one or two machines depending on the cancer center. It is used to detect leukemia in organs.

Spinal fluid tests

Leukemia can travel to the fluid that surrounds the spine or brain. This may cause symptoms. In order to know if leukemia cells are in your spinal fluid, a sample must be taken and tested.

A lumbar puncture is a procedure that removes spinal fluid. It is also called a spinal tap. A lumbar puncture may also be used to inject cancer drugs into spinal fluid. This is called intrathecal chemotherapy.

During a spinal tap, you will be lying down or sitting on an exam table. If lying down, your knees must be tucked up near your chest. If sitting, you must lean forward toward your knees.

The lower part of your back over your spine will be numbed. Next, a thin needle will be inserted between your spinal bones. You may feel some pressure. After the sample is taken, it will be sent to a lab for testing.

A lumbar puncture might be used to rule out a central nervous system (CNS) disease.

Heart tests

Heart or cardiac tests might be needed to see how well your heart works.

Electrocardiogram

An electrocardiogram (ECG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged QT interval (or QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an ECG. Many drugs used to treat AML can affect QT.

Echocardiogram

An echocardiogram (or echo) uses sound waves to make pictures. 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 is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart every time it beats. In low ejection fraction, the amount of blood pumping from the left side of the heart is lower than normal.

MUGA

A multigated acquisition (MUGA) scan is used to evaluate the pumping function of your heart. During the test, a small amount of radiotracer is injected into a vein. A special camera, called a gamma camera, will create computer-generated movie images of your beating heart.

MUGA scan might show low ejection fraction. This is when the amount of blood pumping from the left side of the heart is lower than normal.

Test results

Results from all of these tests will determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

Whether you are going for a second opinion, test, or office visit, keep these things in mind:

- Bring someone with you to doctor visits. Encourage this person to ask questions and take notes.
- Write down questions and take notes during appointments. Don't be afraid to ask questions. Get to know your care team and let them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have. It will be helpful when getting a second opinion.
- Organize your papers into a medical binder or notebook. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your binder or notebook. Hang the list on your fridge or keep by the phone.

Review

- Blood tests check for signs of disease, how well organs are working, and treatment results. Blood clotting tests will also be done.
- A bone marrow aspiration and biopsy are procedures that remove bone and marrow samples. Your marrow will be tested for markers of leukemia cells.
- Genetic test results are used to predict the outcome of AML called a prognosis. Results are also used for treatment planning.
- Genetic testing is recommended for anyone with AML.
- A translocation is the switching of parts between two chromosomes. Possible translocations in AML are t(15;17), t(8;21), and t(16;16).
- An inversion is a switching of parts within one chromosome. A type of inversion in AML is inv(16).
- HLA typing should be done in all patients with newly diagnosed AML for whom allogeneic (donor) blood stem cell transplant is an option.
- Imaging tests are used to look for sites of infection, bleeding, and leukemia that might have spread outside the bloodstream.
- A lumbar puncture may be done to look for leukemia in spinal and brain fluid.
- Heart or cardiac tests might be needed to test how well your heart works.

Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and tests results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments. You never know when you might need it!

3
Treatment options

Treatment is based on the type of AML. This chapter provides a general overview of some therapies you might receive.

Chemotherapy

Chemotherapy is a type of drug therapy used to treat cancer. Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. Chemotherapy drugs used for the treatment of AML affect the instructions (genes) that tell cancer cells how and when to grow and divide. This disrupts the life cycle of cancer cells.

There are 2 types of chemotherapy used to treat AML:

- **Anthracyclines** damage and disrupt the making of DNA causing cell death of both cancerous and non-cancerous cells.
- **Anti-metabolites** prevent the "building blocks" of DNA from being used.

Chemotherapy is most often a liquid that is slowly injected into a vein with a needle. The final dose differs between people because it is based on body weight. Intrathecal chemotherapy is injected into spinal or brain fluid.

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 will have tests to see how well treatment is working. You might spend time in the hospital during treatment.

Anthracyclines

Anthracyclines damage and disrupt the making of DNA, thus causing cell death of both cancerous and non-cancerous cells.

Here is a list of some of the anthracyclines used to treat AML:

- Daunorubicin (Cerubidine®)
- Idarubicin (Idamycin PFS®)
- Mitoxantrone (Novantrone®)

Daunorubicin, idarubicin, and mitoxantrone drugs can cause heart problems. They may not be an option for you. There is a limit to how much you can receive in your lifetime.

Anti-metabolites

Anti-metabolites prevent the "building blocks" of DNA from being used.

Here is a list of some of the anti-metabolites used to treat AML:

- Cytarabine (Cytosar-U®)
- Cladribine (Leustatin®)
- Fludarabine (Fludara®)
- Clofarabine (Clolar®)
- Methotrexate

Dual-drug liposome of cytarabine and daunorubicin (Vyxeos™) includes an anti-metabolite and an anthracycline.

Cytarabine

Cytarabine or Ara-C is used in many treatment regimens. It might be used alone or in combination with other drugs. It might be given as a single dose to reduce a very high white blood cell count.

There are different doses for cytarabine:

- Standard
- High (HiDAC)
- Intermediate
- Low (LDAC)

The dose you will receive is based on many factors. Ask your doctor for the details of your treatment.

- What is the dose?
- How often is treatment received?
- How many treatment cycles are needed?
- Will I need to spend time in the hospital? If so, how long?

Cytarabine or methotrexate may be used to treat AML in the fluid that surrounds the spine or brain. In this case, it is injected into the spinal fluid. This is called intrathecal chemotherapy.

Hypomethylating agents

Methyl groups are molecules that are found in DNA. It can turn genes on or off. 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. Decitabine (Dacogen®) and azacitidine (Vidaza®) are two such agents. They turn silenced genes back on, which allows leukemic blasts to mature.

HMAs may be a good option if you are older or are quite sick. They also work well against leukemia cells with high-risk markers. It will take time to see results. These agents are also sometimes used for maintenance therapy.

Targeted therapy

Targeted therapy is a form of systemic therapy that works throughout the body. It is drug therapy that focuses on specific or unique features of cancer cells. Targeted therapy might be used alone or in combination with chemotherapy.

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.

Here is a list of some targeted therapies you might receive:

- Gemtuzumab (Mylotarg™)
- Gilteritinib (Xospata®)
- Enasidenib (Idhifa®)
- Ivosidenib (Tibsovo®)
- Sorafenib (Nexavar®)
- Midostaurin (Rydapt®)
- Venetoclax (Venclexta™)

Targeted therapy might be used to target:

- CD33 surface protein
- *CBF* mutation
- *FLT3* (ITD and TKD) mutation
- *IDH1* mutation
- *IDH2* mutation

CD33

Gemtuzumab ozogamicin (GO) is a type of targeted therapy that is 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 do not have CD33 and are not affected.

GO may delay count recovery and cause liver issues.

CBF

Gemtuzumab might be used in combination with daunorubicin and cytarabine to treat core binding factor (CBF) and other cytogenetic abnormalities.

FLT3

Gilteritinib or midostaurin is used to treat AML with *FLT3*-ITD and *FLT3*-TKD gene mutations.

Sorafenib with azacitidine or decitabine is used to treat AML with *FLT3*-ITD mutation.

IDH1

Ivosidenib is used to treat AML with *IDH1* mutation.

IDH2

Enasidenib is used to treat AML with *IDH2* mutation.

Clinical trials

Clinical trials study how safe and helpful tests and treatments are for people. Clinical trials find out how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve your care and treatment of cancer.

Clinical trials have 4 phases.

- **Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects.
- **Phase II trials** assess if a drug works for a specific type of cancer.
- **Phase III trials** compare a new drug to a standard treatment.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often are alike in terms of their cancer and general health. This helps to ensure that any change is from the treatment and not because of differences between patients.

If you decide to join a clinical trial, you will need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits. Even after you sign a consent form, you can stop taking part in a clinical trial at any time.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. Discuss the risks and benefits of joining a clinical trial with your care team. Together, decide if a clinical trial is right for you.

Finding a clinical trial

- Search the National Institutes of Health (NIH) database for clinical trials. It includes publicly and privately funded clinical trials, who to contact, and how to enroll. Look for an open clinical trial for your specific type of cancer. Go to ClinicalTrials.gov.
- The National Cancer Institute's Cancer Information Service (CIS) provides up-to-date information on clinical trials. You can call, email, or chat live. Call 1.800.4.CANCER (800.422.6237) or go to cancer.gov.

NCCN experts encourage patients to join a clinical trial when it is the best option for the patient.

Blood stem cell transplant

A blood stem cell transplant (SCT) replaces damaged or destroyed stem cells with healthy stem cells. The healthy stem cells form new marrow and blood cells. It is also called a hematopoietic cell transplant (HCT). You might know it as a bone marrow transplant (BMT).

There are 2 types of blood stem cell transplants:

- **Autologous** – stem cells from you
- **Allogeneic** – stem cells from a donor

Autologous transplant

An autologous transplant is also called HDT/ASCR (high-dose therapy with autologous stem cell rescue) or an autoSCT. First, your healthy stem cells will be removed. Then, you will receive treatment to kill your bone marrow cells. Your healthy stem cells will be returned to "rescue" your marrow. An HDT/ASCR is not used very often in AML.

Allogeneic transplant

An allogeneic transplant uses healthy stem cells from a donor. The donor may or may not be related to you. A donor transplant is not used for induction, the first treatment given to treat a leukemia. It is an option to treat blasts that may have survived induction. An allogeneic HCT is sometimes used to treat a relapse. It is also called an alloSCT.

