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1 AML basics

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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 found in adults. This chapter will provide an overview of AML.

Blood

Acute myeloid leukemia (AML) is a type of 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. Blood also plays an important role for the immune system and in preventing bleeding.

Blood cells

Your blood contains different types of cells.

There are 3 types of blood cells:

- Red blood cells (erythrocytes)
- White blood cells (leukocytes), which include granulocytes, monocytes, and lymphocytes
- Platelets (thrombocytes)

Blood cells are being replaced in your body all the time. Many have a short lifespan. Some white blood cells live less than one day. Your body makes one million red blood cells every second!

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.
How blood cells are formed
Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are early blood-forming cells called blood stem cells (hematopoietic stem cells). All types of blood cells start as blood stem cells. At any given time, bone marrow will have cells in various stages of development, from very immature to almost fully mature. With each stage, the blood stem cell changes and gets closer to what it is meant to be. After a blood stem cell develops into a red blood cell, white blood cell, or platelet, it is released in your bloodstream as needed.

Blood stem cells can copy themselves or self-renew. These cells are rare. Blood stem cells can also make new cells that are committed to becoming a certain type of blood cell. These are called progenitor cells or precursor cells. Progenitor cells are much more common than blood stem cells. Progenitor cells can become red blood cells, white blood cells, or platelets.

There are different types of progenitor cells:

- Lymphoid progenitor cells form into lymphoblasts that mature into lymphocytes.
- Myeloid progenitor cells from into myeloblasts and other non-lymphoid blood cells.

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.
Blasts
A blast is an immature white blood cell. Both lymphoid and myeloid progenitor cells form into blast cells called lymphoblasts or myeloblasts depending on the type. Blasts are committed to becoming a type of blood cell. Lymphoblasts normally mature into lymphocytes, a type of white blood cell. Myeloblasts are responsible for all other non-lymphoid blood cells in bone marrow, such as granulocytes, a type of white blood cell.

Acute myeloid leukemia
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 left untreated, AML is fatal.

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.

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
There are many types of AML. They are grouped and treated based on gene mutations and other features. Genetic and biomarker testing is used 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 myeloid leukemia (AML)
- Acute promyelocytic leukemia (APL)
- Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Key points

- 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.
- Myeloid progenitor cells develop into red blood cells, granulocytes (a type of white blood cell), and platelets.
- 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.
- 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.

Those with AML should be treated at experienced leukemia centers.
2 Testing and diagnosis

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14 General health tests
17 HLA typing
18 Bone marrow tests
18 Immunophenotyping
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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.

### Guide 1 Possible tests for AML

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Test results

Results from blood tests, imaging studies, and biopsy will be used to 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.

Keep these things in mind:

- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don’t be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. 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 phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician informed of changes to this list.

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!
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, herbals, or supplements you take. Tell your doctor about any symptoms you have. A medical history will help determine which treatment is best for you. It is sometimes called a health history.

**Physical exam**
During a physical exam, your health care provider may:

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

**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. Those with a family history of leukemia, blood cancer or abnormalities, or certain genetic mutations might be referred to genetic counseling.

**Blood tests**
Blood tests check for signs of disease and how well organs are working. 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 to check treatment results, blood counts, and the health of organs like your liver and kidneys.
Tests described next are listed alphabetically and not in order of importance.

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

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

It is standard to screen for clotting problems. 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

**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.

**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.

**Complete blood count and differential**
A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. A CBC is a key test that gives a picture of your overall health. AML often causes low counts of healthy blood cells.

There are several types of white blood cells. A 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.

**Creatinine**
Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys aren’t working as well as they were when someone had lower levels of creatinine.
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.

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

Lactate dehydrogenase
Lactate dehydrogenase (LDH) or lactic acid dehydrogenase 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.

Liver function tests
Liver function tests (LFTs) 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.
Phosphate
Cells have a lot of phosphate in them. Therefore, when many cells are breaking down at the same time, the levels of phosphate in the blood can go up. Your kidneys help get rid of extra phosphate, but too much phosphate in the blood can also damage the kidneys, making it harder to get the levels back down to normal.

Uric acid
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. Very high levels of uric acid in the blood can damage the kidneys.

HLA typing
Human leukocyte antigens (HLAs) are proteins found on the surface of most cells. They play 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 blood test that detects a person’s HLA type. This test is done before a donor (allogeneic) blood stem cell transplant. To find a donor match, your proteins will be compared to the donor’s proteins to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood samples from you and your blood relatives will be tested first.

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.
Bone marrow tests

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

If the blastic plasmacytoid dendritic cell neoplasm (BPDCN) subtype of AML is suspected, or if your AML is suspected to be active outside of the bone marrow, you might have a lymph node, organ, or skin biopsy. This would be in addition to the standard bone marrow tests described next.

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

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

For many, this is a painful procedure. Your care team will try to make you as comfortable as possible. The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. For an aspirate, a hollow needle will be inserted 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. You may feel bone pain at your hip for a few days. Your skin may bruise.

Immunophenotyping

Immunophenotyping 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 biomarkers. Certain biomarkers can be targeted with specific AML treatments.

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

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

Flow cytometry may be used on cells from circulating (peripheral) blood or from a bone marrow aspirate.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cells. The cells are then studied using a microscope.
Genetic tests

Genetic tests are used to learn more about your type of AML, to target treatment, and to determine the likely path your cancer will take (prognosis). This testing is different from family history genetic testing. AML genetic testing looks for changes only in the leukemia cells that have developed over time, and not changes in the rest of your body’s cells.

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes tell cells what to do and what to become. Most genes contain information about a specific protein.

AML cells sometimes have changes in genes and chromosomes that can be seen under a microscope or found with other tests. Cytogenetic tests look for these changes or abnormalities.

A karyotype and FISH are two types of cytogenetic tests used in AML.

Karyotype

A karyotype is a picture of the chromosomes in cells. It is a test that shows abnormal changes in chromosomes.
FISH
Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. FISH can look for translocations and inversions that are too small to be seen with other methods. However, it can only be used for known changes. It cannot detect all the possible changes found with a karyotype.

- 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).

Since this test doesn’t need growing cells, it can be performed on either a bone marrow or blood sample. A bone marrow sample is needed to get all the information your doctor needs to help plan your care.

Biomarker testing
Biomarker or molecular testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment. Proteins are written like this: PML. Genes are written like this: *PML*.

Biomarker testing is very important to identify the AML subtype and is a standard part of testing at diagnosis. Test results are used to predict the outcome of AML called a prognosis.

