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Acute Myeloid Leukemia in Adults: In Detail

A companion to AML: The Basics

Revised **2025**

Formerly titled Acute Myeloid Leukemia in Adults

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Inside This Booklet

Acknowledgement

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Support for this publication provided by AbbVie Inc.; Bristol Myers Squibb; Daiichi Sankyo, Inc.; Genentech, a member of the Roche Group; Kura Oncology, Inc.; and Syndax Pharmaceuticals Inc.

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Introduction

This booklet provides information about acute myeloid leukemia (AML) in adults. This type of leukemia is also known as "acute myelogenous leukemia," "acute myelocytic leukemia," "acute myeloblastic leukemia" and "acute granulocytic leukemia."

AML is the most common type of acute leukemia in adults. Although AML can occur at any age, adults aged 60 years and older are more likely to develop the disease than younger people.

For easy-to-read, general information about AML for yourself, family or friends, view LLS's *AML: The Basics.* For information about AML in children, view LLS's *Acute Myeloid Leukemia in Children and Teens: In Detail.* Both booklets are available at www.LLS.org/booklets.

Over the past several decades, advances in AML research have resulted in new treatments, but much work remains to be done. New therapies are needed to extend survival and to increase cure rates, and The Leukemia & Lymphoma Society (LLS) is leading the charge. Approximately one quarter of our annual research funding is dedicated to AML.

This booklet provides information about AML and explains tests and treatments for the disease. It also includes brief descriptions of normal blood and bone marrow, as well as a glossary of health terms related to AML.

We hope you will keep this booklet handy and that, should you ever feel alone in confronting problems, you will turn to it for information and guidance to find the support and resources you need.

We are here to help.

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Leukemia Basics

The human body is made up of trillions of cells. Normally these cells grow and multiply to form new cells as the body needs them. When cells become damaged or old, they usually die, and new cells take their place.

Sometimes cells start collecting mistakes in their DNA (deoxyribonucleic acid). DNA is like an instruction manual for your body, telling cells how to grow, function and make you who you are. A gene mutation is a change in the sequence of the DNA in a cell.

Cancer starts when a gene or several genes in a cell mutate and create a cancerous cell. This abnormal cancer cell grows and divides instead of dying. Cancer cells may spread into, or invade, other areas of the body, disrupting how the body works.

As cancer cells multiply, many types of cancers form solid tumors, but cancers of the blood, such as leukemia, generally do not. Instead leukemia cells affect the amount of blood cells in the body, and they may accumulate in organs such as the liver or spleen.

Cancer can happen in almost any cell anywhere in the body. Leukemia is a cancer of blood cells. It begins in the bone marrow, the spongy tissue in the center of most bones where most blood cells are formed. Blood cells begin as hematopoietic (blood) stem cells in the bone marrow. These stem cells develop into immature cells called “blasts” that go through many stages before they eventually develop into mature red blood cells, white blood cells and platelets.

Leukemia occurs when one of the immature blasts in the bone marrow mutates at some point in its development and becomes a leukemia cell. Leukemia cells do not mature into healthy functioning blood cells. They grow more quickly and live longer than normal blood cells. They divide and copy themselves to make more and more leukemia cells. Over time, the leukemia cells crowd out and suppress the development of healthy blood cells in the bone marrow. When this happens, the body may not have enough red blood cells, white blood cells and/or platelets.

Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clotting (clumping tougher) at the site of an injury. Without sufficient red blood cells, the body’s organs and tissues may not receive enough oxygen to work properly. Low white blood cell counts can lead to serious and frequent infections, and low platelet counts can cause excessive bleeding and bruising.

There are four major types of leukemia. They are:

- Acute myeloid leukemia (AML)
- Chronic myeloid leukemia (CML)

- Acute lymphoblastic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)

Leukemia is classified as either “acute” or “chronic.” These two terms describe how quickly the disease progresses without treatment. Acute leukemias progress rapidly and produce cells that are not fully developed. These immature cells cannot perform their normal functions. Chronic leukemias usually progress slowly, and patients have greater numbers of mature cells. In general, these more mature cells can carry out some or all of their normal functions.

Leukemia is further classified by the type of blood cell (either “myeloid” or “lymphoid”) that becomes cancerous. Blood cells begin as stem cells in the bone marrow. A blood stem cell may become a lymphoid stem cell or a myeloid stem cell. Lymphoid stem cells develop into white blood cells called “lymphocytes.” Myeloid stem cells can develop into red blood cells, platelets or certain other types of white blood cells. Leukemia is classified as “lymphocytic” or “lymphoblastic” if it originates in a lymphoid cell. It is classified as “myeloid” or “myelogenous” if the cancerous changes start in a myeloid cell. See **Figure 5** on page 54, for an illustration of blood cell development.

Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is a type of cancer in which the bone marrow makes too many immature blood cells called "myeloblasts." In AML, a mutation or a series of mutations in the DNA of a single myeloid stem cell results in the formation of an abnormal myeloblast. This abnormal myeloblast does not develop into a healthy, functioning myeloid cell. It becomes a leukemia cell (also referred to as an “AML cell” or a "leukemia blast cell”).

These genetic errors in the mutated cell cause the leukemia cell to keep growing and dividing, whereas a healthy cell would stop dividing and eventually die. Every cell that arises from the initial leukemia cell also has the mutated DNA. As the leukemia cells multiply uncontrollably, they quickly accumulate in the bone marrow. This slows down or stops the production of normal, healthy red blood cells, white blood cells and platelets. As a result, there are too many leukemia blast cells (immature cells) and not enough mature, functioning red and white blood cells and platelets.

Over time, the leukemia cells spill out of the bone marrow into the bloodstream. This can cause the number of white blood cells in the blood to increase, but most of these white blood cells are leukemia cells that do not protect against infection. Once they are in the bloodstream, the leukemia cells can spread to other parts of the body such as the central nervous system (brain and spinal cord).

By the time AML is diagnosed, the number of healthy red blood cells, white blood cells and platelets in the blood is usually lower than normal. Low levels of blood cells may result in anemia, infections and excessive bleeding or bruising.

Medical Term	Definition
Anemia	Low red blood cell count
Thrombocytopenia	Low platelet count (“thrombocyte” is another word for platelet)
Neutropenia	Low neutrophil count (a neutrophil is a type of white blood cell)

In rare instances, AML cells collect outside the bone marrow and form a solid mass (a tumor). This type of tumor, called a “myeloid sarcoma” can form in almost any part of the body. Other names for a myeloid sarcoma are “extramedullary disease,” “chloroma,” “granulocytic sarcoma,” “myeloblastoma” and “monocytoma.” It is important to note that a myeloid sarcoma is different from a true "sarcoma," which refers to a distinct group of cancers arising from connective tissues like muscle, fat, or bone. Surgery and radiation therapy are not effective ways of treating myeloid sarcomas, so myeloid sarcomas are generally treated with chemotherapy regimens used for AML (even if the bone marrow and blood do not appear to be involved). In some cases, treatment for myeloid sarcomas may also include allogeneic stem cell transplantation.

Signs and Symptoms

Signs and symptoms are changes in the body that may indicate the presence of disease. A “sign” is a change the doctor sees during an examination or in a laboratory test result. A “symptom” is a change a patient can notice and/or feel.

A person who has signs and/or symptoms that suggest the possibility of leukemia is referred to a specialist called a “hematologist-oncologist.” This is a doctor who has special training in diagnosing and treating blood disorders and blood cancers such as leukemia, lymphoma and myeloma. In some large medical centers, there are hematologist-oncologists who specialize in treating acute leukemias such as AML.

It is common for someone with AML to feel unwell because of the lack of normal, healthy blood cells. This happens when the leukemia cells in the bone marrow crowd out the normal blood-forming cells. As a result, patients with AML may not have enough mature red blood cells, white blood cells and/ or platelets, so they often have signs and/or symptoms related to low blood cell counts.

Symptoms of anemia (a low red blood cell count) include:

- Fatigue
- Weakness
- Shortness of breath during normal physical activities

- Lightheadedness, dizziness or faintness
- Headaches
- Pale complexion

Symptoms of neutropenia (a low number of neutrophils, a type of white blood cell that is important in fighting infections) include:

- Frequent infections
- Fever

Symptoms of thrombocytopenia (a low platelet count) include:

- Bruising easily
- Pinhead-sized red or purple spots on the skin, called “petechiae”
- Prolonged bleeding from minor cuts
- Frequent or severe nosebleeds
- Bleeding gums
- Heavier or more frequent menstrual periods in females

Other general symptoms of AML include:

- Loss of appetite
- Unexplained weight loss
- Discomfort in bones or joint
- Fullness or swelling in the abdomen, due to an enlarged spleen or liver

The signs and/or symptoms of AML may be similar to those of other blood disorders or medical conditions. Speak with your doctor if you experience any of these symptoms to ensure proper diagnosis and treatment.