The timing for a search to find a donor or for a referral to a transplant center depends on your risk group. Risk group is based on the type of AML and which genetic mutations are present.

Before the transplant, you will receive treatment that destroys bone marrow cells. The death of these cells creates room for the donor cells. It also weakens your immune system so your body won't kill the donor cells.

Treatment before the transplant may include one or more chemotherapies. Sometimes, radiation therapy is added to chemotherapy.

After your bone marrow cells are destroyed, you'll receive the donor cells. These cells will create new marrow with healthy cells. They will also attack blasts that weren't killed by prior treatment.

Possible side effects

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

Review

- Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells.
- Targeted therapies seek out how cancer cells grow, divide, and move in the body.
- A clinical trial, if available, may be an option.
- A blood stem cell transplant (SCT) or hematopoietic cell transplant (HCT) replaces damaged stem cells with healthy stem cells.

Seek treatment at an experienced leukemia center that specializes in your type of cancer.

“I had been battling a “cold” that wouldn’t get better. My doctor ordered blood work and called to say, “I’ve got some bad news…you have leukemia.” I didn’t even know what leukemia was really.”

– Matt

4
Treatment phases

The goal of AML treatment is a complete response or complete remission. Treatment for AML and its subtypes will be in phases. The three phases of treatment are induction, consolidation, and maintenance.

Types of response

There are different types of treatment responses. When there are no signs of cancer, it is called a complete response or complete remission. This does not always mean that AML has been cured. Remission can be short-term (temporary) or long-lasting (permanent).

Definitions for different types of complete response (CR) are listed in Guide 2.

Guide 2
Complete response (CR) types and definitions

Morphologic	• Does not need transfusions • Absolute neutrophil count (ANC) is more than 1,000/mcL • Platelets of 100,000/mcL or more • Less than 5 percent (5%) blasts when marrow is looked at under a microscope • No evidence of extramedullary disease
Cytogenetic	• Cytogenetics (karyotype and FISH) are normal in those who had abnormal cytogenetics before
Molecular	• PCR shows no cancer in blood cells or bone marrow • Molecular remission for APL should be performed after consolidation • Molecular remission in non-APL AML should be performed after induction
CRi	• Less than 5 percent (5%) blasts • ANC is less than 1,000/mcL or platelets are less than 100,000/mcL • Does not need transfusions, but has cytopenia that persists

*Less than a complete response may still be meaningful depending on the therapy.

Types of complete response include:

- **Morphology** refers to the structure of cells, such as size and shape. In AML, the number of blood cells are also measured. With a complete morphologic response, there are less than 5 blasts out of every 100 blood cells in the bone marrow when viewed under a microscope. No evidence of extramedullary disease means no cancer is found in organs outside the bone marrow.
- **Cytogenetics** refers to changes in chromosomes found using karyotype or FISH. In complete remission, treatment corrects abnormal chromosomes.
- **Molecular** refers to proteins and genes. It is a complete remission when PCR cannot find disease in blood cells or bone marrow.
- **CRi** is an incomplete blood count recovery.

In complete remission all of the following are true:

- There is no sign of leukemia after treatment
- Your blood counts have returned to normal
- You have less than 5 percent (5%) blasts in your bone marrow (or less than 5 blasts out of every 100 blood cells)

Other definitions that might be used to describe treatment responses are listed in Guide 3.

Guide 3
Other treatment response definitions

Morphologic leukemia-free state	• Bone marrow has less than 5% blasts • No evidence of extramedullary disease
Partial remission	• Bone marrow aspirate shows number of blasts decreased by half and are now between 5% and 25% • Blood counts are normal
Relapse following complete response	• Blasts re-appear in the blood or more than 5% blasts are found in bone marrow (not caused by treatment or extramedullary disease)
Induction failure	• When complete response isn't achieved after at least 2 courses of intensive induction therapy

Phases of treatment

There are 3 phases of treatment: induction, consolidation, and maintenance.

Induction

Induction is the first phase of treatment. The goal of induction is complete response or remission. Sometimes this initial treatment is called remission induction therapy.

There are 3 types of complete response or complete remission:

- Morphologic
- Cytogenetic
- Molecular

After induction, you will have bone marrow tests to look for a response (remission).

Minimal residual disease

In minimal residual disease (MRD), AML seems to be in remission after induction, but very sensitive lab tests, such as PCR, find leukemia cells in your bone marrow.

Consolidation

Consolidation is the second phase of treatment. It is needed to kill any cancer cells that might be left in the body after induction. This is to prevent cancer from returning. Standard types of consolidation include a stem cell transplant or more chemotherapy. Sometimes, this treatment is called post-remission therapy, which might be a combination of consolidation and maintenance therapy.

Maintenance

Maintenance can be the third phase of treatment. It is treatment to prevent cancer from returning. Treatment might include drugs, vaccines, or antibodies that kill cancer cells. It may be given for a long time and occur over years. Maintenance is also called post-consolidation therapy because it is treatment after (post) consolidation.

Not everyone will receive maintenance therapy. Maintenance may be recommended depending on your type of disease, consolidation, and risk of relapse.

Monitoring

Monitoring or surveillance watches for any changes in your condition. You will have tests during monitoring to check for signs of disease.

Relapse

When leukemia returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. Depending on your type of AML, complete remission might not be possible. You may receive treatment to prevent the blasts from spreading to your brain and spine. A relapse is very serious. It is important to ask about your prognosis.

Refractory

When leukemia has not gone away and does not respond to treatment, it is called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about your prognosis.

Review

- The goal of treatment is a complete response. There are different types of responses. Less than a complete response may still be meaningful depending on the therapy.
- Induction or remission induction is the first phase of treatment.
- Minimal residual disease (MRD) is AML that appears to be in remission, but very sensitive tests find cancer.
- Consolidation or post-remission therapy is the second phase of treatment.
- Maintenance or post-consolidation therapy is the third or final phase of treatment.
- Monitoring watches for any changes in your condition.
- Leukemia that returns after remission is called relapse.
- When leukemia does not respond to treatment, it is called refractory or resistant cancer.

Get to know your care team and let them get to know you.

“My treatment team was amazing. They always discussed what was being done and were very caring.”

– Lew

5
APL

There are different types of AML. Acute promyelocytic leukemia (APL) is one subtype. APL occurs when pieces of chromosomes 15 and 17 break off and trade places. The result is two fused genes called *PML-RARA* and *RARA-PML*. You will be treated for APL if the *PML-RARA* gene is found. Together, you and your doctor will choose a treatment plan that is best for you.

Overview

Acute promyelocytic leukemia (APL) is a rare type 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 types. APL is treated with all-trans retinoic acid (ATRA) in combination with another therapy.

Diagnosis

The initial diagnosis of APL may be confirmed by a chromosome test such as FISH or PCR. APL can be diagnosed quickly and treatment started within just a few hours.

APL occurs when parts of chromosome 15 and chromosome 17 break off and trade places, called translocation. This translocation is referred as t(15;17). It makes two genes that are fused together. These two fused genes are called *PML-RARA* and *RARA-PML*. You will be treated for APL if the *PML-RARA* gene is found. When treatment is successful, the *PML-RARA* gene cannot be found.

APL can cause bleeding that can be fatal. You will start taking retinoid (ATRA) right away if your doctor suspects APL. It can stop the bleeding. If APL is not confirmed, then you will stop taking the retinoid.

What causes APL?

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

Treatment therapies

Unlike other types 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, a targeted therapy, might be given in place of ATRA or arsenic trioxide. Chemotherapy may also be used.

ATRA

All-trans retinoic acid (ATRA) is made in the body from vitamin A, but it is also made in a lab to treat acne and APL. This drug is also called a retinoid. Retinoid forces APL blasts to mature and become normal cells.

Retinoid is a good 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 (Trisenox®)

Arsenic trioxide (or ATO) causes the death of APL cells. When added to ATRA, it improves outcomes. More leukemia cells die. Relapse occurs in fewer people.

Blood stem cell transplant

An autologous hematopoietic cell transplant (HCT) may be an option if less than a molecular response is achieved. In other words, if a PCR test still shows signs of APL, then a blood stem cell transplant using your own cells may be an option. A donor or matched sibling blood stem cell transplant may be an option depending on the circumstances.

Treatment phases

Treatment phases for APL include induction, consolidation, and maintenance. Treatment might take place over a period of years.

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.

Types of complete response (remission) you might have:

- Induction often causes a large drop in the number of blasts. This is called a **morphologic complete response**.
- When the translocation of chromosomes 15 and 17 or t(15;17) is no longer found, it is called a **cytogenetic complete response**.
- 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 is not found. Often, more treatment is needed to achieve a molecular response.
- When there are no signs or symptoms of cancer, it is called **complete remission**.

Bone marrow tests

Bone marrow samples are needed to see how well induction treatment worked. Marrow tests should not occur sooner than 28 days after treatment starts. If the tests are done sooner, the *PML-RARA* gene may still be present. Treatment needs time to work. Your blood needs time to recover.

Tests will look for blasts in the marrow. If absent, induction can be stopped to allow your marrow to make more blood cells. This is called recovery. If present, you may stay on treatment and repeat the marrow tests one week later.

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.

If your white blood cell count is more than 10,000 mcL, you may have a lumbar puncture before starting consolidation. Some types of consolidation 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.