Biomarker testing can also detect fusion genes made by translocations. An example of two fused genes is *PML-RARA*. *PML-RARA* 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 (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies are called PCR product. This is important when testing for treatment response or remission.
Imaging tests

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

Leukemia can spread outside the bloodstream to lymph nodes, liver, spleen, skin, and other organs. It rarely spreads to the lining of the brain and spinal cord.

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.

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.

Contrast material

Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. Contrast might be taken by mouth (oral) or given through a vein (IV). The contrast is not permanent and will leave the body in your urine immediately after the test.

Tell your doctors if you have had allergic reactions to contrast in the past. This is important. You might be given medicines, such as diphenhydramine (Benadryl®) and prednisone (steroids), to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

Brain CT

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the same body part from different angles. All the images are combined to make one detailed three-dimensional (3D) 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 powerful magnets to take pictures of the inside of the body. It does not use x-rays. A device will be placed around your head that sends and receives radio waves. An MRI can show if the outer layer of the brain is swollen. Swelling caused by leukemia is called leukemic meningitis. Contrast should be used.
PET scan
A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and if they are using sugar to grow. Cancer cells show up as bright spots on PET scans. However, not all cancer will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. When a PET scan is combined with CT, it is called a PET/CT scan.

Heart tests
Heart or cardiac tests are used to see how well your heart works. These tests might be used to monitor treatment side effects. You might be referred to a cardiologist.

Electrocardiogram
An electrocardiogram (ECG or EKG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged corrected 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. Certain treatments for AML can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

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.

Cardiac nuclear medicine scan
A nuclear heart scan is an imaging test that uses special cameras and a radioactive substance called a tracer to create pictures of your heart. The tracer is injected into your blood and travels to your heart. This test can also be used to measure the ejection fraction.
Lumbar puncture

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 to rule out a central nervous system (CNS) disease.

A lumbar puncture (LP) 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.
Key points

- Blood tests check for signs of disease, how well organs are working, and treatment results.
- A bone marrow aspiration and biopsy are procedures that remove bone and marrow samples. To diagnose AML samples of bone marrow must be removed and tested before starting any treatment.
- Immunophenotyping can detect subtle differences between types of AML.
- Genetic tests are used to learn more about your type of AML, to target treatment, and to determine the likely path your cancer will take (prognosis).
- Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment.
- 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.
- Online patient portals are a great way to access your test results.
3 Treating AML

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27 Treatment phases
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Treatment for AML and its subtypes will be in phases. The first goal of treatment is often to put the cancer in remission. This chapter provides a general overview of some therapies you might receive and what to expect. Together, you and your doctor will choose a treatment plan that is best for your type of AML.

Treatment team

Those with AML should seek treatment at experienced cancer centers. Treating cancer takes a team approach. Treatment decisions will involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team might include the following specialists:

- **A hematologist** is an expert in blood diseases and blood cancers.
- **A pathologist** analyzes the cells, tissues, and organs removed during a biopsy and provides cancer diagnosis and information about biomarker testing.
- **A diagnostic radiologist** reads the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places ports for treatment.
- **A medical oncologist** treats cancer in adults using systemic therapy.
- **A radiation oncologist** prescribes and plans radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during procedures.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Palliative care nurses** and advanced practice providers provide an extra layer of support to help with your cancer-related symptoms.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.
- **Social workers** help people solve and cope with problems in their everyday lives.
- **A research team** helps to collect research data if you are in a clinical trial.
You know your body better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

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

---

### Treatment phases

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 (CR) or remission. Sometimes this initial treatment is called remission induction therapy. After induction, you will have bone marrow tests to look for a response (remission).

In measurable 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.

#### Remission

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

It takes time for bone marrow to make normal blood cells again. This is called recovery.

In complete remission:

- 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)
**Consolidation**
Consolidation may occur after induction, for those in remission. 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. 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.

**Surveillance**
You will be monitored throughout treatment. Surveillance watches for any changes in your condition after remission or a stem cell transplant. You will have tests during surveillance to check for relapse.

**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.

**Systemic therapy**
Systemic therapy works throughout the body. Types include chemotherapy, targeted therapy, and immunotherapy. Systemic therapy might be used alone or with other therapies. Goals of systemic therapy should be discussed before starting treatment. Your wishes about treatment are important. If you have any religious or personal beliefs about certain kinds of treatment, now would be the time to share them with your doctor.

**Warnings!**
You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction. It is critical to speak
with your care team about any supplements you may be taking.

Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- St. John’s Wort

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. Bring a list with you to every visit.

Chemotherapy

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**

Some of the anthracyclines used to treat AML include:

- 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**

Some of the anti-metabolites used to treat AML include:

- Cladribine (Leustatin®)
- Clofarabine (Clolar®)
- Cytarabine (Cytosar-U®)
- Fludarabine (Fludara®)
- Methotrexate
Dual-drug liposome of cytarabine and daunorubicin (Vyxeos™, CPX-351) 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 of 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, for 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.

**Did you know?**

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

**Hypomethylating agents**
Methyl groups are molecules that are found in DNA. They 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 have other serious health issues. 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 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:

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

Targeted therapy might be used to target:

- CD33 surface protein
- FLT3 mutations
- IDH1 and IDH2 mutations

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 blood count recovery and cause liver issues.

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

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

Sorafenib with azacitidine or decitabine may be used to treat AML with FLT3-ITD mutation.

IDH1 and IDH2
Ivosidenib is used to treat AML with IDH1 mutation.

Enasidenib is used to treat AML with IDH2 mutation.
Stem cell transplant

A stem cell transplant (SCT) replaces bone marrow stem cells. You might hear it called a hematopoietic cell transplant (HCT) or a bone marrow transplant (BMT). This book will refer to it as SCT.

There are 2 types of SCTs:

- **Autologous** – stem cells come from you
- **Allogeneic** – stem cells come from a donor who may or may not be related to you

**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 leukemia. It is an option to treat blasts that may have survived induction. An allogeneic SCT 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 an SCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune system so your body won’t kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

After conditioning, you will receive the healthy stem cells through a transfusion. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks.

Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. Transfusions are also possible. A red blood cell transfusion is used to prevent bleeding and to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding. While waiting for the cells to engraft, you will likely feel tired and weak.

**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 SCT and how this might affect your quality of life.
Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

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

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

- **Phase I trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.

- **Phase II trials** study how well the drug or approach works against a specific type of cancer.

- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.

- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

Finding a clinical trial

**In the United States**

NCCN Cancer Centers
NCCN.org/cancercenters

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

**Worldwide**

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

Need help finding a clinical trial? NCI’s Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact
Who can enroll?
Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

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

Start the conversation
Don’t wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions
There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

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

Are clinical trials free?
There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.
General supportive care

Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. It might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects. Best supportive care, supportive care, and palliative care are often used interchangeably.

It is important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment.