Testing

While certain signs and/or symptoms may indicate a person has AML, laboratory tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis because it helps the doctor to:

- Estimate how the disease will progress
- Determine the appropriate treatment

Talk to your doctor about:

- The diagnostic tests that are being done
- What the results mean
- Getting copies of the results

Some tests may be repeated, both during and after treatment, to evaluate its effectiveness.

Medical History. Your doctor will take a thorough medical history. This may include information about past illnesses, injuries, medications and other treatments. Some illnesses run in families, so the doctor may also ask about the health of your blood relatives. Your doctor should find out whether you have a family history of blood cancer. Certain gene mutations present at birth may increase a person's risk of developing AML, creating an inherited predisposition to the disease. If you have either a personal history of cancer or a family history of leukemia and/or other cancers in closely related relatives or recent generations, the doctor should evaluate you for an inherited predisposition syndrome; this information will help the doctor to manage your treatment selection. For example, it may affect choice of chemotherapy or choice of a related donor for allogeneic stem cell transplantation.

Physical Examination. The doctor will want to know about your current symptoms and will conduct a physical examination. During the physical examination, the doctor may listen to your lungs and heart and carefully check your body for any signs of infection and disease. To check your internal organs, the doctor may feel different parts of your body. For example, the doctor may feel your abdomen to see if you have an enlarged spleen or liver. Your doctor may also check the lymph nodes in your neck, armpits and groin (the top inner part of the thigh) to see if they are enlarged.

Complete Blood Count (CBC) with Differential (diff). This test measures the number of red blood cells, white blood cells and platelets in a blood sample. It also measures the amount of hemoglobin in the red blood cells and the percentage of red blood cells in the sample. The CBC should include a "differential," which measures the numbers of the different types of white blood cells in the sample.

People with AML often have a high number of white blood cells, but most of these are leukemia cells that do not protect against infection. These patients are "immunocompromised," meaning they have a weakened immune system because they do not have enough mature white blood cells. They may also have low numbers of red blood cells and platelets.

Bone Marrow Aspiration and Biopsy. Leukemia starts in the bone marrow, the spongy tissue inside the center of most bones. When blood tests show cytopenias (low blood counts) or the presence of blast cells (immature blood cells), your doctor may recommend a test of the bone marrow to see whether your bone marrow is healthy and if it is making normal amounts of blood cells. Doctors use the findings from bone marrow aspiration and biopsy to diagnose and monitor blood and bone marrow diseases, including leukemia.

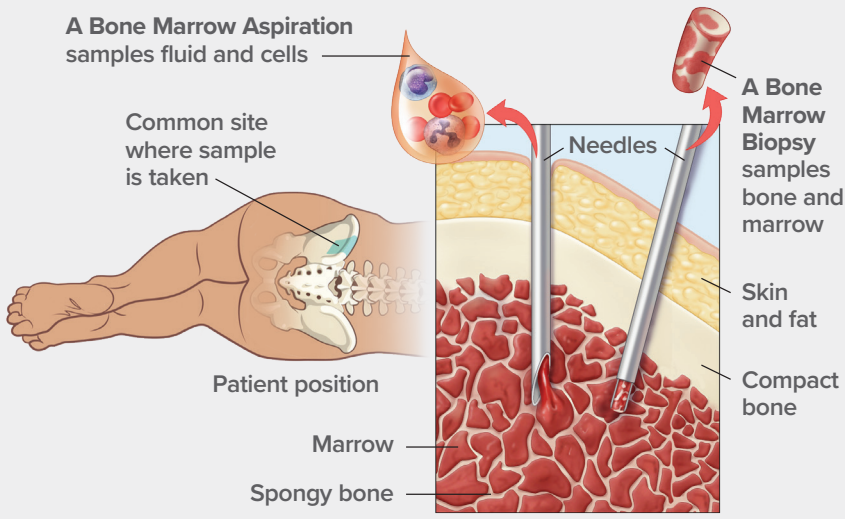
- A bone marrow aspiration is a test to remove a small sample of liquid bone marrow.
- A bone marrow biopsy is a test to remove a small sample of intact bone marrow.

Many people will have both tests done at the same time, but sometimes people just have a bone marrow aspiration. Bone marrow aspiration and biopsy are often performed at the doctor's office or in the hospital. Both samples are usually taken from the large hip bone in the lower back. You will likely lie on your stomach or side.

For many people, this is a painful procedure, so you will receive medicine to numb the skin and the surface of the bone. You may also have the option to take medicine before the procedure to help you relax. Some patients may be given a sedative so they will feel less pain and have no memory of the procedure.

For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both needles are inserted through the skin, generally in the same area. The bone marrow samples (the aspirate and the biopsy) are sent to the laboratory where they are examined under a microscope. See **Figure 1** below for an illustration of the bone marrow tests.

Figure 1. Bone Marrow Aspiration and Biopsy



Left: The place on the back of the patient's pelvic bone where a bone marrow aspiration or biopsy is done. **Right:** Where the needles go inside the bone to collect the liquid sample for aspiration (the needle on the left) and the bone sample for biopsy (the needle on the right). The needles are different sizes for each of these tests.

Visit www.LLS.org/3D and click on "Bone Marrow Biopsy and Aspiration" to view an interactive 3D model that will help you visualize and better understand the bone marrow aspiration and biopsy procedures.

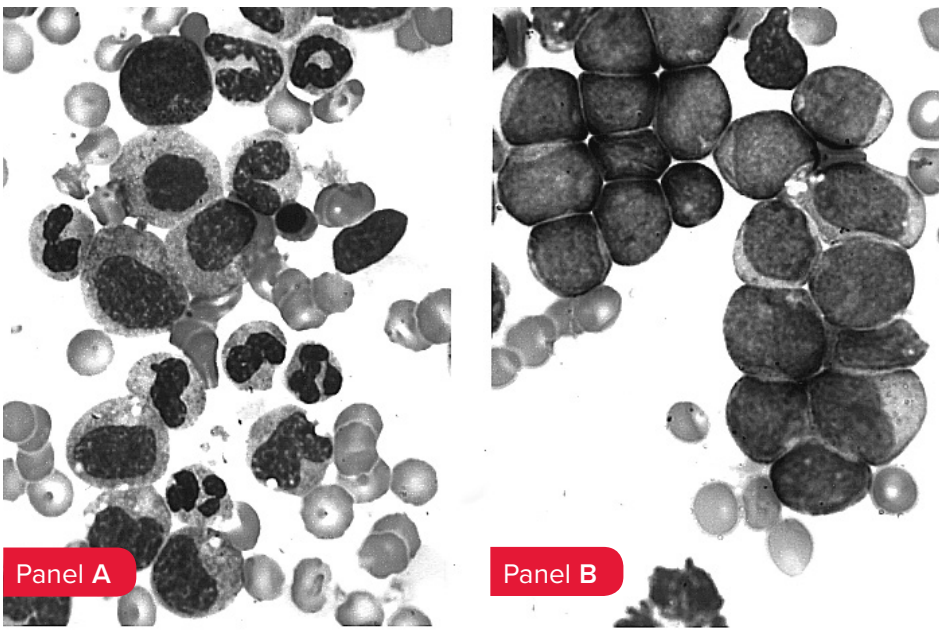
Cell Assessment. At the laboratory, a hematopathologist examines the blood and bone marrow samples. A hematopathologist is a doctor who has special training in identifying blood diseases by studying cells under a microscope and performing other specialized tests on the bone marrow and blood cells.

The hematopathologist examines the cells under a microscope to determine their size, shape and type, and to identify other cell features (see **Figure 2** below). The percentage of blast cells in the bone marrow and blood is another important finding. In individuals without leukemia, there are typically no blast cells in the blood, and no more than 5 percent blasts in the bone marrow.

In some types of AML, a diagnosis requires finding at least 20 percent myeloblasts in the bone marrow. In certain cases, AML can also be diagnosed when the percentage of myeloblasts is less than 20 percent if the myeloblasts have a chromosomal change or genetic mutation that is typically found in a specific type of AML.

The hematopathologist will conduct additional tests on the samples to determine the subtype of AML.

Figure 2. Normal Cells versus AML Cells



Panel A shows normal marrow cells seen through a microscope. The darker shapes are the nuclei of the cells. Some of the nuclei are circular and some are horseshoe shaped, reflecting the different developmental stages and the different types of cells. **Panel B** shows AML blast cells seen through a microscope. These cells are "arrested" in an early stage of development. In panel B, all the AML cells have a similar appearance, in contrast to the varied appearance of the normal cells in panel A.

Biomarker Testing. These laboratory tests look for biomarkers, which are molecules found in the blood, other body fluids or tissues that are signs of a normal or abnormal process, or of a condition or disease. Biomarkers provide information about a person's cancer. Each person's cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose some types of cancer. It may also be used to help plan treatment, make a prognosis or predict whether cancer will come back or spread to other parts of the body. It may also be used to monitor treatment. Important tests may include:

Immunophenotyping (Flow Cytometry). This laboratory test identifies cancer cells based on markers called "antigens." These antigens are proteins found either on the surface of or within white blood cells. Finding (or not finding) certain proteins can help determine the type of leukemia.