PCR should be performed on a blood sample when consolidation is finished to show molecular remission. For those receiving ATRA/arsenic regimen, your doctor should consider a PCR sample at 3 to 4 months during consolidation.

Molecular testing

Bone marrow samples are needed to measure how well your body responded to consolidation treatment. PCR can tell whether or not the *PML-RARA* gene is present. If the *PML-RARA* gene is found, then PCR will be done again within 4 weeks.

Maintenance

Maintenance or post-consolidation therapy is the last phase of treatment. The goal is to prolong the good results of prior treatment. Chances are you will continue on the same treatment, but at a lower dose. Treatment may last for 1 to 2 years or longer.

Some APL treatment regimens include maintenance therapy. Discuss with your doctor if your regimen includes maintenance therapy.

> “Bone marrow biopsies are not fun. I was glad when I didn’t need to do them again.”
>
> – Rhonda

Risk groups

Not all people with APL receive the same treatment. Doctors plan treatment for APL using risk groups. These risk groups are based on the white blood cell count at diagnosis.

The 2 risk groups are:

- **Low-risk group** is white blood cell count of 10,000 mcL or less
- **High-risk group** is white blood cell count of more than 10,000 mcL

Treatment for high risk is based on:

- No heart issues/disease
- Heart issues (such as low ejection fraction or prolonged QTc)

Low-risk group

For low-risk group, the preferred induction therapy option is ATRA with arsenic trioxide and supportive care. If arsenic trioxide is not an option, ATRA with idarubicin can be used for induction therapy.

You will have a bone marrow aspirate and biopsy to document remission before starting consolidation therapy. If you were on arsenic trioxide, you will have a break between treatments to give your blood a chance to recover. See Guide 5.

Consolidation may include one or more of the following:

- ATRA
- Arsenic trioxide
- Gemtuzumab

Guide 5
Low-risk group: Induction followed by consolidation options

Induction		Consolidation
ATRA with arsenic trioxide and suppportive care (preferred option)	→	Bone marrow aspirate and biopsy on day 28 to 35, before starting ATRA with arsenic trioxide. Gemtuzumab may be given in place of ATRA or arsenic trioxide.
If arsenic is not an option		
ATRA with idarubicin	→	At count recovery, start ATRA with idarubicin followed by ATRA with mitoxantrone, then ATRA with idarubicin.

High-risk group

Treatment for high risk is based on those with and without heart issues or heart disease. In all groups, ATRA is used. After induction, a bone marrow aspirate and biopsy will be done on day 28 to look for and confirm remission. Your doctor will consider a lumbar puncture before you start consolidation.

No heart issues

For high-risk group without heart issues, the preferred induction therapy option is ATRA with arsenic trioxide and either a chemotherapy (idarubicin) or targeted therapy (gemtuzumab). See Guide 6.

For other recommended options, see Guide 7.

Guide 6
High-risk group: Preferred therapy options

Induction	Consolidation
ATRA with idarubicin and arsenic trioxide	→ ATRA and arsenic trioxide
ATRA with arsenic trioxide and gemtuzumab	→ ATRA and arsenic trioxide. Gemtuzumab may be given in place of ATRA or arsenic trioxide.

*After induction: bone marrow aspirate and biopsy on day 28 to document remission. Consider lumbar puncture before starting consolidation.

Guide 7
High-risk group: Other recommended options

Induction	Consolidation
ATRA with daunorubicin and cytarabine	→ Arsenic trioxide, then ATRA with daunorubicin
	→ Daunorubicin with cytarabine, then cytarabine with daunorubicin and intrathecal chemotherapy
ATRA with idarubicin	→ ATRA with idarubicin and cytarabine, then ATRA with mitoxantrone, then ATRA with idarubicin and cytarabine

*After induction: bone marrow aspirate and biopsy on day 28 to document remission. Consider lumbar puncture before starting consolidation.

High risk with heart issues

For high-risk group with heart issues such as heart disease, induction options are based on the type of heart issue. See Guide 8.

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 QT interval (or 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

If the drug regimen you were started on includes maintenance or post-consolidation therapy, then you may have this last phase of treatment. The goal is to prolong the good results of prior treatment. Chances are you will continue on the same treatment, but at a lower dose. Treatment may last for 1 to 2 years or longer. See Guide 9.

Guide 8
High-risk group with heart issues: Induction and consolidation options

	Induction		Consolidation
Those with low ejection fraction	ATRA with arsenic trioxide and gemtuzumab	→	ATRA and arsenic trioxide. Gemtuzumab may be given in place of ATRA or arsenic trioxide.
Those with prolonged QTc	ATRA with gemtuzumab	→	ATRA alone or with gemtuzumab

*After induction: bone marrow aspirate and biopsy on day 28 to document remission. Consider lumbar puncture before starting consolidation.

Monitoring

After completing maintenance therapy, you will 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 will have no drug therapy during this time. See Guide 9.

PCR every 3 months for 2 years is advised for those:

- Who are at high risk for relapse
- Over 60 years of age or had long interruptions during consolidation
- Who are not able to tolerate maintenance therapy

If PCR comes back positive, then a repeat PCR will be done on a second blood sample within 4 weeks to confirm it is positive. A positive result means there is cancer. A bone marrow biopsy is usually performed to confirm cancer.

Guide 9
Post-consolidation therapy and monitoring

PCR is negative	Start maintenance therapy (if it was part of first treatment plan) →	After completing maintenance therapy, monitor PCR for up to 2 years →	• If PCR negative, repeat this row • If PCR positive, then follow row below for PCR positive
PCR is positive	Repeat PCR within 4 weeks to confirm PCR is positive →	• If PCR negative, then follow row above • If PCR positive, then see Guide 10	

*First, document molecular remission after consolidation.

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 will have molecular tests to confirm you have relapsed APL instead of AML caused by previous treatment (called therapy-related AML). A bone marrow biopsy tests for morphologic response. PCR tests for molecular response.

Treatment for first relapse APL will be based on your prior therapy and if it is:

- 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 is not always possible. Options for first relapse are found in Guide 10.

Guide 10
First relapse therapy options after morphologic or molecular remission

Early relapse • **Less than 6 months after ATRA and arsenic trioxide (no anthracycline)**	Anthracycline-based treatment as in Guide 6
Did not have arsenic trioxide or has **Early relapse** • **Less than 6 months after ATRA with anthracycline-containing treatment**	Arsenic trioxide
	Arsenic trioxide with ATRA
	Arsenic trioxide with ATRA and gemtuzumab until count recovery with marrow confirmation of remission
Late relapse • **6 or more months after arsenic trioxide-containing treatment**	Arsenic trioxide
	Arsenic trioxide with ATRA
	Arsenic trioxide with ATRA and (anthracycline or gemtuzumab) until count recovery with marrow confirmation of remission

Second therapy

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

If remission, then a bone marrow biopsy will be done to confirm morphologic response. This means the number of blasts in your blood dropped to less than 5 blasts for every 100 blood cells. The goal of treatment is to achieve remission again. Treatment options are based on the PCR result and if you are a candidate for a blood stem cell transplant (HCT). You may receive chemotherapy to prevent APL from spreading to your brain and spine (central nervous system). See Guide 11.

If no remission, then the options are:

- Clinical trial
- Matched sibling or other donor blood stem cell transplant (HCT)

This is the time to have a conversation with your doctor about your prognosis.

Guide 11
Second therapy based on remission or no remission

Second remission (morphologic) • Consider intrathecal chemotherapy of methotrexate or cytarabine to prevent CNS	PCR is negative →	• If transplant candidate, then autologous HCT • Not a transplant candidate, then arsenic trioxide consolidation
	PCR is positive →	• If transplant candidate, then matched sibling or other donor HCT • If not a transplant candidate, then clinical trial
No remission		• Clinical trial • Matched sibling or other donor HCT

Supportive care

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

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant.

Ask your treatment team for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better and to prevent some side effects.

Supportive care for some key health problems in APL are described next.

Arsenic trioxide monitoring

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

You will have an ECG before initial induction therapy. Electrolyte and creatinine levels will be measured. If you are taking medicines that cause prolonged QT, your doctor may reduce or stop these medicines.

Bleeding

APL can cause bleeding, or coagulopathy, that can be fatal. Your blood will be tested to see how well it clots. Wait to have any procedure that may cause bleeding until your blood clots well. If you have issues with bleeding, then you will be monitored daily until your condition improves.

Bleeding can usually be managed. Platelet transfusions can help keep platelet levels at 50,000 mcL or higher. The normal range is 150,000 to 450,000 mcL.

Fibrinogen is needed for blood clots to form. Its normal range is 150 to 400 mg/dL. Cryoprecipitate and fresh frozen plasma can be used to help maintain a minimum level of 150 mg/dL. Cryoprecipitate comes from thawed frozen blood.

Differentiation syndrome

Differentiation syndrome is caused by a large release of cytokines (immune substances) from leukemia cells. Anti-cancer drugs used to treat APL may cause differentiation syndrome.

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 drop 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.

Differentiation syndrome is most often caused by ATRA or arsenic trioxide. It also occurs during relapse treatment but not during consolidation or maintenance. Less often, differentiation syndrome starts before any treatment. Other types of treatment can also trigger it.

Prevention

Not every person gets differentiation syndrome. A white blood cell count higher than 10,000 mcL puts you at risk. Your doctor may prescribe steroids, such as prednisone or dexamethasone, to try to prevent it.

Tests

During treatment, you will be monitored for differentiation syndrome. Your doctor will ask about any new or worsening symptoms. It might be helpful to keep a list of symptoms or journal of how you are feeling.