Anemia
Anemia is a condition where your body does not make enough healthy blood cells, resulting in less oxygen being carried to your cells. Treatment depends on the type of anemia and its cause.

It might include:

- Iron supplements to treat iron deficiency.
- Vitamin B supplements for low vitamin levels.
- Blood transfusions to increase red blood cell levels.
- Medicine to induce blood creation.

Supportive care resources from NCCN

Anemia
For more information, see NCCN Guidelines for Patients: Anemia and Neutropenia, available at NCCN.org/patientguidelines.

Distress
For more information, see NCCN Guidelines for Patients: Distress During Cancer Care, available at NCCN.org/patientguidelines.

Nausea and Vomiting
For more information, see NCCN Guidelines for Patients: Nausea and Vomiting, available at NCCN.org/patientguidelines.
Distress
Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt.

Depression, anxiety, and sleeping problems are common in cancer. Talk to your doctor and with those whom you feel most comfortable about how you are feeling. There are services and people who can help you. Support and counseling services are available.

Fatigue
Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. There are treatments for fatigue. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

Nausea and vomiting
Nausea and vomiting are a common side effect of treatment. You will be given medicine to prevent and treat nausea and vomiting.

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

Keep a pain diary
A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:
- The time and dose of all medicines
- When pain starts and ends or lessens
- Where you feel pain
- Describe your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt).
- Does pain get in the way of you doing the things you enjoy?
Treating AML General supportive care

Treatment side effects
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 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.

Trouble eating
Sometimes side effects from cancer or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining your weight.

It is important to tell your care team about all side effects so they can be managed.
Key points

- The goal of treatment is a complete response (CR).
- Induction or remission induction is the first phase of treatment.
- Measurable residual disease (MRD) is AML that appears to be in remission, but very sensitive tests find cancer.
- Consolidation may occur after induction for those in remission. It is needed to kill any cancer cells that might be left in the body after induction.
- Maintenance or post-consolidation therapy is given to prevent the return of cancer.
- 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.
- Systemic therapy works throughout the body. AML is treated with systemic therapy.
- A stem cell transplant (SCT) replaces damaged or destroyed stem cells with healthy stem cells.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.

- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.

Take our survey
And help make the NCCN Guidelines for Patients better for everyone!
NCCN.org/patients/comments
4 AML

- Overview
- Treatment phases
- Treatment overview
- Under 60 years of age
- 60 years of age and over
- Maintenance
- Surveillance
- Relapse and refractory
- Supportive care
- Key points
Overview

There are different types of AML. This chapter is for those with AML that is not APL or BPDCN. It is sometimes referred to as non-APL AML. Together, you and your doctor will choose a treatment plan that is best for you.

Diagnosis

To be diagnosed with AML, 20 percent (20%) or more myeloblasts must be present in the bone marrow or blood. This means that at least 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 biopsy. 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 known reason. Certain treatments for other cancers, such as radiation or certain class of chemotherapy, can later cause AML. Myelodysplastic syndrome (MDS) or other chronic marrow cancers 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. AML can also run in certain families, although this is thought to be quite uncommon.

Treatment phases

The goal of the induction phase of treatment is to put AML into complete remission. In complete remission, both bone marrow and blood cell blasts are suppressed, allowing marrow function to resume. However, a remission does not equal cure, since undetected leukemia cells may persist and can return causing relapse. A cure requires several years of continued remission. Consolidation therapy is needed to prolong remission.

Treatment for AML can occur over years. The several phases are 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. When blood counts are normal, bone marrow tests will be repeated to see if the leukemia is in remission. You might be referred to a palliative care specialist before starting induction.

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 and 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.
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.

**Measurable residual disease**
In measurable residual disease (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 (alloSCT). When testing finds MRD, it is called a positive MRD result or MRD positive. Ask your doctor what this might mean and what will be the next steps.

**Consolidation**
Your blood will be given time to recover before starting consolidation. Consolidation is the second phase of treatment. It is also called post-remission therapy. Consolidation treats blasts that may have survived induction.

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

**Monitoring**
You will have frequent blood tests during induction and consolidation. Bone marrow tests are possible.

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

**Surveillance**
Surveillance watches for any changes in your condition after remission or a stem cell transplant. You will have tests during surveillance to check for relapse.
Treatment overview

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 genetic risk 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

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)
- Those who had myelodysplastic syndrome (MDS) or chronic myelomonocytic leukemia (CMML) before called antecedent MDS or CMML
- AML with myelodysplasia-related changes called AML-MRC

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 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
Risk groups
Risk groups for non-APL AML are based on the presence of abnormal or mutated genes. 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.

For genetic risk groups, see Guide 2.

Guide 2
Genetic risk groups for AML

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Genetic Abnormalities</th>
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<tbody>
<tr>
<td><strong>Favorable</strong></td>
<td>Includes any of the following abnormal genes:</td>
</tr>
<tr>
<td></td>
<td>- t(8;21)(q22;q22.1); RUNX1-RUNX1T1</td>
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<tr>
<td></td>
<td>- inv(16)(p13.1q22) or t(16;16)(p13.1q22); CBFB-MYH11</td>
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<tr>
<td></td>
<td>- Biallelic mutated CEBPA</td>
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<tr>
<td></td>
<td>- Mutated NPM1 without FLT3-ITD or with FLT3-ITD&lt;sub&gt;low&lt;/sub&gt;</td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td>Includes any of the following abnormal genes:</td>
</tr>
<tr>
<td></td>
<td>- Mutated NPM1 and FLT3-ITD&lt;sub&gt;high&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td>- Wild-type NPM1 without FLT3-ITD or with FLT3-ITD&lt;sub&gt;low&lt;/sub&gt; (without adverse-risk genetic lesions)</td>
</tr>
<tr>
<td></td>
<td>- t(9;11)(p21.3;q23.3); MLLT3-KMT2A</td>
</tr>
<tr>
<td></td>
<td>- Other abnormalities not classified as favorable or adverse</td>
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<tr>
<td><strong>Poor or adverse</strong></td>
<td>Includes any of the following abnormal genes:</td>
</tr>
<tr>
<td></td>
<td>- t(6;9)(p23;q34.1); DEK-NUP214</td>
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<tr>
<td></td>
<td>- t(v;11q23.3); KMT2A rearranged</td>
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<tr>
<td></td>
<td>- t(9;22)(q34.1;q11.2); BCR-ABL1</td>
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<td>- inv(3)(q21.3q26.2) or t(3;3)(q21.3; q26.2); GATA2,MECOME(EVI1)</td>
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<tr>
<td></td>
<td>- -5 or del(5q); -7; -17/abn(17p)</td>
</tr>
<tr>
<td></td>
<td>- Complex karyotype, monosomal karyotype</td>
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<tr>
<td></td>
<td>- Wild-type NPM1 and FLT3-ITD&lt;sub&gt;high&lt;/sub&gt;</td>
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<td></td>
<td>- Mutated RUNX1</td>
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<td></td>
<td>- Mutated ASXL1</td>
</tr>
<tr>
<td></td>
<td>- Mutated TP53</td>
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</table>
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 of each treatment and why a certain treatment might be better for you. Find out how treatment might affect your quality and length of life.