Immunophenotyping is done with an instrument called a "flow cytometer." A flow cytometer measures the number of cells in a sample, as well as specific characteristics of the cells, including their size and shape, and identifies specific markers on the cell surface. A sample of cells from blood, bone marrow or other sample is tagged with a panel of antibodies that are specific to areas on the cell. The cells are stained with a light-sensitive dye and are passed through a laser beam in the flow cytometer. If they have an antibody-specific surface marker, the cells light up and are counted.

Leukemia cells can have different antigens on their surfaces, depending on the type of leukemia. Certain antigens, called "cluster of differentiation (CD)" proteins, help identify the type of leukemia cells. While the specific pattern of antigens varies among different AML subtypes, most AML cells express CD13, CD33 and/or CD34.

In addition to its use for diagnosis, flow cytometry is also used after treatment for evaluating measurable residual disease (MRD), also called "minimal residual disease." This term refers to the small number of cancer cells that may remain in the body after treatment. Flow cytometry can find one cancer cell among 10,000 to 100,000 normal bone marrow cells. Testing for MRD helps doctors plan additional treatments. It is also used to find out how well treatment is working or if the cancer has come back.

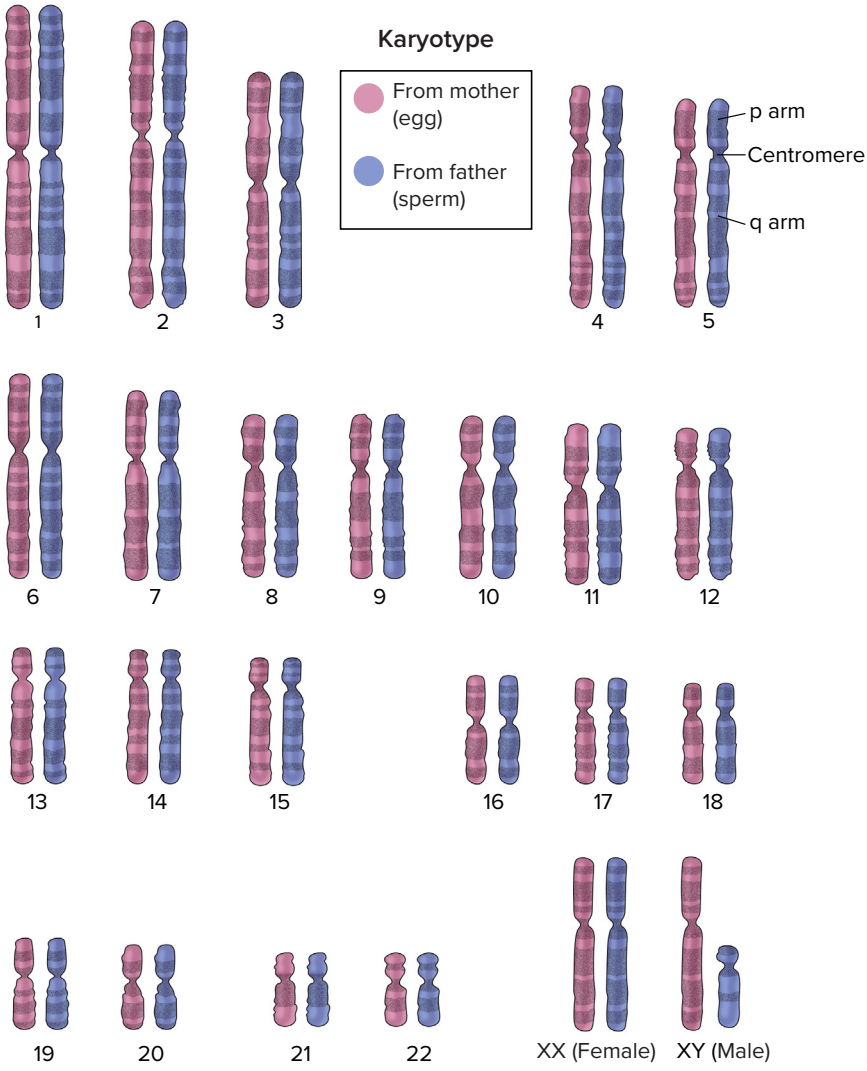
Cytogenetic Analysis (Karyotyping). In this test, a hematopathologist uses a microscope to examine the chromosomes inside of cells. In patients with AML, cytogenetic analysis is used to look for abnormal changes in the chromosomes of the leukemia cells.

Normal human cells contain 23 pairs of chromosomes, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. Each chromosome is divided into two sections or "arms." The short arm of the

chromosome is labeled the “p arm.” The long arm of the chromosome is labeled the “q arm.” See **Figure 3** below, for an illustration of human chromosomes lined up in pairs, an arrangement called a “karyotype.”

In some cases of AML, the chromosomes of the leukemia cells have abnormal changes that can be seen under a microscope. Cytogenetic testing is done with either a bone marrow sample or a blood sample. The leukemia cells in the sample are allowed to grow in a laboratory and then are stained prior to examination. The sample is then examined under a microscope and photographed to show the arrangement of the chromosomes.

Figure 3. Normal Karyotype



Chromosomal abnormalities in leukemia cells can be identified in many patients with AML. These abnormalities can be “numerical” or “structural.” A “numerical abnormality” is when there is a different number of chromosomes in the cells than is usually found. For example, instead of the typical 46 chromosomes in each cell of the body, there may be 45 or 47 chromosomes in the leukemia cells. A "structural" abnormality occurs when the chromosome’s structure has been altered in one of several ways including:

- Translocation, which occurs when a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes trade places with each other.
- Inversion, which occurs when a part of a chromosome breaks off, turns upside down and then reattaches in that position.
- Deletion, which occurs when a part of the chromosome is missing.
- Duplication, which occurs when part of the chromosome is copied too many times, resulting in extra genetic material.

In some cases, cytogenetic analysis provides important information for doctors determining a patient’s treatment options and prognosis. For example, a translocation between chromosomes 15 and 17, abbreviated t(15;17), is associated with a diagnosis of acute promyelocytic leukemia (APL). This AML subtype has a more favorable prognosis and requires a different treatment approach than that of other AML subtypes. For more information on APL, see page 30.

Fluorescence In Situ Hybridization (FISH). This very sensitive test is used to examine genes or chromosomes in cells and tissues. Doctors use FISH to detect certain abnormal changes in the chromosomes and genes of leukemia cells. Pieces of DNA that contain special fluorescent dyes are prepared in the laboratory and added to the leukemia cells on a glass slide. The pieces of DNA that bind to certain genes or areas of chromosomes light up when the slide is viewed under a specialized “fluorescence” microscope. Not only can FISH identify most abnormal changes that can be seen with karyotype testing under a microscope, but it can also detect some changes that are too small to be seen with karyotype testing. It is not, however, used as a general screening tool as FISH has one disadvantage—before the test is performed, the doctor must select the specific chromosomes or genes that are going to be examined.

Polymerase Chain Reaction (PCR). This very sensitive test is used to detect and measure certain genetic mutations and chromosomal changes that are too small to be seen with a microscope. Essentially, PCR amplifies (increases) small amounts of specific pieces of either RNA (ribonucleic acid) or DNA to make them easier to detect and measure in a cell sample. It can find a single leukemia cell in approximately 100,000 to 1 million normal cells. This test is used to measure MRD in patients because it can identify a small amount of cancer cells that may remain in the body after treatment.

Next-Generation Sequencing (NGS). Next-generation sequencing (NGS), also called "molecular testing" or "genomic testing" refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. These technologies allow for sequencing of DNA and RNA much more quickly and cheaply than sequencing methods that were used previously.

This makes it possible to identify a variety of genetic changes in a patient's cancer cells. These changes are important in guiding risk assessment and prognosis and may also inform treatment decisions. The information it provides can help doctors to determine which patients are at high risk and may need more intensive treatment or may benefit from treatment with novel therapies.

There are targeted sequencing tests (also called "multigene panels") that look for specific mutations in the cancer cells. These tests focus on specific sets of genes or areas of DNA. There are also broad DNA sequencing tests (genomic screening tests) that analyze the sequence of large regions of DNA, rather than looking for mutations of specific genes. Doctors may also order sequencing of all the DNA in your entire genome. This test is known as "whole genome sequencing."

Next-generation sequencing finds gene mutations in approximately 90 percent of people with AML. Standard protocols combine cytogenetic analysis with testing for mutations of a number of single genes, including *ASXL1, BCOR, EZH2, FLT3*-ITD, *FLT3*-TKD, *KIT, NPM1, CEBPA, IDH1, IDH2, RUNX1, SF3B1, SRSF2, STAG2, TP53, U2AF1, ZRSR2, BCR::ABL* and *PML::RARα.* These markers are important in guiding risk assessment and prognosis and are also used to guide treatment decisions. For example, some patients may be eligible to receive drugs called "inhibitors" that target specific gene mutations expressed by leukemia cells, such as *FLT3, IDH1* and *IDH2*. These inhibitors may be taken alone or in combination with other chemotherapy drugs, but they only work against leukemia cells with these specific mutations.