Treatment

At the first signs or symptoms of differentiation syndrome, you will start on a steroid. If you were already on a steroid, then a different steroid will be used. This can help your blood count return to normal. ATRA or arsenic trioxide may be stopped.

For differentiation syndrome that is difficult to treat, your doctor might try:

- Cytoreduction (the removal of cancerous cells)
- Anthracycline, a chemotherapy
- Hydroxyurea, an anti-metabolite

Review

- Acute promyelocytic leukemia (APL) is a rare type of AML. With treatment, APL is cured more often than other AML types.
- You will start taking retinoid right away if your doctor suspects APL. It may stop fatal bleeding.
- Treatment for APL involves several phases.
- Doctors plan treatment for APL using low- and high-risk groups. Risk groups are based on white blood cell count. ATRA-based treatment is advised for both risk groups.
- Supportive care can help to prevent death from health issues caused by APL or its treatment.

Before I was sick, I was a very active person. I'm not one to sit down. I had to adjust my life. I knew that I could find things that would make me happy and move on and get stronger."

– Patsy

6
AML

There are different types of AML. This chapter is for treatment of AML that is not APL or BPDCN. Together, you and your doctor will choose a treatment plan that is best for you.

Overview

There are many subtypes of AML. Most people with leukemia do not have acute promyelocytic leukemia (APL). In the past, all non-APL subtypes were treated the same way. As doctors learn more, treatment is being improved to better target each subtype.

Diagnosis

Acute leukemia is defined by a high number of blasts in the bone marrow or blood. The standard cutoff is at least 2 out of every 10 marrow cells are blasts. If there are fewer blasts, then a common biomarker must be present. Subtypes of AML are based on features of the cells.

At diagnosis, most people will have a bone marrow biospy. Some may have a lumbar puncture if there are signs and symptoms of central nervous system (CNS) leukemia.

What causes AML?

AML can happen for no reason. Sometimes, certain treatments for other cancers later causes AML.

Myelodysplastic syndrome (MDS) can become AML. MDS is a type of cancer that occurs when bone marrow stops making enough healthy blood cells and abnormal cells are found.

Risk groups

Risk groups for non-APL AML are based on the gene mutations or cytogenetics of the cancer. 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. Some people may do better than expected. Some will do worse. Risk groups will be used in addition to other factors such as your age and overall health. See Guide 12.

There are 3 risk groups for non-APL AML:

- Favorable
- Intermediate
- Poor or adverse

Guide 12
Risk groups for non-APL AML

Favorable	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* • Biallelic mutated *CEBPA* • Mutated *NPM1* without *FLT3*-ITD
Intermediate	Includes any of the following abnormal genes: • Mutated *NPM1* and *FLT3*-ITD^{high} • Wild-type *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low} (without adverse-risk genetic lesions) • t(9;11)(p21.3;q23.3); *MLLT3-KMT2A* • Cytogenetic abnormalities not classified as favorable or adverse
Poor or adverse	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* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOME(EVI1)* • -5 or del(5q);-7;-17/abn(17p) • Complex karyotype, monosomal karyotype • Wild-type *NPM1* and *FLT3*-ITD^{high} • Mutated *RUNX1* • Mutated *ASXL1* • Mutated *TP53*

Treatment phases

The goal of treatment is to put AML into complete remission. In complete remission, the bone marrow and blood cell counts return to normal. This is different than a complete molecular remission where no signs of leukemia are found in the bone marrow. A complete molecular remission is preferred.

Treatment for AML can occur over years. It involves several phases. These phases are briefly described next.

Induction

Induction is the first phase of treatment. It is 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 types of marrow cells will also decrease. Your marrow will need time to recover so blood cells can return to normal levels. Treatment attempts to restore the process of making normal blood cells.

Monitoring

Blood samples will be needed to check treatment results. Your blood counts will be measured. Blood tests also look at the health of organs like your liver and kidneys.

Bone marrow samples will be needed about 2 to 3 weeks after the start of chemotherapy. Marrow tests will show how well treatment is working. Bone marrow tests may be repeated.

If blasts are not found in the bone marrow, then no treatment will be given for 2 to 4 weeks. During this time, your marrow will begin to make normal blood cells again. This is called recovery.

When blood counts are normal, marrow tests will be repeated. Your doctor will check to see if the leukemia is in remission. A complete remission is an absence of all signs and symptoms.

If treatment does not reduce the number of blasts, you may receive more treatment called re-induction. After more induction, the blasts may persist. In this case, treatment options will be listed with those for relapse.

Minimal residual disease

You will have a PCR or flow cytometry to look for minimal residual disease (MRD). In MRD, AML seems to be in remission, but very sensitive lab tests, such as PCR, find leukemia cells in your bone marrow. It is suggested you be tested for MRD after finishing the first round of induction and before an allogeneic stem cell transplant. See Guide 13.

When testing finds MRD (called a positive MRD result), it does not prove that your cancer has relapsed. If tests find residual disease, ask your doctor what this might mean and what will be the next steps.

Consolidation

This is the second phase of treatment. It is also called post-remission therapy. Consolidation treats blasts that may have survived induction.

You may receive the same drugs used for induction. If not, you may receive one drug at a higher dose. A blood stem cell transplant may also be an option. It is sometimes done if the leukemia is likely to return after treatment.

You may have a lumbar puncture before consolidation. The removed spinal fluid will be tested for blasts. This test is based on your pre-treatment white blood cell count, leukemia subtype, and other factors.

Some types of consolidation 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.

Your blood will be given time to recover before starting consolidation.

Maintenance

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

Surveillance

Surveillance is a period of testing that is started after consolidation. A complete blood count (CBC) every 1 to 3 months for 2 years is advised. Then, it should then be repeated every 3 to 6 months for up to 5 years. If results aren't normal, bone marrow tests may be needed.

Relapse

When leukemia returns it is 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.

Refractory

When leukemia does not respond to treatment, it is called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment.

Guide 13 Minimal residual disease (MRD)
Participation in a clinical trial is encouraged.
MRD in AML refers to the presence of leukemia cells that are not seen on conventional tests.
You can achieve a complete response and still have a large number of leukemia cells in bone marrow.
Tests needed are PCR or flow cytometry.
Tests should be reviewed by an experienced hematopathologist.
MRD is not proof of relapse.
Tests will be repeated.
Testing should take place after initial induction is finished, before allogeneic transplant, and as needed.

Treatment therapies

AML is not treated the same for everyone. As the body ages, it can have difficulty tolerating higher doses or more intense cancer treatments. Your overall health and general level of fitness, called performance status, also play a role in treatment decisions. Since AML behaves differently in those 60 years of age and over, age as well as your overall health and cytogenetics will play a role. Your wishes are also important.

Treatment is divided into 2 groups:

- Those under 60 years of age
- Those 60 years of age and over

Keep in mind that these age ranges are just guidelines. A very healthy 61 year old might be treated as someone under 60 years of age. A 55 year old with serious health issues might be treated as someone 60 years of age and over.

Chemotherapy

Some treatments are specific to an AML subtype such as:

- Therapy-related AML (AML caused by an earlier treatment for a different cancer)
- Acute myeloid leukemia with myelodysplasia-related changes (AML-MRC)
- Those who had antecedent MDS or chronic myelomonocytic leukemia (CMML). Antecedent MDS or CMML means you had MDS or CMML before.

AML-MRC is a type of AML in which blood or marrow has at least 20% immature white blood cells (blasts) with one of the following:

- Has had myelodysplastic syndrome (MDS) or a myeloproliferative neoplasm (MPN) before
- Cells that have changes in certain chromosomes that are similar to those found in MDS
- At least half of the cells of at least 2 types of blood cells appear abnormal under a microscope

Under 60 years of age

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 low- or non-intensive therapy. Depending on your performance status, if you have any heart or other serious health issues, treatment is usually more intensive for those under 60 years of age. Remission or a complete response is still possible in lower-intensity treatments.

There are always risks with treatment. Talk with your doctor about the risks with each treatment and why a treatment might be better for you. Find out how treatment might affect your quality and length of life.

Helpful tips

- ✓ Keep a list of contact information of all of your health care providers.
- ✓ Ask a caregiver to help you plan your appointments.
- ✓ Use a calendar or day planner to keep track of your upcoming tests and doctors' appointments.

"The treatment was tough due to nausea, vomiting, and weakness. It was important to try and eat, drink water and exercise every day—this I did."

– Gillian

Induction

Most people have one round of induction. But, it is possible you will have more than one round. For induction options, see Guide 14.

Guide 14
Under 60 years of age: Induction options

Favorable-risk cytogenetics	Standard-dose cytarabine with idarubicin or daunorubicin CD33-positive: • Standard-dose cytarabine with daunorubicin and gemtuzumab	→ See Guide 15
Intermediate-risk cytogenetics and *FLT3*-mutated (ITD or TKD)	Standard-dose cytarabine with daunorubicin and midostaurin	→ See Guide 15
• **Therapy-related AML other than CBF or APL** • **Antecedent MDS or CMML** • **Cytogenetic changes consistent with MDS (AML-MRC)**	Standard-dose cytarabine with idarubicin or daunorubicin Dual-drug liposome of daunorubicin and cytarabine	→ See Guide 15
Other recommended options for intermediate-risk or poor-risk disease	Standard-dose cytarabine with: • Idarubicin or daunorubicin • Daunorubicin or cladribine CD33-positive or intermediate-risk AML: • Standard-dose cytarabine with daunorubicin and gemtuzumab High-dose (HiDAC) cytarabine with idarubicin or daunorubicin Fludarabine with HiDAC, idarubicin, and granulocyte colony-stimulating factor (G-CSF)	→ See Guide 17

Options after standard-dose cytarabine induction

Your next round of induction will be based on which therapy you had first and how AML responded to treatment.