**Induction options**
Most people have one round of induction. But, it is possible you will have more than one round. A follow-up bone marrow aspirate and biopsy will be done 14 to 21 days after the start of therapy. For induction options, see Guide 3.
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<thead>
<tr>
<th>Guide 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Under 60 years of age: Induction options</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Favorable-risk cytogenetics</th>
<th>Standard-dose cytarabine with idarubicin or daunorubicin</th>
<th>Guide 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>For CD33-positive:</td>
<td>• Standard-dose cytarabine with daunorubicin and gemtuzumab</td>
<td></td>
</tr>
<tr>
<td><strong>FLT3, ITD, or TKD with intermediate- or poor-risk cytogenetics</strong></td>
<td>Standard-dose cytarabine with daunorubicin and midostaurin</td>
<td>Guide 4</td>
</tr>
<tr>
<td><strong>Unfavorable-risk cytogenetics and TP53-mutated</strong></td>
<td>Other options will be considered</td>
<td>Guide 4</td>
</tr>
<tr>
<td><strong>• Therapy-related AML other than CBF or APL</strong></td>
<td>Standard-dose cytarabine with idarubicin or daunorubicin</td>
<td>Guide 4</td>
</tr>
<tr>
<td><strong>• Antecedent MDS or CMML</strong></td>
<td>CPX-351/dual-drug liposome of daunorubicin and cytarabine</td>
<td></td>
</tr>
<tr>
<td><strong>• Cytogenetic changes consistent with MDS (AML-MRC)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended options for intermediate-risk or poor-risk disease</th>
<th>Standard-dose cytarabine with idarubicin or daunorubicin</th>
<th>Guide 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD33-positive or intermediate-risk AML:</strong></td>
<td>• Standard-dose cytarabine with daunorubicin and gemtuzumab</td>
<td></td>
</tr>
<tr>
<td><strong>High-dose (HiDAC) cytarabine with idarubicin or daunorubicin, and etoposide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fludarabine with HiDAC, idarubicin, and granulocyte colony-stimulating factor (G-CSF)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NCCN Guidelines for Patients®
Acute Myeloid Leukemia, 2022
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. Treatment options are based on the amount of cancer or blasts that remain after induction. In hypoplasia, bone marrow is starting to recover, but isn’t there yet. For treatment after standard-dose cytarabine induction, see Guide 4.

Guide 4
Under 60 years of age: After standard-dose cytarabine induction or re-induction

<table>
<thead>
<tr>
<th>Significant amount of cancer remains</th>
<th>Cytarabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard-dose cytarabine with idarubicin or daunorubicin</td>
<td></td>
</tr>
<tr>
<td>FLT3-mutated ITD or TKD:</td>
<td></td>
</tr>
<tr>
<td>• Standard-dose cytarabine with daunorubicin and midostaurin (bone marrow aspirate and biopsy on day 21)</td>
<td></td>
</tr>
<tr>
<td>Therapy-related AML (other than CBF-AML or APL) or those who had MDS or CMML or AML-MRC before:</td>
<td></td>
</tr>
<tr>
<td>• CPX-351/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)</td>
<td></td>
</tr>
<tr>
<td>Treatment for induction failure (no response):</td>
<td></td>
</tr>
<tr>
<td>• Matched sibling or other donor SCT</td>
<td></td>
</tr>
<tr>
<td>• HiDAC (if not previously used as treatment for persistent disease at day 15) with or without anthracycline (daunorubicin or idarubicin) if a clinical trial is not available while waiting to find a donor</td>
<td></td>
</tr>
<tr>
<td>• Therapy for relapsed or refractory disease</td>
<td></td>
</tr>
<tr>
<td>• Best supportive care</td>
<td></td>
</tr>
</tbody>
</table>

| 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) |
| Intermediate or high-dose cytarabine |

| Hypoplasia | Wait for recovery |

Notes: Follow-up bone marrow aspirate and biopsy 14 to 21 days after start of therapy.
Further treatment is 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. A lumbar puncture might be done. For induction failure, the options include:

- Matched sibling or other donor stem cell transplant (SCT)
- HiDAC (if not previously used as treatment for persistent disease at day 15) with or without anthracycline (daunorubicin or idarubicin) if a clinical trial is not available while waiting to find a donor
- Therapy for relapsed or refractory disease
- Best supportive care

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. Options are based on the amount of cancer or blasts that remain after induction. In hypoplasia, bone marrow is starting to recover, but isn’t there yet. For treatment after high-dose cytarabine, see Guide 5.

---

Guide 5
Under 60 years of age: After high-dose cytarabine induction

| Significant amount of cancer remains | • Therapy for relapsed or refractory disease (Guide 9)  
<table>
<thead>
<tr>
<th></th>
<th>• Best supportive care</th>
</tr>
</thead>
</table>
| Significant cancer reduction with low percent of residual blasts or hypoplasia | Wait for recovery, then:  
|                                      | • Bone marrow aspirate and biopsy  
|                                      | • Genetic and biomarker testing as needed  
|                                      | • Test for measurable residual disease (MRD)  
| If complete response, then consolidation |                           |
| If induction failure, then:         | • Therapy for relapsed or refractory disease (Guide 9)  
|                                      | • Matched sibling or other donor SCT  
|                                      | • Best supportive care |

Notes: Follow-up bone marrow aspirate and biopsy 21 to 28 days after start of therapy.
If complete response (remission) was achieved, then you will have consolidation therapy.

If there was no response or cancer progressed, then options include treatment for relapsed or refractory disease, a stem cell transplant (SCT), or best supportive care. Best supportive care is treatment to improve quality of life and relieve discomfort.

**Consolidation**
Consolidation therapy is treatment to kill any remaining blasts after a complete response (remission). Treatment is based on genetic and biomarker test results. See Guide 6.