Generally, NGS should be done when the cancer is first diagnosed. It is also increasingly used to measure MRD in patients because it can detect very low levels of residual leukemia-specific genetic mutations with high sensitivity, allowing for early identification of disease persistence or relapse. In addition, NGS should be done after a relapse. This is because the cancer may acquire additional genetic abnormalities after the patient completes their initial treatment. If this is the case, it is important to know about these additional genetic abnormalities because the presence or absence of mutations in leukemia cells affects treatment options both at the time of the initial diagnosis and again at the time of relapse.

Visit www.LLS.org/booklets to view the free LLS booklets *Understanding Genetics* and *Biomarker Testing for Cancer Treatment*.

Pre-Treatment Tests. Before you start treatment, your doctor will perform tests to learn more about your overall health and your disease. Doctors use this information for treatment planning.

Blood Chemistry Profile. This blood test measures the levels of certain substances released into the blood by organs and tissues in the body. These substances include electrolytes (such as sodium, potassium and chloride), proteins, glucose (blood sugar), creatinine, uric acid and liver enzymes. The test findings indicate how well a person's kidneys, liver and other organs are working. Although a blood chemistry profile is not used to diagnose leukemia, if the results show there is an abnormal amount of a particular substance in the blood, it may be a sign of disease or some other health problem. A blood chemistry profile also provides helpful information about any potential organ damage caused by leukemia cells or cancer treatments.

Human Leukocyte Antigen (HLA) Typing. This blood test is done to identify certain proteins, called "human leukocyte antigens (HLAs)," found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. While HLA typing is not used to diagnose leukemia, it is an important test for newly diagnosed patients with AML if allogeneic stem cell transplantation is being considered as a treatment option. See *Allogeneic Stem Cell Transplantation* on page 26 for more information.

Heart Tests. Some chemotherapy drugs, such as the class of drugs called "anthracyclines," can damage heart tissue. Because of this, your doctor may want to test your heart function before starting each new cycle of chemotherapy. Some heart tests that may be given to patients include:

- **Echocardiogram.** In this test, a computerized image of the heart is created by bouncing sound waves off internal tissues or organs in the chest. An echocardiogram shows the size, shape and position of the heart, as well as its internal structures. It also shows if the heart is beating and pumping blood normally.
- **Multigated Acquisition (MUGA) Scan.** For this test, patients receive a shot containing a radiotracer into a vein, and pictures of the heart are taken with a special camera. The pictures show the radiation being released by the radiotracer, making it possible to see how much blood the heart pumps with each heartbeat.

Coagulation Tests. The body stops bleeding by turning blood into a gel-like form called a blood clot. Blood clots help control excessive bleeding when a person has a cut. Blood moving through blood vessels, however, should not clot. Thrombosis is the formation of a blood clot inside an artery or a vein. If clots form in blood vessels, they can travel through the bloodstream to the heart, lungs or brain. This can cause heart attack, stroke or even death.

Clotting problems are common in AML, particularly in one subtype called acute promyelocytic leukemia (APL). Coagulation tests measure the blood's ability to clot, and how long it takes to clot. This can help the doctor measure the risk of excessive bleeding and thrombosis

Key Questions to Ask Your Treatment Team:

- What tests are necessary before I start treatment?
- When will the tests take place?
- Where will the tests take place? How long will the tests take?
- Will my insurance pay for all of my tests? If not, is there someone who can assist me with getting my tests covered?
- What are my options if my insurance plan does not cover the tests?
- Will the tests need to be repeated after the end of first-line (initial) treatment?

Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Lab and Imaging Tests*.

Visit www.LLS.org/3D to view interactive 3-dimensional illustrations of some laboratory and imaging tests.

Diagnosis

AML is a diverse group of diseases classified into many subtypes. Knowing your AML subtype is very important, as it can affect both your prognosis and your best treatment plan. If you are not sure of your AML subtype, ask your doctor what it is and to explain how it may affect your treatment.

The International Consensus Classification (ICC) has classified AML into subtypes (see **Table 1** on page 17). The subtypes of AML are based on the genetic abnormalities (gene or chromosome changes) in the myeloblasts (leukemia cells) and the percentage of myeloblasts present in the bone marrow and blood.

In some types of AML, a diagnosis requires finding at least 20 percent myeloblasts in the bone marrow. In certain cases, AML can also be diagnosed when the percentage of myeloblasts is less than 20 percent if the myeloblasts have a chromosomal change or genetic mutation that is typically found in a specific type of AML. There is another group of blood cancers called myelodysplastic syndromes (MDS). MDS can also have increased myeloblasts in the bone marrow and MDS with 10 to 19 percent myeloblasts is called "MDS/AML."

Table 1. Classification of AML with Percentage of Blast Cells Required for Diagnosis

APL with t(15;17)(q24.1;q21.2)/*PML*::*RARA* ≥10%
APL with other *RARA* rearrangements ≥10%
AML with t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1* ≥10%
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11* ≥10%
AML with t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A* ≥10%
AML with other *KMT2A* rearrangements ≥10%
AML with t(6;9)(p22.3;q34.1)/*DEK*::*NUP214* ≥10%
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2; MECOM(EVI1)* ≥10%
AML with other *MECOM* rearrangements ≥10%
AML with other rare recurring translocations ≥10%
AML with t(9;22)(q34.1;q11.2)/*BCR*::*ABL1* ≥20%
AML with mutated *NPM1* ≥10%
AML with in-frame bZIP *CEBPA* mutations ≥10%
AML and MDS/AML with mutated *TP53* 10%-19% (MDS/AML) and ≥20% (AML)
AML with myelodysplasia-related gene mutations 10%-19% (MDS/AML) and ≥20% (AML) Defined by mutations in *ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1* or *ZRSR2*
AML with myelodysplasia-related cytogenetic abnormalities 10%-19% (MDS/AML) and ≥20% (AML) Defined by detecting a complex karyotype (≥3 unrelated clonal chromosomal abnormalities in the absence of other class-defining recurring genetic abnormalities), del(5q)/t(5q)/add(5q), −7/del(7q), +8, del(12p)/t(12p)/add(12p), i(17q), −17/add(17p) or del(17p), del(20q), and/or idic(X)(q13) clonal abnormalities
AML not otherwise specified (NOS) 10%-19% (MDS/AML) and ≥20% (AML)
Myeloid sarcoma
Diagnostic qualifiers that should be used following AML diagnosis: Therapy-related • prior chemotherapy, radiotherapy, immune interventions
Progressing from MDS • MDS should be confirmed by standard diagnostics
Progressing from MDS/MPN (specify) • MDS/MPN should be confirmed by standard diagnostics
Germline predisposition

Key: AML, acute myeloid leukemia; add, addition of genetic material; APL, acute promyelocytic leukemia; del, deletion of genetic material; i, isochromosome; inv, an inversion in a chromosome; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasm; p, the short arm of a chromosome (the upper half); q, the long arm of a chromosome (the lower half); t, a translocation between chromosomes.

Source: Adapted from: Arber DA, Orazi A, Hasserjian RP, et al. International consensus classification of myeloid neoplasms and acute leukemias: Integrating morphologic, clinical and genomic data. *Blood*. 2022;140(11):1200-1228.

The latest ICC classification also has a list of “diagnostic qualifiers” that should be used after diagnosis. They include:

- **Therapy-related AML.** Certain treatments for other cancers such as prior chemotherapy and radiation can cause AML.
- **AML progressing from MDS.** Myelodysplastic syndromes (MDS) are a group of blood cancers in which the bone marrow does not make enough healthy blood cells. In some people, MDS can transform into AML.
- **AML progressing from MDS/MPN.** Myeloproliferative neoplasm (MPN) is a type of blood cancer in which the bone marrow makes too many red blood cells, white blood cells and/or platelets. Certain MPNs may become AML.
- **AML with germline predisposition.** Germline mutations are DNA mutations that are inherited during conception. These mutations occur in a parent's reproductive cells (egg or sperm). These changes may be inherited directly from the parent or may occur spontaneously in the reproductive cells. Some people with AML have germline mutation that increased their risk of developing AML.

These diagnostic qualifiers are not separate subtypes of AML, but doctors use these qualifiers when planning treatment.

Treatment Planning

Choosing a Hospital and Doctor. When you find out you have cancer, you want to get the best possible medical care and treatment. AML is an aggressive blood cancer that can be difficult to treat, and a diagnosis of AML is associated with a wide range of possible outcomes. So, you may want to seek treatment in a center with hematologist-oncologists who have significant experience in the care of patients with AML.