If you had standard-dose cytarabine as your first induction, see Guide 15.

Treatment options are based on the following:

- Significant amount of cancer (residual disease) remains after treatment
- Significant reduction of cancer with a low amount of remaining (residual) blasts
- Hypoplasia (bone marrow is starting to recover, but isn't there yet)

Guide 15
Under 60 years of age: After standard-dose cytarabine induction or re-induction

Significant amount of cancer remains	High-dose cytarabine
	Standard-dose cytarabine with idarubicin or daunorubicin
	FLT3-mutated ITD or TKD: • Standard-dose cytarabine with daunorubicin or midostaurin (bone marrow aspirate and biopsy on day 21)
	Therapy-related AML or those who had MDS or CMML or AML-MRC before: • Dual-drug liposome of daunorubicin and cytarabine (preferred only if given in induction) (bone marrow aspirate and biopsy 14 to 21 days after start of therapy)
	See treatment for induction failure (no response) in Guide 16
Significant cancer reduction with low number of residual blasts	Standard-dose cytarabine with idarubicin or daunorubicin
	FLT3-mutated ITD or TKD: • Standard-dose cytarabine with daunorubicin and midostaurin (bone marrow aspirate and biopsy on day 21)
Hypoplasia	Wait for recovery

*Follow-up bone marrow aspirate and biopsy 14 to 21 days after start of therapy.

For treatment after standard-dose cytarabine induction therapy, see Guide 16. Options are based on if there was a complete response or no response (induction failure) to standard-dose induction.

If there was a complete response, then consolidation can begin.

If induction therapy did not work, then the options include:

- Blood stem cell transplant (HCT)
- HiDAC
- Clinical trial (if not available then HiDAC with anthracycline)
- Therapy for relapsed or refractory disease
- Best supportive care

Options after high-dose cytarabine induction

Your next round of induction will be based on which therapy you had first and how AML responded to treatment. If you had high-dose cytarabine as your first induction, see Guide 17.

After induction, doctors will look for the amount of cancer left in the body.

- If there is still a lot of cancer left (significant residual disease), then you might be treated for relapsed or refractory disease.
- If the number of blasts decreased significantly and there is low residual disease, then you will wait until recovery. After your bone marrow recovers, it will be tested to see if AML is in remission.
- In hypoplasia, bone marrow is starting to recover, but isn't there yet. After your bone marrow recovers, it will be tested to see if AML is in remission.

Guide 16
Under 60 years of age: Options after standard-dose cytarabine induction

Complete response	• Consolidation post-remission therapy (Guide 18)
No response	• Matched sibling or other donor HCT • HiDAC (if not used before for persistent disease at day 15) • If clinical trial not available or waiting for HCT donor, then HiDAC (see above) with anthracycline (daunorubicin or idarubicin) • Therapy for relapsed or refractory disease (Guide 25) • Best supportive care

*First, bone marrow aspirate and biopsy to document remission status upon blood recovery. Cytogenetics and molecular testing as needed. For measurable (minimal) residual disease (MRD) assessment, see Guide 13.

Complete response

If complete response (remission) was achieved, then you will have consolidation post-remission therapy.

No response

If there was no response or cancer progressed, then options include treatment for relapsed or refractory disease, a blood stem cell transplant, or best supportive care. Best supportive care is treatment to improve quality of life and relieve discomfort. It is not cancer treatment. It might include pain relief, emotional or spiritual support, or family counseling.

Guide 17
Under 60 years of age: After high-dose cytarabine induction

Significant amount of cancer remains	• Therapy for relapsed or refractory disease (Guide 25) • Best supportive care	
Significant cancer reduction with low percent of residual blasts	Wait for recovery, then: • Bone marrow aspirate and biopsy to document remission status after blood recovery • Cytogenetics and molecular testing as needed • For minimal residual disease (MRD) assessment (Guide 13)	→ If complete response, then consolidation post-remission therapy (Guide 18)
Hypoplasia		→ If induction failure, then: • Therapy for relapsed or refractory disease (Guide 25) • Matched sibling or other donor HCTs • Best supportive care

*Follow-up bone marrow aspirate and biopsy 21 to 28 days after start of therapy. Can repeat bone marrow biopsy 5 to 7 days before start.

Consolidation post-remission therapy

Consolidation post-remission therapy is treatment to kill any remaining blasts after a complete response (remission). This treatment guide is for those who had a complete response and is based on cytogenetic and molecular test results. See Guide 18.

Guide 18
Under 60 years of age: Consolidation post-remission therapy options

Core binding factor (CBF) cytogenetic translocations without *KIT* mutation	• High-dose cytarabine (HiDAC) • HiDAC with gemtuzumab for CD33-positive • Cytarabine with daunorubicin and gemtuzumab for CD33-positive
• **Intermediate-risk cytogenetics** • **Molecular abnormalities**	• Matched sibling or other donor HCT • HiDAC • HiDAC with oral midostaurin for *FLT3*-mutated AML • Cytarabine with daunorubicin and gemtuzumab for CD33-positive
• **Therapy-related AML other than CBF** • **Unfavorable cytogenetics** • **Molecular abnormalities**	• Matched sibling or other donor HCT • HiDAC • HiDAC with oral midostaurin for *FLT3*-mutated AML • Dual-drug liposome of daunorubicin and cytarabine for therapy-related AML, or those who had MDS, CMML, or AML-MRC before (preferred only if given in induction)

60 years of age and over

As the body ages, it can have difficulty tolerating higher doses or more intense cancer treatments. Your overall health and general level of fitness, called performance status, also 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 low- or non-intensive therapy. An intensive therapy is not necessarily better. Remission or a complete response is still possible in lower-intensity treatments.

Depending on your performance status, if you have any heart or other serious health issues, treatment will be:

- Low- or non-intensive
- Intensive

There are always risks with treatment. Talk with your doctor about the risks and why a treatment might be better for you. Find out how treatment might affect the quality and length of life.

Treatment induction is based on:

- Favorable-risk cytogenetics
- Unfavorable-risk cytogenetics
- Intermediate-risk or poor-risk disease
- *FLT3*-mutated (ITD or TKD)
- Therapy-related AML
- If you were treated for MDS or CMML in the past
- AML with myelodysplasia-related changes called AML-MRC

Antecedent MDS or CMML means you had MDS or CMML before.

AML-MRC or acute myeloid leukemia with myelodysplasia-related changes is a type of AML in which blood or marrow has at least 20% immature white blood cells (blasts) with one of the following:

- Has had myelodysplastic syndrome (MDS) or a myeloproliferative neoplasm (MPN) before
- Cells that have changes in certain chromosomes that are similar to those found in MDS
- At least half of the cells of at least 2 types of blood cells appear abnormal under a microscope

If intensive induction is an option

The goal of intensive remission induction is to reduce the number of blasts and put AML in remission. You might have more than one round of induction in order to achieve a complete response.

For those 60 years of age and over, intensive remission induction options can be found in Guide 19.

If you forgot your risk group, risk groups can be found in Guide 12.

Guide 19
60 years of age and over: Intensive remission induction options

Favorable-risk cytogenetics	CD33-positive AML: • Standard-dose cytarabine with daunorubicin and gemtuzumab Standard-dose cytarabine with (idarubicin or daunorubicin or mitoxantrone)	→ See Guide 20
***FLT3*-mutated (ITD or TKD)**	Standard-dose cytarabine with daunorubicin and midostaurin	→ See Guide 20
• **Therapy-related AML** • **Antecedent MDS or CMML** • **AML-MRC**	Dual-drug liposome of daunorubicin and cytarabine	→ See Guide 21
Unfavorable-risk cytogenetics	Venetoclax with one from below: • Decitabine • Azacitidine • Low-dose cytarabine (LDAC) Low-intensity therapy of azacitidine or decitabine	→ See Guide 21
Other recommended options for intermediate-risk or poor-risk disease	Standard-dose cytarabine with (idarubicin or daunorubicin or mitoxantrone) CD33-positive or intermediate-risk AML: • Standard-dose cytarabine with daunorubicin and gemtuzumab	→ See Guide 20

Residual disease after standard-dose cytarabine induction

There might be cancer left after intensive induction treatment called residual disease. If standard-dose cytarabine was part of your intensive remission induction therapy, then see Guide 20.

Blood needs time to recover after treatment. When blood cell counts have not returned to normal (hypoplasia), then you will wait for recovery.

Post-remission therapy after intense induction

After induction is finished, your blood will be given time to recover, about 4 to 6 weeks. A bone marrow aspirate and biopsy will be done to determine remission status and to look for minimal residual disease (MRD).

The goal of induction is a complete response. This section is called post-remission because it includes a variety of options depending on the type of response and where you are in the treatment phase. See Guide 21.

Guide 20
60 years of age and over: Options after standard-dose cytarabine induction

Residual disease	Another standard-dose cytarabine with anthracycline (idarubicin or daunorubicin) or mitoxantrone
	FLT3-mutated ITD or TKD: • Standard-dose cytarabine with daunorubicin or midostaurin
	Therapy-related AML, AML-MRC, or those who had MDS or CMML before: • Dual-drug liposome of daunorubicin and cytarabine (preferred only if given in induction)
	Regimens with intermediate-dose cytarabine
	Reduced-intensity allogeneic blood stem cell transplant (HCT)
	Therapy for relapsed or refractory disease (Guide 25)
	Wait for recovery
	Best supportive care
Hypoplasia	Wait for recovery

*Follow-up bone marrow aspirate and biopsy 14 to 21 days after start of therapy.