**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.

| Guide 6 |
|------------------|--------------------------------------------------|
| **Under 60 years of age: Consolidation therapy options** | |
| **• Core binding factor (CBF) translocations and MRD negative** | • High-dose cytarabine (HiDAC)  |
| | • HiDAC with gemtuzumab for CD33 positive, NPM1 positive, or FLT3 negative  |
| | • Cytarabine with daunorubicin and gemtuzumab for CD33 positive  |
| **• Intermediate-risk cytogenetics** | • Matched sibling or other donor SCT  |
| **• Molecular abnormalities including MRD positive** | • HiDAC  |
| | • HiDAC with oral midostaurin for FLT3-mutated AML  |
| | • Cytarabine with daunorubicin and gemtuzumab for CD33 positive  |
| **• Therapy-related AML other than CBF** | • Matched sibling or other donor SCT (preferred)  |
| **• Unfavorable cytogenetics** | • HiDAC  |
| **• Molecular abnormalities** | • HiDAC with oral midostaurin for FLT3-mutated AML  |
| | • CPX-351/dual-drug liposome of cytarabine and daunorubicin for therapy-related AML, or those who had MDS, CMML, or AML-MRC before (preferred only if given in induction)  |
Depending on your performance status, if you have any heart or other serious health issues, treatment will be:

- Intensive
- Low- or non-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 your quality and length of life.

### Guide 7

#### 60 years of age and over: Intensive induction options

<table>
<thead>
<tr>
<th>Favorable-risk cytogenetics</th>
<th>For CD33-positive AML:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Standard-dose cytarabine with daunorubicin and gemtuzumab</td>
</tr>
<tr>
<td>Standard-dose cytarabine with (idarubicin or daunorubicin or mitoxantrone)</td>
<td></td>
</tr>
</tbody>
</table>

| FLT3, ITD, or TKD with intermediate-risk or poor-risk cytogenetics | Standard-dose cytarabine with daunorubicin and midostaurin |

| • Therapy-related AML  
| • Antecedent MDS or CMML  
| • AML-MRC | CPX-351/dual-drug liposome of cytarabine and daunorubicin (Vyxeos®) |

<table>
<thead>
<tr>
<th>Unfavorable-risk cytogenetics</th>
<th>Venetoclax with one from below:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Decitabine</td>
</tr>
<tr>
<td></td>
<td>• Azacitidine</td>
</tr>
<tr>
<td></td>
<td>• Low-dose cytarabine (LDAC)</td>
</tr>
<tr>
<td>Low-intensity therapy of azacitidine or decitabine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended options for intermediate-risk or poor-risk disease</th>
<th>Standard-dose cytarabine with (idarubicin or daunorubicin or mitoxantrone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For CD33-positive or intermediate-risk AML:</td>
<td></td>
</tr>
<tr>
<td>• Standard-dose cytarabine with daunorubicin and gemtuzumab</td>
<td></td>
</tr>
</tbody>
</table>
**Intensive induction is an option**
The goal of intensive remission induction is to reduce the number of blasts and put AML into remission. You might have more than one round of induction to achieve a complete response. Follow-up bone marrow aspirate and biopsy will occur 14 to 21 days after the start of therapy. Intensive induction options can be found in Guide 7.

**After standard-dose cytarabine induction**
Blood needs time to recover after treatment. When blood cell counts have not returned to normal (hypoplasia), then you will wait for recovery. There might be cancer left after treatment called residual disease.

Treatment options for residual disease include:

- Additional standard-dose cytarabine with anthracycline (idarubicin or daunorubicin) or mitoxantrone
- For FLT3, ITD, or TKD genetics: Standard-dose cytarabine with daunorubicin and midostaurin
- For therapy-related AML, AML-MRC, or those who had MDS or CMML before: Dual-drug liposomal encapsulation of cytarabine and daunorubicin (preferred only if given in induction)
- Regimens containing intermediate-dose cytarabine
- Consider allogeneic SCT (alloSCT)
- Therapy for relapsed or refractory disease
- Await recovery
- Best supportive care

**After intense induction**
Post-induction therapy is treatment after 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 measurable residual disease (MRD).

The goal of induction is a complete response (remission). Consolidation therapy may be given to kill any remaining blasts after a complete response (remission).

- If induction caused a complete response, then you might have an allogeneic stem cell transplant (SCT), have cytarabine-based therapy, or be placed on maintenance therapy.
- If induction did not cause a complete response or remission, then you might have a low-intensity therapy of azacitidine or decitabine, have an alloSCT, or be treated for relapsed or refractory disease. Best supportive care is an option. It is preferred that the SCT be part of a clinical trial.
**Intensive induction is not an option**
Not everyone wants or can tolerate intensive induction treatment. Age, overall health, and disease features 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. Actionable mutations include *FLT3*, *IDH1*, and *IDH2*. Treatment options for both actionable mutations and AML without actionable mutations can be found in Guide 8.

### Guide 8
**60 years of age and over: Low- and non-intensive induction options**

<table>
<thead>
<tr>
<th>AML without actionable mutations</th>
<th>Preferred</th>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Venetoclax and azacitidine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Venetoclax and decitabine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Venetoclax and low-dose cytarabine (LDAC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Low-intensity therapy of azacitidine or decitabine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Glasdegib and LDAC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Gemtuzumab for CD33 positive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Best supportive care (hydroxyurea and transfusion support)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IDH1 or IDH2 mutation</th>
<th>Preferred</th>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Venetoclax-based therapy in combination with azacitidine or decitabine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Ivosidenib for <em>IDH1</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Enasidenib for <em>IDH2</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Venetoclax-based therapy in combination with LDAC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Low-intensity therapy of azacitidine or decitabine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FLT3 mutation</th>
<th>Preferred</th>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Venetoclax-based therapy in combination with azacitidine or decitabine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Low-intensity therapy (of azacitidine or decitabine) with sorafenib for <em>FLT3</em>-ITD positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Venetoclax-based therapy in combination with LDAC</td>
</tr>
</tbody>
</table>
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.

Options 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 measurable residual disease (MRD).

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

- Allogeneic stem cell transplant (alloSCT)
- Continue with lower intensity treatment
- Hypomethylating agents (HMAs) such as azacitidine or decitabine
- Enasidenib for IDH2-mutated AML or ivosidenib IDH1-mutated AML
- Venetoclax with (decitabine or azacitidine or LDAC)
- Glasdegib and LDAC for those 75 years of age or older or for those with other serious health issues
- Azacitidine or decitabine and sorafenib for FLT3-ITD-mutated AML
- Gemtuzumab for CD33 positive

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.
Maintenance

Maintenance therapy is given to maintain remission. For those who had intensive chemotherapy and AML is now in remission, maintenance therapy with oral azacitidine can be considered if you were unable to complete chemotherapy consolidation and are not a candidate for allogeneic stem cell transplant (alloSCT). If those with FLT3-positive AML in remission after alloSCT, maintenance therapy with a FLT3-inhibitor may be considered.

Surveillance

Surveillance is a period of testing that begins after remission to monitor for relapse or the return of cancer. 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.