In general, larger cancer centers, and particularly academic medical centers, are more likely to have AML specialists who are the most up to date on the latest treatment options. A local oncologist may only see a few people with AML. In large medical centers, there are hematologist-oncologists who specialize in treating acute leukemias including AML. These specialists see hundreds of patients with AML, and they develop experience and expertise in diagnosing and treating AML.

Typically, people with AML need to start treatment as soon as possible after diagnosis. However, if time allows, you may want to seek a second opinion from another doctor, as it may help you feel more confident about the recommended treatment plan. The second opinion should come from another hematologist-oncologist, preferably one who treats AML. These doctors will usually have the most knowledge and experience about the latest treatment options for patients who have AML. Some AML specialists conduct telehealth visits, so you may have the opportunity to see an expert without traveling.

When you schedule a second opinion, ask that the biopsy of your leukemia cells be reviewed by the cancer center’s hematopathologist. Often, you will have to

sign a release for one medical center to send the biopsy specimen to another cancer center.

If you are either unsure about getting a second opinion or feel uncomfortable about how to tell your doctor you are seeking one, call our Information Specialists at (800) 955-4572, to discuss an approach that makes you feel comfortable. You may also want to check with your insurance company to be sure your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

Visit www.LLS.org/booklets to view the free LLS booklet *Choosing a Specialist or Treatment Center.*

Fertility. If you are of child-bearing age, you should be aware some cancer treatments may affect your fertility (the ability to have children in the future). Before you begin treatment, it is important to talk with your doctor about whether the treatment could affect your fertility. You may also want to speak with a fertility specialist, a doctor who has special training helping people who have trouble conceiving or carrying a pregnancy to term. This specialist can talk to you about possible options for preserving your fertility. You may be able to take steps to preserve your fertility. However, delaying treatment to address fertility options may not always be recommended. You may need to start treatment right away.

Visit www.LLS.org/booklets to view the free LLS booklet *Fertility and Cancer*.

Prognostic Factors. Certain factors can affect a patient's prognosis—the probable outcome of their cancer. These are called "prognostic factors." Doctors use prognostic factors to help predict how a patient's disease is likely to respond to treatment. These factors help doctors plan the most appropriate initial treatment regimen for each patient. In addition, they help determine whether stem cell transplantation should be considered as a treatment option for the patient, and if so, when to perform the transplant.

The following prognostic factors are taken into account for adults with AML:

AML Subtype. Chromosomal and genetic abnormalities are the most significant prognostic factors in people with AML. **Table 2** on page 20, lists some of the more common genetic abnormalities by their risk category. The risk categories in **Table 2** apply to younger patients (age less than 60 to 65 years) treated with intensive chemotherapy. They may not apply to older patients, those with treatment-related AML and those receiving lower intensity therapy. **Table 3** on page 21, outlines a proposed genetic risk classification framework for people with newly diagnosed AML receiving less-intensive therapies.

Patient's Age. AML occurs mostly in older adults; the median age at diagnosis is 67 to 70 years. Patients with AML are considered to be "young" if they are younger than 60 years old. Usually, the older the patient, the poorer the

prognosis. Unfavorable genetic abnormalities increase with age. Additionally, older patients sometimes have comorbidities (other medical conditions) that can make it difficult for them to tolerate intense chemotherapy treatments.

Response to Induction Therapy. Patients who do not achieve a remission after one cycle of induction therapy (the first phase of treatment for AML) have a poorer prognosis.

Therapy-related AML. People who received chemotherapy in the past to treat a different type of cancer may develop AML. This is known as therapy-related or treatment-related AML. In these cases, the disease is more resistant to treatment and is associated with a poorer prognosis.

Prior Blood Cancer. In patients who have had a prior blood cancer, such as a myelodysplastic syndrome (MDS) or a myeloproliferative neoplasm (MPN), AML is associated with a poorer prognosis.

High White Blood Cell Count. A high white blood cell count (40,000/mcL or more) at the time of diagnosis is an adverse risk factor for long-term remission.

Table 2. 2022 European LeukemiaNet (ELN) Risk Classification by Genetics at Initial Diagnosis

Risk Category	Genetic Abnormality
Favorable	○ t(8;21)(q22;q22.1)/*RUNX1::RUNX1T1* ○ inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB::MYH11* ○ Mutated *NPM1* without *FLT3*-ITD ○ bZIP in-frame mutated *CEBPA*
Intermediate	○ Mutated *NPM1* with *FLT3*-ITD ○ Wild-type *NPM1* with *FLT3*-ITD (without adverse-risk genetic lesions) ○ t(9;11)(p21.3;q23.3); *MLLT3::KMT2A* ○ Chromosome and/or gene abnormalities not classified as favorable or adverse
Poor/Adverse	○ t(6;9)(p23.3;q34.1)/*DEK::NUP214* ○ t(v;11q23.3)/*KMT2A*-rearranged ○ t(9;22)(q34.1;q11.2)/*BCR::ABL1* ○ t(8;16)(p11.2;p13.3)/*KAT6A*::*CREBBP* ○ inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*, *MECOM(EVI1)* ○ t(3q26.2;v)/*MECOM(EVI1)*-rearranged ○ -5 or del(5q); -7; -17/abn(17p) ○ Complex karyotype, monosomal karyotype ○ Mutated *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1* and/or *ZRSR2* ○ Mutated *TP53*

Key: abn, abnormal; del, deletion of part of a chromosome; inv, an inversion in a chromosome; p, the short arm of a chromosome (the upper half); q, the long arm of a chromosome (the lower half); t, a translocation between chromosomes; v, variable.

Source: Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood.* 2022;140(12):1345-1377.

Table 3. European LeukemiaNet (ELN) Proposed Risk Classification for Patients Receiving Less-Intensive Therapies

Risk Category	Genetic Abnormality
Favorable	Mutated *NPM1* (*FLT3*-ITD^{neg}, *NRAS*^{wt}, *KRAS*^{wt}, *TP53*^{wt}) Mutated *IDH2* (*FLT3*-ITD^{neg}, *NRAS*^{wt}, *KRAS*^{wt}, *TP53*^{wt}) Mutated *IDH1** (*TP53*^{wt}) Mutated *DDX41*† Other chromosome and/or gene abnormalities‡ (*FLT3*-ITD^{neg}, *NRAS*^{wt}, *KRAS*^{wt,} *TP53*^{wt})
Intermediate	Other chromosome and gene abnormalities‡ (*FLT3*-ITD^{pos} and/or *NRAS*^{mut} and/or *KRAS*^{mut}; *TP53*^{wt})
Poor/Adverse	Mutated *TP53*

This classification does not apply to patients who have received prior treatment with a hypomethylation agent.

Key: mut, mutated; neg, negative; pos, positive; WT, wild-type (a term used to describe a gene when it is found in its natural, non-mutated form).

* Favorable risk applies to patients treated with azacitidine + ivosidenib, irrespective of the presence of activating signaling gene mutations.

† Identification of a *DDX41* mutation at near-heterozygous frequency should prompt consideration of germ line *DDX41* mutation.

‡ For many chromosome and gene abnormalities, single or as coaberrations, no data are currently available; they are tentatively categorized as favorable and intermediate-risk depending on the absence or presence of activating signaling gene mutations.

Adapted from: Döhner H, DiNardo CD, Appelbaum FR, et al. Genetic risk classification for adults with AML receiving less-intensive therapies: The 2024 ELN recommendations. *Blood.* 2024;144(21):2169-2173.

Treatment

New treatments may have been approved since this booklet was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Treatment Overview. Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. A clinical trial is a type of research study that tests how well new medical approaches work in people. Like all treatment options, clinical trials have possible risks and benefits. By considering all your treatment options, including participation in a clinical trial, you will be taking an active role in a very important treatment decision that affects you. For more information on clinical trials, see page 36.

Talk to your doctor about:

- Your treatment options and the results you can expect from treatment
- The possibility of participating in a clinical trial

In the past, a diagnosis of AML was generally considered a medical emergency, and treatment usually started as soon as the diagnosis was made. This often

did not allow time for doctors to obtain the specific genetic profile of a patient's leukemia prior to making treatment decisions. Preliminary research has recently found that in many cases of AML, waiting up to 7 days to obtain genetic data and other laboratory test results on the AML cells, may be safe for most patients. This is an important consideration when assigning patients to the best available treatment option before starting therapy.

Not everyone with AML receives the same treatment. The choice of therapy for AML depends on a series of factors, including:

- The biology of the disease (measured by the genetic profile of the leukemia cells)
- The patient's age, overall health and general level of fitness (called "performance status")
- Consideration of the patient's goals for treatment and eligibility to undergo stem cell transplantation

Doctors often give the most intensive chemotherapy regimens to people younger than 60 years of age. However, this age limit is just a guideline. Some older patients in good health may also benefit from intensive regimens or slightly less-intensive treatments. For example, a person with AML aged 63 years with no other health issues and someone younger than 60 years old may be treated in a similar way. Likewise, a person aged 57 years with serious health issues may get the sort of treatment usually given to someone aged 60 years and older.