Complete response
If induction caused a complete response, then there a few options. You might have an allogeneic stem cell transplant (HCT), cytarabine-based therapy, maintenance therapy, or enter observation.

No response
If induction did not cause a complete response or remission, then you might have an allogeneic stem cell transplant (HCT), a low-intensity therapy, or be treated for relapsed or refractory disease. Best supportive care is an option.

Guide 21
60 years of age and over: Post-remission therapy if had intense therapy before

Complete response	Allogeneic blood stem cell transplant (HCT)
	Cytarabine options: • Standard-dose cytarabine • Standard-dose cytarabine with anthracycline (idarubicin or daunorubicin) • Consider intermediate-dose cytarabine for those with good performance status, normal kidney function, and better-risk or normal karyotype with favorable markers • Intermediate-dose cytarabine with midostaurin
	Maintenance therapy with hypomethylating regimens (of azacitidine or decitabine) every 4 to 6 weeks until progression
	Observation
	CD33-positive AML: • Cytarabine with daunorubicin and gemtuzumab
	Therapy-related AML, AML-MRC, or those who had MDS or CMML before: • Dual-drug liposome of daunorubicin and cytarabine (preferred only if given in induction)
No response	• Low-intensity therapy of azacitidine or decitabine • Allogeneic blood stem cell transplant (HCT) • Therapy for relapsed or refractory disease (Guide 25) • Best supportive care

*Bone marrow aspirate and biopsy to document remission status upon blood recovery (4 to 6 weeks). Test for minimal residual disease (MRD) (Guide 13).

If intensive induction is not an option

Not everyone wants or can tolerate intensive induction treatment. Age, overall health, and cytogenetics play an important role. Low- or non-intensive induction therapy can still cause a complete response.

Treatment options are based on the presence or absence of certain actionable gene mutations. An actionable mutation is one that is likely to respond to a targeted therapy.

Treatment will target these actionable mutations:

- *FLT3*
- *IDH1*
- *IDH2*

Treatment options for both actionable mutations and AML without actionable mutations can be found in Guide 22.

Guide 22
60 years of age and over: Low- and non-intensive induction options

AML without actionable mutations	• Venetoclax and decitabine (preferred) • Venetoclax and azacitidine (preferred) • Venetoclax and low-dose cytarabine (LDAC) (preferred)
	• Low-intensity therapy of azacitidine or decitabine • Glasdegib and LDAC • Gemtuzumab for CD33-positive • Best suppportive care
***IDH1* mutation**	• Ivosidenib • Low-intensity therapy of azacitidine or decitabine • Venetoclax-based therapy in combination with (azacitidine or decitabine or LDAC)
***IDH2* mutation**	• Enasidenib • Low-intensity therapy of azacitidine or decitabine • Venetoclax-based therapy in combination with (azacitidine or decitabine or LDAC)
***FLT3* mutation**	• Low-intensity therapy (of azacitidine or decitabine) with sorafenib for *FLT3*-ITD-positive • Venetoclax-based therapy in combination with (azacitidine or decitabine or LDAC

Treatment after low- and non-intensive induction

After induction is finished, your bone marrow will be given time to recover, about 4 to 6 weeks. A bone marrow aspirate and biopsy will be done to check for type of remission response and to look for minimal residual disease (MRD). Treatment options can be found in Guide 23.

If your bone marrow responded to treatment, the options are:

- Have an allogeneic stem cell transplant
- Continue on a lower-intensity treatment

If there was no response or your cancer progressed, the options are:

- Treatment for relapsed or refractory disease
- Best supportive care

Best supportive care is treatment to improve quality of life and relieve discomfort. It is not cancer treatment. It might include pain relief, emotional or spiritual support, or family counseling.

Guide 23
60 years of age and over: Post-induction if had low- or non-intense therapy before

Response	Allogeneic blood stem cell transplant (HCT)
	Continue on lower-intensity regimen options: • Hypomethylating regimens of azacitidine or decitabine until progression • Enasidenib for *IDH2*-mutated AML until progression • Ivosidenib for *IDH1*-mutated AML until progression • Venetoclax with decitabine • Venetoclax with azacitidine • Venetoclax with low-dose cytarabine (LDAC) • Glasdegib with LDAC • Azacitidine or decitabine with sorafenib for *FLT3*-ITD-mutated AML
	CD33-positive AML: • Gemtuzumab
No response or AML has progressed	• Therapy for relapsed or refractory disease (Guide 25) • Best supportive care

*Bone marrow aspirate and biopsy to document remission status upon blood recovery (4 to 6 weeks). Test for minimal residual disease (MRD) (Guide 13).

Non-intensive therapy for 75 years of age and over

Glasdegib with low-dose cytarabine (LDAC) is an option for those who have one of the following:

- Are newly diagnosed with AML and are 75 years of age and over
- Have other serious health issues that might prevent the use of a more intense therapy
- Do not have actionable mutations or decide they do not want treatment.

Venetoclax is another low-intense (less-aggressive) therapy. It might be used alone or in combination with azacitidine, decitabine, or LDAC for those who are newly diagnosed with AML and are 75 years of age and over. It is also used in those who have other serious health issues.

Surveillance

Surveillance is a period of testing that is started after consolidation. You will enter surveillance if treatment puts your cancer in remission. During surveillance you will 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. If results aren't normal, bone marrow tests may be needed.

Relapsed or refractory disease

When leukemia returns it is called a relapse. The goal of treatment is to achieve remission again. If you are a candidate for a blood stem cell transplant, then at the sign of first relapse your doctor will start the search for a donor if you do not have a sibling donor match.

When leukemia does not respond to treatment, it is called refractory or resistant cancer.

For relapsed AML or AML that stops responding to treatment after consolidation, see Guide 24 and Guide 25.

Guide 24
Therapy options for relapsed or refractory disease after consolidation

Determine mutation status of these actionable genes: • ***FLT3*** **(ITD or TKD)** • ***IDH1*** • ***IDH2***	Clinical trial (strongly preferred)
	Targeted therapy (Guide 25, followed by matched sibling or other donor blood stem cell transplant)
	Chemotherapy (Guide 25, followed by matched sibling or other donor blood stem cell transplant)
	Repeat first successful induction treatment regimen if 12 or more months since induction
	Best supportive care

*Molecular testing should be repeated at each relapse or progression.

Guide 25
Therapy options for relapsed or refractory disease after consolidation

Clinical trial	A clinical trial is strongly preferred
Targeted therapy	AML with *FLT3*-ITD mutation: • Gilteritinib • Hypomethylating agents of azacitidine or decitabine with sorafenib
	AML with *FLT3*-TKD mutation: • Gilteritinib
	AML with *IDH2* mutation: • Enasidenib
	AML with *IDH1* mutation: • Ivosidenib
	CD33-positive AML: • Gemtuzumab
Aggressive therapy for certain people	• Cladribine with cytarabine and G-CSF • Cladribine with cytarabine and G-CSF with mitoxantrone or idarubicin
	• High-dose cytarabine (if not had before) • High-dose cytarabine (if not had before) with (idarubicin or daunorubicin or mitoxantrone)
	• Fludarabine with cytarabine and G-CSF • Fludarabine with cytarabine, G-CSF, and idarubicin
	• Etoposide with cytarabine • Etoposide with cytarabine and mitoxantrone
	• Clofarabine • Clofarabine with cytarabine and G-CSF • Clofarabine with cytarabine, G-CSF, and idarubicin
Less-aggressive therapy	• Hypomethylating agents (HMAs) of azacitidine or decitabine • Low-dose cytarabine (LDAC) • Venetoclax with HMAs or LDAC

Supportive care

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

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Some side effects are very serious.

Ask your treatment team for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

Supportive care for AML treatment-related side effects are described next.

Abnormal blood cells counts

Before treatment, your white blood cell count may be very high. A high count can cause severe health problems. 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. Hydroxyurea is a drug.

During chemotherapy, you may need blood transfusions. Most white blood cells should be removed from donor blood. Donor blood should also be treated with radiation if your treatment will suppress your immune system. These steps will help prevent donor blood from attacking your body. They will also help prevent infections.

G-CSF

Growth factors, called granulocyte colony-stimulating factor (G-CSF), trigger the bone marrow to make blood cells. It is 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.

Brain impairment

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.

High-dose cytarabine can cause these problems in people of any age. Mid-dose cytarabine increases the chance among people over 60 years of age. With either dose, your risk of these problems rises if your kidneys don't work well.

You will be assessed for brain problems before each dose of cytarabine. Cytarabine might be stopped if problems are found. Once resolved, treatment will continue, but at a lower dose.

Tumor lysis syndrome

Tumor lysis syndrome (TLS) occurs when the waste released by dead cells is not quickly cleared out of your body. This results in kidney damage and severe blood electrolyte disturbances. It can be life threatening.

Induction chemotherapy may cause TLS. Many cells are killed during induction. This results in too much waste too quickly. TLS is more likely if your blast count is very high.

Allopurinol or rasburicase are drugs that decrease uric acid levels. Rasburicase may be given first if your blast count is quickly rising. It may also be first received if your uric acid level is high or your kidneys are damaged.