We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback
Relapse and refractory

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. A search for a stem cell donor should begin at first relapse, if this is an option being considered.

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. Biomarker testing (including IDH1, IDH2, and FLT3 mutations) should be done to determine next treatment options. See Guide 9.

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

- Clinical trial (strongly preferred)
- Targeted therapy (see Guide 9) followed by matched sibling or other donor SCT
- Chemotherapy (see Guide 9) followed by matched sibling other donor SCT
- Repeat initial successful induction regimen if 12 months or more since induction regimen
- Best supportive care
### Guide 9
Therapy options: Relapsed or refractory disease

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>A clinical trial is strongly preferred</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targeted therapy</strong></td>
<td></td>
</tr>
</tbody>
</table>
| AML with \(FL3\)-ITD mutation: | • Gilteritinib  
  • Hypomethylating agents of azacitidine or decitabine with sorafenib |
| AML with \(FL3\)-TKD mutation: | • Gilteritinib |
| AML with \(ID2\) mutation: | • Enasidenib |
| AML with \(ID1\) 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 cell 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.

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

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

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

If you do not want blood transfusions, your care team will:

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

> Consider using acetaminophen to manage fever.

> Consider iron, folate, and vitamin B12 supplementation. Iron supplementation may be avoided if you have excess iron levels.

> Consider use of erythropoiesis-stimulation agent (ESA), granulocyte colony-stimulating factor (G-CSF), and thrombopoietin (TPO) after a thorough discussion of potential risks, benefits, and uncertainties.

> Consider bed rest and supplemental oxygenation if you have severe anemia.

Based on your disease, your care team might:

> Test for actionable mutations and consider use of targeted agents instead of intensive chemotherapy.

> Consider use of less myelosuppressive induction including dose reduction of anthracyclines, and use of non-intensive chemotherapy.

> Consider referring you to centers with experience in bloodless autologous stem cell transplant (autoSCT).

**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 having 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.

**Differentiation syndrome**

Differentiation syndrome is a potentially serious side effect of taking certain anti-cancer drugs. It is caused by 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.

> 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 sign of 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 (Hydrea®) 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.

**Growth factors**
A type of growth factor, called granulocyte colony-stimulating factor (G-CSF), triggers the bone marrow to make granulocytes (white 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. Filgrastim (Neupogen®) is a G-CSF. A biosimilar might be used in place of filgrastim. A biosimilar is a drug that is very much like one that has been approved by the U.S. Food and Drug Administration (FDA). It must be used in the exact same way and at the same dose as the other drug.

**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. Antifungals can treat fungal infections. You may be given anti-viral drugs to prevent viral infections.

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

- The whole process can take about 1 to 4 hours, depending on how much blood is needed.
- Most transfusions use blood from a donor. Some choose a family member or friend to donate blood.
- Blood transfusions are usually very safe. Donated blood is carefully tested, handled, and stored.
- Most people’s bodies handle blood transfusions very well. But, like any medical procedure, there are some risks. Speak with your doctor for specific information about your risks.
- Chemotherapy can affect how bone marrow makes new blood cells. Some people getting treatment for cancer might need a transfusion of red blood cells or platelets.
**Tumor lysis syndrome**
In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. TLS can be life-threatening.

Induction chemotherapy may cause TLS. TLS is more likely if your blast count is very high. If you are at risk for TLS, you will have blood tests daily.

**Key points**
- Most people with AML have a subtype other than APL.
- Treatment for AML involves several phases.
- Treatment 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.
- Treatment of AML requires the use of blood and blood products for supportive care. If you do not wish to receive transfusions or certain blood products, please make your wishes known.
## 5 APL

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<td>Treatment phases</td>
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Acute promyelocytic leukemia (APL) is a rare type of AML. With treatment, APL is cured more often than other AML types. APL occurs when pieces of chromosomes 15 and 17 break off and trade places creating 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 can be started within just a few hours.

APL occurs when parts of chromosome 15 and chromosome 17 break off and trade places, called a 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.

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

**Consolidation**
Consolidation 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. PCR can tell whether 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 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.

**Treatment overview**
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. 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. Your heart and electrolytes will be monitored during treatment with arsenic trioxide.

Low-risk group
Those with a white blood cell count of 10,000 mcL or less at diagnosis are placed into the low-risk group. For low risk, the preferred induction therapy option is ATRA with arsenic trioxide and supportive care. Consolidation will include ATRA with arsenic trioxide.

Guide 10
Low-risk group: Induction followed by consolidation options

<table>
<thead>
<tr>
<th>Induction</th>
<th>Consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA with arsenic trioxide and supportive care (preferred option)</td>
<td>If blood counts are normal, then start ATRA with arsenic trioxide. Bone marrow aspirate and biopsy might be done before starting consolidation.</td>
</tr>
</tbody>
</table>

If arsenic is not an option

<table>
<thead>
<tr>
<th>Induction</th>
<th>Consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA with idarubicin</td>
<td>At blood count recovery, start ATRA with idarubicin followed by ATRA with mitoxantrone, then ATRA with idarubicin.</td>
</tr>
<tr>
<td>ATRA with gemtuzumab</td>
<td>Bone marrow aspirate and biopsy on day 28 to 35 before starting ATRA. Gemtuzumab may be given.</td>
</tr>
</tbody>
</table>
High-risk group

Those with a white blood cell count of more than 10,000 mcL at diagnosis are placed into the high-risk group.

Treatment for high risk is based on if you have:

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

For high risk, ATRA is used as part of induction therapy. 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 starting consolidation.

Guide 11
High-risk group and no heart issues: Induction followed by consolidation options

<table>
<thead>
<tr>
<th>Induction</th>
<th>Consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA with idarubicin and arsenic trioxide (preferred)</td>
<td>→ ATRA and arsenic trioxide</td>
</tr>
<tr>
<td>ATRA with arsenic trioxide and gemtuzumab (preferred)</td>
<td>→ ATRA and arsenic trioxide. Gemtuzumab may be given.</td>
</tr>
<tr>
<td>ATRA with daunorubicin and cytarabine</td>
<td>→ Arsenic trioxide, then ATRA with daunorubicin</td>
</tr>
<tr>
<td></td>
<td>→ Daunorubicin with cytarabine, then cytarabine with daunorubicin and intrathecal chemotherapy</td>
</tr>
<tr>
<td>ATRA with idarubicin</td>
<td>→ ATRA with idarubicin and cytarabine, then ATRA with mitoxantrone, then ATRA with idarubicin and cytarabine</td>
</tr>
</tbody>
</table>

*After induction: Bone marrow aspirate and biopsy on day 28 to document remission. A lumbar puncture before starting consolidation is possible.

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 11.