There are always risks associated with treatment. Talk with your doctor about how the treatment may affect your quality and length of life.

Supportive Care. Supportive care is health care that relieves symptoms caused by cancer and by cancer treatment. The goal of supportive care is to improve the patient's quality of life and to relieve discomfort as much as possible. Supportive care for AML should be given whenever a person has symptoms that need to be controlled. For patients with AML, supportive care may include blood transfusions, antibiotics, antiviral drugs, growth factors, pain medications and specialized nursing care and may be given during any phase of treatment.

Therapy for Patients Younger Than 60 Years of Age and "Fit" Patients Aged 60 Years and Older. For this group of patients, the goal of treatment is to increase long-term survival with the possibility of a cure. Treatment is more intensive and may have more serious side effects. It typically consists of multidrug chemotherapy given in two phases: induction and consolidation. Some patients may also receive a third phase of treatment called maintenance.

Chemotherapy works by either stopping or slowing the growth of cancer cells. Different types of chemotherapy drugs work in different ways to eliminate leukemia cells or stop new leukemia cells from forming. So, more than one chemotherapy drug is usually used. Chemotherapy may be given in many ways

including orally (in pills, capsules or liquids that you take by mouth and swallow), intravenously (directly into a vein), or subcutaneously (beneath the skin).

The specific drugs, the dosages used and timing of administration depend on several factors, including the genetics of the leukemia cells, the patient's age and the overall health of the patient. Clinical trials, whenever available, remain the best option for the treatment of AML.

Induction. The first phase of therapy is called induction. The goal of induction is to destroy as many cancer cells as possible in order to induce (achieve) a complete remission and restore normal blood cell production. Although obtaining a remission is the first step in controlling AML, it is also important for patients to emerge from the induction phase physically fit enough to tolerate the intensive treatments given during the consolidation phase.

The most common chemotherapy induction regimen for AML includes cytarabine (Ara-C, Cytosar-U®) and an anthracycline drug, such as daunorubicin (Cerubidine®) or idarubicin (Idamycin®). This is called the "7+3 regimen," because cytarabine is most often given by continuous intravenous (IV) infusion over 7 days, while the anthracycline drug is given by an IV infusion in a single dose for 3 days during the first week of treatment.

Induction therapy is usually given in the hospital and lasts about a week. However, patients typically remain in the hospital for an additional 3 to 5 weeks for a total of 4 to 6 weeks while their blood counts recover following 7+3 therapy.

In addition to the chemotherapy, patients may receive targeted therapies during induction. Targeted therapy is a type of treatment that uses drugs or other substances to target specific molecules that cancer cells need to survive and spread. These may include:

- **FLT3 Inhibitors.** Approximately one-third of people with AML have a mutation in the *FLT3* gene that can increase the growth and division of AML cells. *FLT3* inhibitors such as midostaurin (Rydapt®) or quizartinib (Vanflyta®) target these specific gene mutations.
- **CD33-Directed Antibody.** More than 90 percent of AML cells have the CD33 protein on their surface. Gemtuzumab ozogamicin (Mylotarg™) is a targeted therapy linked to the chemotherapy drug calicheamicin. It binds to and then enters cells with the CD33 protein on their surface. Once inside, it releases the chemotherapy drug that kills the cells.

Other drugs may be substitutes for the 7+3 regimen including:

- CPX-351 (Vyxeos®), a liposomal formulation of daunorubicin and cytarabine. A liposomal medication contains the active drug inside small, fat-like particles. This special fatty preparation allows more medication to reach its target (the bone marrow) and stay in the bone marrow to kill leukemia cells.

- High-dose cytarabine with idarubicin or daunorubicin and etoposide (VP-16, Etopophos®, VePesid®)
- High-dose cytarabine with mitoxantrone (Novantrone®)
- FLAG-IDA (fludarabine [Fludara®], high-dose cytarabine, granulocyte colony-stimulating factor [G-CSF] and idarubicin)

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for each drug's prescribing information.

Fourteen to 21 days after the start of induction, bone marrow tests are done to see how well the treatment is working and whether a second round of induction therapy is needed. If there are less than 5 percent blasts in the bone marrow, the leukemia is generally considered to have a good chance of entering a remission with the single round of induction therapy. Patients then receive supportive care until their blood counts recover. A follow-up bone marrow biopsy is performed to confirm that a remission has been achieved prior to moving on to consolidation. Some medical centers, however, give all medically-fit patients a second round of induction even if they have achieved optimal cytoreduction (ie, no persistent blasts in the bone marrow at day 14).

If the first round of induction does not achieve optimal cytoreduction, the therapy can be repeated, usually with a new chemotherapy regimen. Patients who continue to have a high level of blasts in their bone marrow after the second round of induction should be considered as candidates for a clinical trial, allogeneic stem cell transplantation or drug regimens for relapsed or refractory AML.

Patients who achieve a remission are given a few weeks to prepare for consolidation, the next phase of treatment. The large doses of chemotherapy given during induction destroys most of the leukemia cells, as well as healthy bone marrow cells. Most patients develop dangerously low blood cell counts and some may become very ill. Following the induction phase, patients typically remain in the hospital while blood cells start recovering in the bone marrow. Patients often require transfusions of red blood cells and platelets. In order to reduce the risk of infection, antibiotics are given to prevent and treat bacterial and fungal infections. Blood cell growth factors can help bring a patient's white blood cell count back more quickly, which may increase the chances of a faster recovery (particularly in patients who develop an infection).

Measurable Residual Disease (MRD). Even when a complete remission is achieved, some leukemia cells that cannot be seen with a microscope may remain in the bone marrow. This is referred to as "measurable residual disease (MRD)," also called "minimal residual disease." When patients test positive for MRD, it means that residual cancer cells were found. When a patient tests negative, no residual cancer cells were found.

Patients who achieve remission after initial treatment, but who are MRD-positive, are at increased risk of disease relapse. Testing for MRD may help doctors identify patients who may benefit from further treatment with intensified therapies such as allogeneic stem cell transplantation.

The tests used most often to detect MRD are flow cytometry, polymerase chain reaction (PCR) and next-generation sequencing (NGS). These tests usually use samples of bone marrow cells or blood cells. These tests can be done at various times, including after induction, during therapy and after therapy completion.

Even when patients test negative for MRD, some residual leukemia cells that cannot be detected, even with very sensitive tests, are believed to remain in the body after remission. Therefore, to optimize the chances of a cure, consolidation (additional intensive therapy) is generally recommended.

Visit www.LLS.org/booklets to view the free LLS booklet *Measurable Residual Disease (MRD)*.

Consolidation. In many patients, blood cell production should return to normal several weeks after induction is completed. Blood cell counts gradually approach acceptable levels, and AML blast cells cannot be detected in the blood or bone marrow. The cancer is now said to be "in remission." If there are a small number of residual AML cells, they will not generally interfere with normal blood cell development. However, they do have the potential to multiply and cause a relapse.

Even when a patient achieves a complete remission, more treatment is always needed to destroy any residual leukemia cells in the body. Without additional therapy, the leukemia will relapse within weeks or months. To prevent a relapse, intensive consolidation therapy is given after the patient recovers from induction therapy.

The goal of consolidation is to "consolidate" the remission by lowering the number of residual leukemia cells in the body or eliminating them entirely. There are two basic treatment options for postremission therapy:

- Additional intensive chemotherapy
- Allogeneic stem cell transplantation

Patients with favorable risk factors are often given intensive chemotherapy with intermediate or high-dose cytarabine and other drugs for their consolidation therapy. In the consolidation phase, patients generally receive multiple cycles of chemotherapy. The number of chemotherapy cycles varies from patient to patient. Patients may be hospitalized or receive consolidation therapy in an outpatient setting, depending on the type of treatment and other factors.

Patients with high-risk AML, based on their prognostic factors, receive more aggressive therapy, such as allogeneic stem cell transplantation (see *Stem Cell Transplantation* on page 26 for more information), during the consolidation

phase of treatment. Allogeneic stem cell transplantation is a complex treatment that can cause serious, life-threatening side effects. So, it is important to discuss the benefits and risks of this procedure with your doctor.

Doctors consider many important factors when deciding if allogeneic stem cell transplantation is a treatment option. These factors include:

- Patient age and general health
- Availability of a suitable donor
- MRD status
- Caregiver support

Whether or not to have an allogeneic stem cell transplant after the first remission is an important treatment decision for a patient. Often, this is when transplantation offers the best chance of preventing AML from recurring. However, allogeneic stem cell transplantation is associated with higher treatment-related morbidity and death compared to other treatment options, especially in older patients. Patients who are candidates for an allogeneic stem cell transplant should begin a search for an HLA-matched stem cell donor (someone with compatible human leukocyte antigens) as soon as possible, ideally while they are receiving induction therapy.