Drinking lots of water can help flush out cell waste. If your blast count is very high, you may need to get fluids at a hospital. These fluids will be injected into a vein.

If you are at risk for TLS, you will have blood tests every day including:

- Chemistry profile
- Electrolytes
- Liver function tests
- Blood urea nitrogen
- Creatinine
- Uric acid
- Phosphate

Differentiation syndrome

Differentiation syndrome is a potentially serious side effect of taking certain anti-cancer drugs. It is caused be a large, fast release of cytokines (an immune protein) as the leukemia cells respond to treatment. Differentiation syndrome may occur among people taking *IDH* inhibitors (enasidenib or ivosidenib) or *FLT3* inhibitors. It used to be called retinoic acid syndrome. Its 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 drop in blood oxygen. Fluid can build up around your lungs or heart. Damage to your kidneys and liver may occur.

Treatment must be started at the first signs or symptoms. Steroids are one effective option for treatment. If there is a rising white blood cell count with differentiation, then an anti-metabolite called hydroxyurea is also frequently used.

Eye problems

High-dose cytarabine can cause eye problems. The white part of your eyes may become red. Your eyes may feel painful and make more tears. These problems may be prevented with saline or steroid eye drops.

Infections

You are at risk for infections. If not treated early, infections can be fatal. Infections can be caused by viruses, fungus, or bacteria. Antibiotics can treat bacterial infections. Anti-fungals can treat fungal infections. You may be given anti-viral drugs to prevent viral infections.

Review

- Most people with AML have a subtype other than APL.
- Treatment for AML involves several phases.
- Treatment for AML is divided into those under 60 years of age and those 60 years of age and over.
- Your doctor will plan treatment based on your age and other factors such as your overall health and performance status. Performance status is your general level of fitness.
- Chemotherapy is a key part of treatment. Targeted therapy may be added if certain gene mutations are present.
- The goal of treatment is a complete response or remission.
- Supportive care can help to prevent or relieve health problems caused by AML or its treatment.

My biggest shock came when I was told that I had about 9 months to live or undergo a bone marrow transplant. Six years later, I have a great life with a wonderful support team of my husband, friends, and a terrific doctor and her entire team."

– Rima

7
BPDCN

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a very rare, aggressive blood cancer. It is similar to AML. But unlike AML, BPDCN can be found in blood, bone marrow, lymph nodes, or skin. It is often misdiagnosed. Together, you and your doctor will choose a treatment plan that is best for you.

Overview

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive blood cancer. It has features of leukemia, lymphoma, and skin cancer. Leukemia starts in blood-forming tissue of bone marrow. Lymphoma begins in the cells of the immune system.

BPDCN is cancer of the immature plasmacytoid dendritic cells, a rare type of immune cell. These blood cells start in the bone marrow and travel to the lymphatic organs such as the spleen and lymph nodes. Like skin cancer, those with BPDCN have areas of skin that look abnormal (skin lesions).

BPDCN can also affect the central nervous system (CNS). Often, BPDCN is misdiagnosed because the symptoms and signs vary greatly and the disease is rare. Therefore, seek treatment at a center that specializes in BPDCN. Ideally, your treatment team should include doctors from different fields of medicine.

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?

Myelodysplastic syndrome (MDS) can become BPDCN. 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.

Chronic myelomonocytic leukemia (CMML) can become BPDCN. 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

You will have several tests if BPDCN is suspected. See Guide 26.

Diagnosis

Almost everyone with BPDCN gets skin lesions. BPDCN is often found through a skin biopsy after a visit to the dermatologist for skin lesions. A dermatologist is an expert in skin problems. It may be diagnosed through a lymph node or bone marrow biopsy.

A protein called CD123 is found at higher than normal levels on cancer cells in those with BPDCN. Molecular testing will be done to confirm BPDCN.

A BPDCN diagnosis requires at least 4 of the following 6 proteins:

- CD123
- CD4
- CD56
- TCL-1
- CD2AP
- CD303/BDCA-2 without myeloid markers, T lineage markers, or B lineage markers

Myeloid markers include: MPO, lysozyme, CD14, CD34, CD116, and CD163.

BPDCN occurs in all races. It is more common in men. This treatment guide is for those 18 years of age and older.

Guide 26
Testing for BPDCN

Medical history and physical exam
Complete blood count (CBC), platelets, differential, and comprehensive metabolic panel (CMP)
Analysis of skin lesions (collaboration with a dermatologist is advised)
Bone marrow aspirate, bone marrow biopsy, and lymph node biopsy
Immunohistochemistry, flow cytometry, and cytogenetic analysis (karyotype and/or FISH)
Analysis of dendritic cell structure and blood blasts
Molecular analysis of at least: *ASXL1, IDH1-2, IKZF1-3, NPM1, NRAS, TET1-2, TP53, U2AF1, and ZEB2*
PET/CT scan for other areas, if extramedullary disease and/or lymphadenopathy suspected
Lumbar puncture to rule out central nervous system (CNS) disease

Treatment therapies

Treating BPDCN takes a team approach. NCCN recommends that treatment decisions involve a multidisciplinary team or a team of doctors from different fields of medicine, including a dermatologist.

Treatment for BPDCN includes tagraxofusp-erzs or high-dose chemotherapy followed by stem cell transplant. Not everyone can tolerate this approach. This cancer usually returns soon after treatment. Speak to your doctor about your goals for treatment and about the possible side effects.

Chemotherapy

There are 3 chemotherapy induction options:

- Cytarabine with idarubicin or daunorubicin
- HyperCVAD
- CHOP

HyperCVAD

In hyperCVAD chemotherapy, treatment alternates between two groups of drugs. Hyper means the 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.

HyperCVAD is an intense therapy that has serious side effects. Testing is needed to look at your overall health before starting hyperCVAD.

CHOP

CHOP stands for cyclophosphamide, doxorubicin, vincristine, and prednisone (a steroid). Doxorubicin can cause heart damage. It will not be an option if you have heart issues or are at risk for heart issues.

Tagraxofusp-erzs

Tagraxofusp-erzs (Elzonris®) is a biologic therapy. A biologic is made from a living organism or its by-product like in a vaccine. Tagraxofusp-erzs targets the CD123 protein marker found at higher levels on BDPCN cancer cells. This leads to cancer cell death.

The first cycle of this drug should be given in a hospital where it is 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 will probably spend more than one week in the hospital.

Before each infusion, you will be given a medicine such as:

- Steroid
- Anti-histamine
- Acetaminophen

Before each infusion the following should be checked:

- Vital signs
- Albumin (baseline level of 3.2 g/dL or higher is needed to start tagraxofusp-erzs)
- Transaminases
- Creatinine

You must be in good overall health to receive this treatment. Tagraxofusp-erzs can cause harmful side effects.

Tagraxofusp-erzs will be stopped if you have:

- Fever of 100.4 F (38 C) or higher
- Weight gain of 1.5 kilograms (3 pounds) or more in one day
- Systolic blood pressure of 160 mmHg or higher
- Systolic blood pressure of 80 mmHg or lower
- Heart rate of 130 beats per minute (BPM) or higher
- Heart rate of 40 BPM or lower
- Edema, fluid overload, and/or hypertension
- Mild to severe hypersensitivity reaction
- Low levels of albumin protein called hypoalbuminemia
- High levels of creatinine and liver enzymes

Radiation therapy

Radiation therapy uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill or shrink cancer cells. Although BPDCN is usually treated with chemotherapy or biologic therapy, radiation therapy might be used to treat skin lesions.

Treatment phases

BPDCN is a difficult disease to treat. However, there are treatment options. It is important to find a doctor and hospital that has experience treating BPDCN.

Induction

BPDCN is treated with a biologic therapy called tagraxofusp-erzs or with a combination of chemotherapies. A biologic therapy helps to improve the body's natural response against cancer.

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 doctor about what to expect from treatment and what you want from treatment.

Candidate for intensive therapy

The goal of intensive therapy is to put BPDCN in remission (to achieve a complete response). Intensive remission induction therapy is not an option for everyone. If intensive remission induction such as tagraxofusp-erzs or combined chemotherapies are an option for you, then see Guide 27.

After a complete response, options are to:

- Continue tagraxofusp-erzs
- Consider a blood stem cell transplant (HCT)

If treatment does not work or causes less than a complete response, then see Guide 29.

Not a candidate for intensive therapy

If intensive remission induction is not an option, then see Guide 28.

Guide 27
Candidate for intensive remission induction therapy

Options

Tagraxofusp-erzs with supportive care

Chemotherapy options:
- AML induction: standard-dose cytarabine with idarubicin or daunorubicin
- ALL induction: HyperCVAD regimen
- Lymphoma induction: CHOP regimen

Intrathecal chemotherapy (methotrexate or cytarabine) in those with CNS disease

→

If complete response, options include:
- Consider allogeneic or autologous HCT followed by surveillance
- Tagraxofusp-ersz until progression, then see treatment for relapsed or refractory disease (Guide 29)

Induction failure or less than complete response, see
- Treatment for relapsed or refractory disease (Guide 29)

Guide 28
Not a candidate for intensive remission induction therapy or tagraxofusp-erzs

Localized or isolated skin disease	→	Options include: • Surgery to remove lesion(s) • Focused radiation
Systemic disease with palliative care	→	Options include: • Systemic steroids • Supportive care

Treatment options are based on whether BPDCN is systemic or localized. Systemic means the cancer is throughout the body and treatment is to palliate or to give relief. If BPDCN is localized to the skin or a certain area of the body, then treatment will focus on those areas.