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. All induction options include ATRA. Consolidation will be a continuation of induction therapy. A chemotherapy might be added. A lumbar puncture is possible.
There are 2 types of heart issues that affect treatment:

- **Low ejection fraction** is when the amount of blood pumping from the left side of the heart is lower than normal. This is measured using a multigated acquisition (MUGA) scan or echocardiogram.

- **Prolonged 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).

Treatment options for high-risk group with heart issues can be found in Guide 12.

### 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 the same treatment, but at a lower dose. Treatment may last for 1 to 2 years or longer.

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.

---

### Guide 12

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

<table>
<thead>
<tr>
<th>Induction</th>
<th>Consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Those with low ejection fraction</strong></td>
<td>ATRA with arsenic trioxide and gemtuzumab</td>
</tr>
<tr>
<td><strong>Those with prolonged QTc</strong></td>
<td>ATRA with gemtuzumab</td>
</tr>
<tr>
<td></td>
<td>ATRA with daunorubicin and cytarabine</td>
</tr>
<tr>
<td></td>
<td>ATRA with idarubicin</td>
</tr>
</tbody>
</table>

*After induction: Bone marrow aspirate and biopsy on day 28 to document remission. A lumbar puncture before starting consolidation is possible.*
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 13.

<table>
<thead>
<tr>
<th>Guide 13</th>
<th>First relapse: Therapy options after remission</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early relapse</strong></td>
<td>Anthracycline-based treatment as in Guide 12</td>
</tr>
<tr>
<td>• Less than 6 months after ATRA and arsenic trioxide (no anthracycline)</td>
<td></td>
</tr>
<tr>
<td><strong>Did not have arsenic trioxide or has</strong></td>
<td>Arsenic trioxide</td>
</tr>
<tr>
<td><strong>Early relapse</strong></td>
<td>Arsenic trioxide with ATRA</td>
</tr>
<tr>
<td>• Less than 6 months after ATRA with anthracycline-containing treatment</td>
<td>Arsenic trioxide with ATRA and gemtuzumab</td>
</tr>
<tr>
<td><strong>Late relapse</strong></td>
<td>Arsenic trioxide</td>
</tr>
<tr>
<td>• 6 or more months after arsenic trioxide-containing treatment</td>
<td>Arsenic trioxide with ATRA</td>
</tr>
<tr>
<td></td>
<td>Arsenic trioxide with ATRA and (anthracycline or gemtuzumab)</td>
</tr>
</tbody>
</table>
**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 and aspirate 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 stem cell transplant (SCT). A clinical trial or arsenic trioxide might be options if you are not a candidate for an SCT. You may receive chemotherapy to prevent APL from spreading to your brain and spine (central nervous system).

If no remission, then the options are:

- Clinical trial
- Matched sibling or other donor SCT

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

**Stem cell transplant**
An autologous stem cell transplant (autoSCT) 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 an stem cell transplant (SCT) using your own cells may be an option. A donor or matched sibling (allogeneic) blood SCT may be an option depending on the circumstances.

**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. Tell your treatment team about any new or worsening symptoms.

Supportive care for APL is described next.

**Arsenic trioxide monitoring**
Arsenic trioxide can cause serious irregular heart rhythms (arrhythmias). You 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 taking 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
Key points

- 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.

Let us know what you think!

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

NCCN.org/patients/response
BPDCN

- Overview
- Testing and diagnosis
- Treatment overview
- Intensive therapy
- No intensive therapy
- Surveillance
- Relapse and refractory
- Supportive care
- Key points
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 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.

Skin lesions are common in BPDCN. BPDCN can also affect the central nervous system (CNS).

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

You might have BPDCN if you have:

- Skin lesions that might be dark purple and large or small spots across the skin. It might look like a rash or bruises. Everyone is different.
- Enlarged lymph nodes

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 and 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. BPDCN 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. Biomarker 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, T lineage, or B lineage expression markers. Myeloid markers include: MPO, lysozyme, CD14, CD34, CD116, and CD163.

You will have several tests if BPDCN is suspected. See Guide 14.

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Guide 14
Possible tests for BPDCN

<table>
<thead>
<tr>
<th>Test Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history and physical exam</td>
</tr>
<tr>
<td>Complete blood count (CBC), platelets, differential, and comprehensive metabolic panel (CMP)</td>
</tr>
<tr>
<td>Analysis of skin lesions (your doctor will likely work with a dermatologist)</td>
</tr>
<tr>
<td>Bone marrow aspirate and biopsy with lymph node biopsy</td>
</tr>
<tr>
<td>Immunohistochemistry, flow cytometry, and cytogenetic analysis (karyotype and/or FISH)</td>
</tr>
<tr>
<td>Analysis of dendritic cell structure and blood blasts</td>
</tr>
<tr>
<td>Molecular tests of at least these mutations: ASXL1, IDH1, IDH2, IKZF1, IKZF2, IKZF3, NPM1, NRAS, TET1, TET2, TP53, U2AF1, and ZEB2</td>
</tr>
<tr>
<td>PET/CT scan of other areas, if extramedullary disease and/or lymphadenopathy suspected</td>
</tr>
<tr>
<td>Lumbar puncture (LP)</td>
</tr>
</tbody>
</table>
BPDCN is a difficult disease to treat. However, there are treatment options. It is important to find a doctor and hospital that have experience treating BPDCN.

Treating BPDCN takes a team approach. Treatment decisions should 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 (SCT). Not everyone can tolerate this approach. BPDCN 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. It helps to improve the body’s natural response against cancer.

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

The first cycle of this drug should be given in a hospital where it 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.

Radiation therapy

Radiation therapy (RT) 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.
Intensive therapy

Intensive therapy is not for everyone. Treatment will be based on factors such as your overall health and your body’s ability to tolerate drug therapies that could be toxic. Your wishes are also important. Talk with your doctor about what to expect from treatment and what you want from treatment.

The goal of intensive therapy is to put BPDCN in remission (to achieve a complete response). If tagraxofusp-erzs or combined chemotherapies are an option for you, then see Guide 15.

Less than complete remission

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

Complete remission

After a complete response, options are to continue tagraxofusp-erzs until disease progression or consider a stem cell transplant (SCT). Surveillance follows an SCT.

Guide 15

Intensive 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
No intensive therapy

If intensive therapy is not an option for induction, then treatment options are based on whether BPDCN is systemic or localized. In both cases, treatment is to palliate or to give relief. See Guide 16.

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

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

Surveillance

After a stem cell transplant (SCT), you will enter 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) should be performed every 1 to 3 months for 2 years, then 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.