Stem Cell Transplantation. For some patients whose disease is in remission and can tolerate intensive chemotherapy, the doctor may recommend stem cell transplantation during consolidation. The goal of stem cell transplantation is to cure the patient's cancer. The process typically involves administering intensive chemotherapy, followed by an infusion of healthy stem cells.

There are two main types of stem cell transplantation. They are:

- Allogeneic, in which a patient receives stem cells either from a matched or a partially matched donor, either related or unrelated to the patient. This type of transplant, typically done for patients who have AML with higher risk features, relies on the donor's immune system cells to fight off any residual leukemia within the recipient. Simply put, allogeneic stem cell transplantion can be regarded as a form of immunotherapy.
- Autologous, in which a patient's own stem cells are collected before chemotherapy and stored. Then, after the patient has completed chemotherapy, these cells are reinfused into the patient's bloodstream. This type of transplant is not typically used for treating AML.

Allogeneic Stem Cell Transplantation. This is the most common type of stem cell transplantation used to treat AML. In preparation for the transplant, patients receive conditioning therapy. This consists of intensive chemotherapy, either with or without radiation, to kill the remaining leukemia cells in their bodies. Importantly, it is also given to suppress their immune systems, so their bodies do not reject the donor stem cells.

After the conditioning therapy, patients receive donor stem cells by IV infusion. Allogeneic transplantation uses healthy blood-forming cells from an HLA-matched donor. The cells can come from a family member, an unrelated person or from a donated umbilical cord. The donated stem cells restore the bone marrow's ability to form new blood cells.

Ideally, an allogeneic stem cell transplant will generate a new immune system for the patient, one that helps the body fight infections and other diseases. The new immune system also has the potential to recognize and attack any remaining cancer cells in the patient's body. The transplanted immune cells (the "graft") perceive the leukemia cells as foreign and destroy them. This is called the "graft-versus-leukemia (GVL)" effect.

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality. However, it may be considered for patients with higher-risk AML, based on their cytogenetic and molecular test results and other prognostic factors. The decision to perform an allogeneic transplant also depends on other factors, including the patient's age, physical fitness, comorbidities (other coexisting medical conditions) and social supports (from family members, caregivers, friends, etc), as well as the patient's understanding of the potential benefits and risks.

One possible serious side effect of allogeneic stem cell transplantation is graft-versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify the normal cells in the patient's body (the host) as foreign and attack them. Most patients need to be closely monitored for acute GVHD for at least the first 100 days after the transplant, and for chronic GVHD for many months after the transplant.

Research to determine which patients are most likely to benefit from stem cell transplantation after their first complete remission is evolving. Studies show that allogeneic stem cell transplantation may benefit fit patients with high-risk or intermediate-risk AML who have an HLA-matched stem cell donor.

Timing of allogeneic transplantation is one of the most important factors influencing its outcomes. In most cases, it is very important to start a donor search as soon as possible after an AML diagnosis in order to identify a suitably matched, related or unrelated donor and to plan for the best time to perform a transplant safely and successfully.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplant may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used in preparation for a standard allogeneic stem cell transplant. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation. With a reduced-intensity conditioning regimen, the patient's blood counts may not fall as low as they would with high-dose chemotherapy. Additionally, the less toxic regimens put less strain on the patient's organs, making this regimen safer and more tolerable.

The success of reduced-intensity transplantation depends on the graft-versus-leukemia effect of the donor stem cells, rather than on high-dose treatments to kill the cancer cells. This therapy reduces the number of cancer cells, but it does not completely destroy the patient's bone marrow. The goal is to have the donor stem cells become established in the patient's bone marrow and produce white blood cells that will attack the patient's remaining cancer cells. As with standard allogeneic stem cell transplantation, the risk of GVHD is an important consideration and a potentially disabling side effect.

Talk to your doctor about:

- ○ Stem cell transplantation and ask whether it is a treatment option for you.

Visit www.LLS.org/booklets to view the free LLS booklets *Blood and Marrow Stem Cell Transplantation* and *Graft-Versus-Host Disease*.

Maintenance. The third phase of treatment is called "maintenance." The main objective of maintenance is to deliver a less toxic therapy to prevent relapse after intensive chemotherapy. Maintenance is often an extended course of treatment that may last for months or years. Not everyone with AML will receive maintenance. Your doctor may recommend maintenance depending on your subtype of AML, your consolidation treatment and your risk of relapse. For some adult patients, the doctor may prescribe an oral formulation of azacitidine (Onureg®) as maintenance therapy. For patients with *FLT3* mutation maintenance therapy with an FLT3 inhibitor such as quizartinib (Vanflyta®) or sorafenib (Nexavar®) are now commonly used.

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for each drug's prescribing information.

Therapy for Patients Aged 60 Years and Older. AML occurs more frequently in older adults; adults aged 60 years and older are more likely to develop the disease than younger people. Treatment approaches for these patients range from standard intensive induction chemotherapy to less-intensive therapies, or the best supportive care. Additionally, there are a growing number of new treatment options available for older adults.

Treating AML in older adults is a challenge. Genetic abnormalities in the leukemia cells occur much more frequently in older patients than they do in younger patients. This makes the disease more resistant to standard chemotherapy. Also, as people age, they may have more difficulty tolerating more intense cancer treatments. Older patients are also more likely to have comorbidities (other medical problems), including diabetes, high blood pressure, high cholesterol levels and heart disease. They may also have a history of stroke or lung disease. These comorbidities can limit treatment options. Many older patients are not offered standard treatment options with intensive chemotherapy because they

are considered unlikely to survive the rigors of this treatment. In some cases, intensive chemotherapy can actually shorten their lives.

There are, however, treatments for patients of all ages. Remission is still possible with lower-intensity treatments. These treatments may prolong survival and improve quality of life.

The choice of therapy for older adults with AML also depends on the specific genetic profile of the leukemia cells; a patient's genetic profile is also the best way to predict how the disease will respond to chemotherapy as some specific genetic mutations may lead to poorer outcomes. In addition, consideration needs to be given to whether patients have available support from friends and family during treatment. You should discuss your treatment goals with your doctor. The doctor should explain the risks and benefits of your different treatment options and also provide realistic expectations about the likely results of each of them.

Older patients who are physically fit and have no serious health problems may benefit from intensive treatment (See T*herapy for Patients Younger Than 60 Years of Age and "Fit" Patients Aged 60 Years and Older* on page 22). Fit older patients may even be candidates for reduced-intensity allogeneic transplantation (See *Reduced-Intensity Allogeneic Stem Cell Transplantation* on page 27).

Not all patients can tolerate intensive therapies or even want them. Patients whose comorbidities and performance status make them poor candidates for intensive chemotherapy may still be able to participate in clinical trials. Clinical trials, whenever available, remain the best option for the treatment of AML.

Older patients may benefit from lower-intensity therapies which may relieve symptoms, improve quality of life and potentially extend survival. Treatment may include hypomethylating agents alone or combined with venetoclax (Venclexta®) or another drug. Hypomethylating agents work by blocking the DNA that helps cancer cells grow. They also help genes that are involved in cell growth and differentiation work the way they should. Using one of these drugs may help improve blood cell counts, which, in turn, may lead to fewer blood transfusions and improve quality of life. They may also slow the progression of AML. These drugs are, in general, less likely to produce severe side effects. Two hypomethylating agents used to treat AML are azacitidine (Vidaza®) and decitabine (Dacogen®).

Below is a list of some lower-intensity treatments for AML induction. Treatment options are based on the presence or absence of certain gene mutations found in the leukemia cells of the patient. In the list below, treatments with "azacitidine" refer to azacitidine (Vidaza®).

- Azacitidine ± venetoclax
- Decitabine ± venetoclax
- Cladribine (Leustatin®), low-dose cytarabine + venetoclax

- Low-dose cytarabine ± venetoclax
- Low-dose cytarabine + glasdegib (Daurismo™)
- Gemtuzumab ozogamicin for AML which is CD33 positive
- Ivosidenib (Tibsovo®) ± azacitidine for AML with an *IDH1* mutation
- Enasidenib (Idhifa®) ± azacitidine for AML with *IDH2* mutation
- Gilteritinib (Xospata®) ± azacitidine for AML with *FLT3* mutation

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for each drug's prescribing information.

Assessing Treatment Response. For patients treated with a venetoclax containing regimen, the response to therapy is often evaluated early during the first cycle, usually between days 14 and 21. Blood and bone marrow tests are done to check for a remission and to look for measurable residual disease (MRD). A complete remission is achieved when no more than 5 percent of the cells in the bone marrow are blast cells. Testing after the initial evaluation is usually repeated when there are concerns of relapse or prolonged cytopenias (low blood counts) to distinguish between relapse and low blood counts due to prolonged chemotherapy toxicity.

For patients who are tolerating and responding to treatment, the doctor will generally continue the treatment indefinitely as maintenance therapy. If there is no response or the cancer progresses, patients may want to consider participating in a clinical trial or trying other treatments for relapsed or refractory disease. Patients may also want to consider only supportive care to improve quality of life and alleviate discomfort.