Surveillance

Surveillance is a plan that closely watches your condition. You might hear it called watch-and-wait. During this time you will have tests on a regular basis to look for changes in your blood. You will not have any treatment during surveillance.

A complete blood count (CBC) every 1 to 3 months for 2 years is advised. Then, it should be repeated every 3 to 6 months for up to 5 years. If results aren't normal, you might have a bone marrow aspirate and biopsy. You might also have a PET/CT if you had extramedullary disease before. This is cancer than might be in the lymph nodes or other organs. Skin or other lesions might be biopsied.

Relapse

When leukemia returns it is 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 responds to treatment in the same way.

A clinical trial is the preferred treatment for relapsed BPDCN, but there are other options. See Guide 29.

Refractory

When leukemia does not respond to treatment, it is 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 refractory BPDCN, but there are other options. See Guide 29.

Guide 29
Treatment for relapsed or refractory BPDCN

Evaluate central nervous system (CNS) for disease or to prevent spread of BPDCN to CNS

Consider the following:

- Clinical trial (preferred)
- Tagraxofusp-erzs (if not used before) with supportive care
- Chemotherapy (if not used before) (Guide 27)
- Local radiation to isolated areas or specific lesions
- Systemic steroids
- Venetoclax-based therapy (Guide 22)

Start donor search at first relapse in those who are candidates and no sibling donor match.

Supportive care

Supportive care is health care that relieves your symptoms caused by cancer and improves your quality of life. It is not cancer treatment. It might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling.

In BPDCN, supportive care might include radiation therapy or surgery to treat skin lesions. If you are taking tagraxofusp-erzs, you will have supportive care. Everyone with BPDCN should have a dermatologist as part of their care team.

Dermatologist

It is important to see a dermatologist and that your doctors work together on your treatment.

Tagraxofusp-erzs

Tagraxofusp-erzs can have very serious side effects. You will 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.

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 will be monitored for capillary leak syndrome. You might 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 is most often the result of capillary leak syndrome.

Review

- Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive blood cancer.
- BPDCN affects the blood, bone marrow, and skin. It can also affect the lymph nodes, spleen, and central nervous system (CNS).
- 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. An allogeneic stem cell transplant (HCT) 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.

8
Making treatment decisions

It is important to choose a cancer treatment that you are comfortable with. This starts with an open and honest conversation with your doctor.

It's your choice

In shared decision-making, you and your doctors share information, discuss options, and agree on a treatment plan. It starts with an open and honest conversation with your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else. Think about what you want from treatment. Discuss the risks and benefits of specific treatments. Weigh options. Share your concerns. Take the time to build a relationship with your doctor.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Even if you like and trust your doctor, get a second opinion. If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan. Bring someone with you to appointments, when possible. Ask questions and take notes during doctor visits.

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs for doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

You can also reach out to a social worker or a counselor. They can help you find ways to cope or refer you to supportive care services. These services may also be available to your family and friends.

Questions to ask your doctors

Possible questions to ask your doctors are on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Questions to ask about diagnosis and testing

1. What subtype of AML do I have? What does this mean in terms of my prognosis and treatment options?
2. What tests do I need? What other tests do you recommend?
3. How soon will I know the results and who will explain them to me?
4. Where will the tests take place? How long will the tests take?
5. Is there a cancer center or hospital nearby that specializes in my type and subtype of cancer?
6. What will you do to make me comfortable during testing?
7. How do I prepare for testing?
8. Would you give me a copy of the pathology report and other test results?
9. Who will talk with me about the next steps? When?
10. Will I start treatment before the test results are in?

Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, health, and other factors affect my options?
3. What if I am pregnant? What if I plan to become pregnant in the near future?
4. Am I a candidate for a blood stem cell transplant?
5. Am I a candidate for a clinical trial?
6. Which option is proven to work best for my subtype, age, and other risk factors?
7. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
8. How do you know if treatment is working? How will I know if treatment is working?
9. What are my options if my treatment stops working?
10. Are there any life-threatening side effects of this treatment? How will I be monitored?
11. What should I expect from this treatment?
12. Can I stop treatment at any time? What will happen if I stop treatment? How will I know when to stop blood transfusions or antibiotics?

Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks?
2. Which treatment do you recommend and why?
3. How long do I have to decide?
4. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?
5. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?
6. How much will the treatment hurt? What will you do to make me comfortable?
7. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?
8. What type of home care will I need? What kind of treatment will I need to do at home?
9. What can I do to prevent or relieve side effects? What will you do?
10. Which treatment will give me the best quality of life? Which treatment will extend my life? By how long?

Questions to ask about blood stem cell transplants

1. Which type of blood stem cell transplant is an option for me?
2. What do I need to do to prepare?
3. What will you do to prepare?
4. What are the risks to myself and/or the donor?
5. How will the transplant affect my prognosis?
6. How will a transplant affect the quality and length of my life?
7. What should I expect from a blood stem cell transplant?
8. How long should I expect to be in the hospital?
9. How will I feel before, during, and after the transplant?
10. How many blood stem cell transplants has this center done for my subtype of AML?

Questions to ask your doctors about their experience

1. What is your experience treating my subtype of AML?
2. What is the experience of those on your team?
3. Do you only treat AML? What else do you treat?
4. I would like to get a second opinion. Is there someone you recommend?
5. I would like another pathologist or hemopathologist to review my blood samples. Is there someone you recommend?
6. How many patients like me (of my age, gender, race) have you treated?
7. Will you be consulting with AML experts to discuss my health care? Who will you consult?
8. How many procedures like the one you're suggesting have you done?
9. Is this treatment a major part of your practice?
10. How many of your patients have had complications? What were the complications?

Websites

Aplastic Anemia & MDS International Foundation (AAMDSIF)
aamds.org

Be The Match®
bethematch.org

BMT InfoNet
Bone Marrow & Transplant Information Network
bmtinfonet.org

The Leukemia & Lymphoma Society
LLS.org/patientsupport

National Cancer Institute (NCI)
cancer.gov/types/leukemia

National Bone Marrow Transplant Link
nbmtlink.org

NCCN for Patients®
nccn.org/patients

NCCN Reimbursement Virtual Resource
nccn.org/reimbursement_resource_room/default.aspx

National Organization for Rare Disorders (NORD)
https://rarediseases.org/

Patient Advocate Foundation
panfoundation.org/apply

“Consider attending a support group for patients and caregivers.”

– Jim

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 hematopoietic cell transplant (HCT)
A cancer treatment that replaces abnormal blood stem cells with healthy donor cells. 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.

anti-metabolite
A drug that interferes with normal cell division and cell function.

arsenic trioxide (ATO)
A drug used to treat APL that has a fusion gene *PML-RARA*.

autologous hematopoietic cell transplant (HCT)
A cancer treatment that destroys your bone marrow then rebuilds it with your healthy stem cells. Also called high-dose therapy with autologous stem cell rescue (HDT/ASCR) stem cell transplant.

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

blast
An immature white blood cell.

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.

bone marrow aspiration
A procedure that removes a liquid bone marrow sample to test for a disease.

bone marrow biopsy
A procedure that removes bone and solid bone marrow samples to test for a disease.

chemotherapy
Cancer drugs that stop the cell life cycle so cells don't increase in number.

chromosome
The structures within cells that contain coded instructions for cell behavior.

complete blood count (CBC)
A lab test that includes the number of blood cells.

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

comprehensive metabolic panel (CMP)
Tests of up to 14 chemicals in your blood.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the insides of the body.

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

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

cytochemistry
The study of chromosomes using a microscope.

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

cytogenetics
The study of chromosomes using a microscope.

cytopenia
A health condition when the number of blood cells is lower than normal.

deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions for making and controlling 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 is caused by leukemia or its treatments.

extramedullary
Taking place outside 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 coded instruction in a cell (gene) made from parts of two coded instructions.

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

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

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

hematopoietic cell transplant (HCT)
A cancer treatment that replaces abnormal blood stem cells with healthy cells.

human leukocyte antigen (HLA)
A cell protein by which your body knows its own cells from foreign cells.

immunohistochemistry (IHC)
A lab test of cancer cells to find specific cell traits involved in abnormal cell growth.

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

induction
The first treatment that is given to greatly reduce the amount of cancer.

induction failure
When complete remission does not happen after two courses of chemotherapy.

karyotype
Lab test that makes a map of chromosomes to find defects.

lactate dehydrogenase (LDH)
A protein in blood that helps to make energy in cells.

lumbar puncture
A procedure that removes spinal fluid with a needle. Also called a spinal tap.

magnetic resonance imaging (MRI)
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

maintenance
A treatment phase that is given to prolong good treatment results.

molecular complete response
The absence of the *PML-RARA* gene after treatment for acute promyelocytic leukemia.

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

monitoring
A period of testing for changes in cancer status.

morphologic complete response
A large drop in number or percent of blasts after treatment for acute leukemia.

mutation
An abnormal change in the instructions within cells for making and controlling cells.

myelodysplastic neoplasm (MDS)
A cancer of blood-forming cells that causes too few blood cells to form.

myeloproliferative neoplasm (MPN)
A cancer of blood-forming cells that causes too many blood cells to form.

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 DNA part are made.

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

prognosis
The pattern and outcome of a disease.

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

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

refractory cancer
A cancer that does not improve with treatment.

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

supportive care
Treatment for the symptoms or health conditions caused by cancer or cancer treatment. Also sometimes called palliative care.

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

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

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

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