Guide 16
Not a candidate for intensive therapy or tagraxofusp-erzs

<table>
<thead>
<tr>
<th>Localized or isolated skin disease</th>
<th>Palliative options include:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Surgery to remove lesion(s)</td>
</tr>
<tr>
<td></td>
<td>• Focused radiation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Systemic disease for palliative care</th>
<th>Options include:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Venetoclax-based therapy</td>
</tr>
<tr>
<td></td>
<td>• Systemic steroids</td>
</tr>
<tr>
<td></td>
<td>• Supportive care</td>
</tr>
</tbody>
</table>
Relapse and refractory

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.

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 relapsed and refractory BPDCN. Tagraxofusp-erzs (Elzonris®) is also a preferred option, if it was not used before. Other options include systemic therapy or radiation. See Guide 17.

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.

Guide 17

Therapy options: Relapsed and refractory BPDCN

Evaluate central nervous system (CNS) for disease

Consider the following:
- Clinical trial (preferred)
- Tagraxofusp-erzs (preferred, if not used before) with supportive care
- Chemotherapy (if not used before)
- Local radiation to isolated areas or specific lesions
- Systemic steroids
- Venetoclax-based therapy

Start donor search at first relapse in those who are candidates and no sibling donor match.
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 be asked to weigh yourself every day while taking tagraxofusp-erzs. Sudden weight gain might be a sign of capillary leak syndrome.

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

Key points
- Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive blood cancer of immature plasmacytoid dendritic cells, a type of immune cell.
- 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 (alloSCT) 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.
Making treatment decisions

- 79 It’s your choice
- 79 Questions to ask your doctors
- 89 Resources
It’s important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It’s your choice

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

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

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!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see 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 people 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.

Questions to ask your doctors

Possible questions to ask your doctors are listed 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, overall health, and other factors affect my options?

3. What if I am pregnant? What if I plan to become pregnant soon?

4. Am I a candidate for a stem cell transplant?

5. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?

6. Which option is proven to work best for my cancer, age, and other risk factors?

7. Does any option offer long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?

8. Are there any life-threatening side effects of this treatment? How will I be monitored?

9. What should I expect from this treatment?

10. 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?

11. What decisions must be made today? Is there a social worker or someone who can help me decide?

12. Is there a hospital or treatment center you can recommend for treatment?
Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks? Which treatment do you recommend and why?

2. Which treatment will give me the best quality of life? Which treatment will extend life? By how long?

3. How will my age, performance status, and other health conditions limit my treatment choices?

4. Does the order of treatment matter?

5. How long do I have to decide about treatment?

6. Does this hospital or center offer the best treatment for me?

7. When will I start treatment? How long will treatment take?

8. How much will the treatment cost? How much will my insurance help pay for the treatment?

9. How do you know if treatment is working? How will I know if treatment is working?

10. What are my options if my treatment stops working?

11. What are the chances my cancer will return? How will it be treated if it returns?

12. I would like a second opinion. Is there someone you can recommend?

13. How will treatment affect my ability to do things I enjoy?
Questions to ask your doctors about their experience

1. What is your experience treating my type 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 hematopathologist to review my blood samples. Is there someone you recommend?

6. How many patients like me (of the same age, gender, race) have you treated?

7. Will you be consulting with AML experts to discuss my health care? Whom 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?

11. Who will manage my day-to-day care?
Questions to ask about side effects

1. What are the side effects of this treatment?

2. What are the side effects of this cancer?

3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?

4. What side effects should I watch for? What side effects are expected and which are life threatening?

5. When should I call the doctor? Can I text? What should I do on weekends and other non-office hours?

6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?

7. What medicines can I take to prevent or relieve side effects?

8. What can I do to help with pain and other side effects?

9. Will you stop treatment or change treatment if there are side effects? What do you look for?

10. What can I do to lessen or prevent side effects? What will you do?

11. What medicines may worsen side effects of treatment?
Questions to ask about blood transfusions

1. How often will I need blood transfusions?
2. How long does a transfusion take?
3. How will I feel after a transfusion?
4. Can I be given blood donated by family members?
5. Should my friends and family donate blood?
6. What are the side effects of blood transfusions?
7. Can my body reject blood transfusions? Is this serious?
8. If my body rejects a blood transfusion, will I be able to have more blood transfusions?
Making treatment decisions  Questions to ask your doctors

Questions to ask about radiation therapy

1. What type of radiation therapy (RT) will I have?

2. What will you target?

3. What is the goal of this RT?

4. How many treatment sessions will I require? Can you do a shorter course of RT?

5. Do you offer this type of RT here? If not, can you refer me to someone who does?

6. What side effects can I expect from RT?

7. Should I eat or drink before RT?

8. Will I be given medicine to help me relax during RT?

9. What should I wear?
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 about clinical trials

1. What clinical trials are available for my type of cancer?

2. What are the treatments used in the clinical trial?

3. What does the treatment do?

4. Has the treatment been used before? Has it been used for other types of cancer?

5. What are the risks and benefits of this treatment?

6. What side effects should I expect? How will the side effects be controlled?

7. How long will I be in the clinical trial?

8. Will I be able to get other treatment if this doesn’t work?

9. How will I know if the treatment is working?

10. Will the clinical trial cost me anything? If so, how much?
Resources

American Cancer Society
cancer.org/cancer/leukemia.html

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

Be The Match®
bethematch.org

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

CancerCare
cancercare.org

Cancer Support Community
cancersupportcommunity.org/living-cancer

Chemocare
chemocare.com

MedlinePlus
medlineplus.gov/acutemyeloidleukemia.html

My Survival Story
mysurvivalstory.org

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

National Bone Marrow Transplant Link
nbmtlink.org

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox

patientadvocate.org/explore-our-resources/national-financial-resource-directory/

National Hospice and Palliative Care Organization
nhpco.org/patients-and-caregivers

NCCN Reimbursement Virtual Resource
NCCN.org/reimbursement

National Organization for Rare Disorders (NORD)
rarediseases.org

OncoLink
oncolink.org

Patient Access Network Foundation
panfoundation.org

Radiological Society of North America
radiologyinfo.org

Testing.com
testing.com

The Leukemia & Lymphoma Society
LLS.org
Words to know

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

- **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 called *PML-RARA*.

- **autologous stem cell transplant (autoSCT)**
  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).

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

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

- **blast**
  An immature white blood cell.

- **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 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.

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. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

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 induction treatment does not cause complete remission.

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.
**Words to know**

**lumbar puncture (LP)**
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.

**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.

**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.

**stem cell transplant (SCT)**
A cancer treatment that replaces abnormal blood stem cells with healthy cells. Also called hematopoietic cell transplant (HCT) or bone marrow transplant (BMT).

**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.
**NCCN Contributors**

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia, Version 1.2022. It was adapted, reviewed, and published with help from the following people:

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