Special Treatment Considerations

Acute Promyelocytic Leukemia (APL). This aggressive subtype of AML is associated with potentially life-threatening simultaneous bleeding and clotting complications. While in the past APL was nearly always fatal, it is now one of the most curable subtypes of AML in adults, if it is diagnosed early and treated appropriately. APL accounts for approximately 10 percent of all AML cases and occurs primarily in middle-aged adults, although it can occur at any age. It can also develop after a patient receives chemotherapy for another disease.

APL is due to a translocation between chromosome 15 and chromosome 17, abbreviated t(15;17), in a myeloid stem cell that is developing in the bone marrow. A translocation is a genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. An abnormal fusion gene called

PML::RARα forms as a result of the translocation. A diagnosis of APL depends upon confirmation of t(15;17) in the patient's AML cells.

The abnormal *PML::RARα* makes a protein that causes blood cells to get stuck in the promyelocytic stage, unable to develop into mature white blood cells. In people with APL, the promyelocytes build up in the bone marrow. Over time, the promyelocytes crowd out and suppress the development of healthy blood cells. When this happens, the body may not have enough healthy red blood cells, white blood cells and/or platelets.

People with APL are particularly susceptible to severe bleeding and blood clots. This occurs, in part, due to the low number of platelets in the blood and to the leukemia cells releasing substances that alter the balance between bleeding and clotting. This may lead to prolonged and excessive bleeding from cuts, nose bleeds, bleeding gums, blood in the urine and heavy menstrual bleeding. Serious bleeding events may occur including bleeding in the brain or lungs, which can be fatal. Thrombosis, the formation of a blood clot inside a blood vessel, may also cause life-threatening conditions.

If APL is suspected, treatment should begin immediately even before laboratory tests have confirmed the presence of the t(15;17) translocation or the *PML::RARα* gene mutation. This is because fatal bleeding events may occur. If laboratory tests show that the patient does not have APL, APL therapy should be discontinued and standard AML therapy started.

APL treatment is often divided into three phases: induction, consolidation and maintenance.

Induction. Standard treatment for APL is the nonchemotherapy drug all-trans retinoic acid (ATRA, Tretinoin, Vesanoid®). This drug is given orally. It is a differentiating agent that helps the abnormal promyelocytes mature into healthy white blood cells. ATRA causes a marked decrease in the number of leukemia cells in the bone marrow, and a remission frequently occurs.

For patients with low-risk APL (those with a white blood cell count of $10X10^9$/L or less at diagnosis), the preferred induction treatment option is ATRA with arsenic trioxide (ATO, Trisenox®). ATO is given by slow intravenous injection.

For patients with high-risk disease (those with a white blood cell count of more than $10x10^9$/L at diagnosis), ATRA and ATO may be combined with idarubicin or gemtuzumab ozogamicin. Other recommended regimens may include ATRA and ATO with daunorubicin or cytarabine.

Consolidation. Even when a patient achieves remission after induction, more treatment is needed to destroy any residual leukemia cells in the body. Typically, consolidation uses the same drugs as during induction.

Maintenance. The third phase of treatment is called maintenance. The main objective of maintenance is to deliver lower doses of drugs to prevent relapse. Maintenance for APL often lasts for a year. Not everyone with APL will receive maintenance. Your doctor may recommend maintenance depending on your risk of relapse.

Relapsed or Refractory Disease. Despite high remission rates, treatment resistance and relapse do occur in some patients with APL. Treatment options for patients with refractory or relapsed AML may include:

- Clinical trial (see page 36)
- Re-treatment with ATRA and ATO
- Salvage therapy followed by a stem cell transplant either autologous or allogeneic (see page 26)

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for each drug's prescribing information.

Treatment Complications. APL treatment can cause unwanted and unpleasant side effects. If you have any concerns about your side effects, talk to your doctor to get help. Most side effects are temporary and resolve when treatment is completed.

Bleeding. The ability to form blood clots (a process called "coagulation") is impaired in APL patients because they have decreased numbers of platelets and clotting factors. When coagulopathy symptoms are present, patients are supported with transfusion therapy that contains platelets or fresh frozen plasma. Plasma is the liquid part of the blood that carries the blood cells. The proteins that form blood clots are found in the plasma. Plasma can be frozen and preserved after blood donation to help prevent and control bleeding disorders, which frequently occur in APL.

Differentiation Syndrome. See page 40 for more information.

Pseudotumor cerebri. This disorder, also known as intracranial hypertension, is related to high pressure in the brain that causes signs and symptoms of a brain tumor – hence the term "pseudo" (or false) tumor. It happens when the fluid that surrounds the spinal cord and the brain—called cerebrospinal fluid—accumulates abnormally in the brain, causing pressure and pain. Pseudotumor cerebri can be a rare side effect of ATRA therapy and is most often observed in children and adolescents. The main symptom of this disorder is headache. Pseudotumor cerebri can be treated with the use of painkillers, glaucoma drugs that might reduce production of cerebrospinal fluid, steroids to reduce inflammation, and/or diuretic medication to reduce fluid buildup. Sometimes the temporary discontinuation of ATRA is necessary.

High White Blood Cell (WBC) Count. Elevated WBC counts, also known as "hyperleukocytosis," is a frequent side effect that occurs in APL patients receiving ATO and/or ATRA therapy. A WBC count higher than 10,000/microliter is considered elevated. This side effect is generally managed with medications such as hydroxyurea, gemtuzumab ozogamicin and anthracyclines (idarubicin and daunorubicin).

Changes in Liver Function. Liver enzymes can become elevated as a result of therapy with ATO, ATRA and/or gemtuzumab ozogamicin. Liver function should be routinely monitored during APL treatment. If needed, therapy can be temporarily discontinued until liver function returns to normal.

QT Interval Prolongation. The use of ATO can affect electrolyte levels. Electrolytes are essential minerals in the blood such as potassium, magnesium, and calcium. Electrolyte imbalance can cause a heart rhythm disorder known as "QT interval prolongation." This disorder causes a fast heartbeat that may lead to sudden fainting or seizures. Electrolytes should be monitored before and during APL treatment to ensure that they stay within a normal reference range. The doctors on your treatment team may order routine blood work and electrocardiograms to monitor any negative effects of ATO or other drugs.

Central Nervous System (CNS) Involvement. AML cells can spread to the cerebrospinal fluid (CSF), the fluid that flows around the brain and spinal cord. Involvement of the CNS occurs in less than 5 percent of AML patients. Because CNS involvement is rare in cases of AML, doctors usually do not test for it at the time of diagnosis unless the patient is experiencing neurologic symptoms, such as headaches or confusion. If neurologic symptoms are present, the doctor may order an imaging test, such as a computed tomography (CT) or a magnetic resonance imaging (MRI) scan, to evaluate the symptoms further.

The doctor will also obtain a sample of the patient's CSF by lumbar puncture. A lumbar puncture (also called a "spinal tap") is a procedure used to collect CSF from the spinal column. A thin needle is inserted between two bones in the spine and into the fluid. A sample of the fluid is removed and examined under a microscope to look for leukemia cells.

If leukemia cells are found in the CSF, the patient will be given "intrathecal chemotherapy." In this treatment, chemotherapy drugs such as cytarabine or methotrexate are injected directly into the spinal fluid. Intrathecal chemotherapy needs to be administered 2-3 times per week until the leukemia cells are eliminated, followed by weekly or monthly treatments to prevent disease recurrence in the CNS. Treatments with intrathecal chemotherapy can be administered at the same time that the patient is receiving other chemotherapy treatments for AML.

Visit www.LLS.org/3D to view interactive 3-dimensional illustrations of a lumbar puncture and intrathecal therapy.

Relapsed and Refractory Disease

Some patients have AML that returns after remission. This is referred to as a "relapse" of the disease (or "relapsed AML"). Some patients are unable to achieve a remission after two cycles of induction therapy. In these cases, the disease is referred to as "refractory" (or "refractory AML").

Relapsed and refractory disease is generally more difficult to treat, but there are treatment options available. Treatment for relapsed and refractory AML is usually more intensive or more complex than the treatment used following the initial diagnosis. For these reasons, it is particularly important to consider getting opinions on treatment options from someone with expertise in managing relapsed and refractory AML.

At the time of relapse, genetic testing of the leukemia cells may be performed. The mutational pattern at the time of relapse may be different from the pattern seen when the disease was first diagnosed, and this can affect treatment decisions.

Allogeneic stem cell transplantation is the only potential cure for patients with relapsed AML. Patients, however, must be considered fit enough to undergo the procedure. There are treatments that may help patients who cannot undergo a stem cell transplant live longer with a higher quality of life.

Treatment options for refractory or relapsed AML include:

- **A clinical trial** (see *Clinical Trials for Blood Cancers* on page 36). Treatment in a clinical trial should be considered first for all patients with refractory or relapsed AML. The Leukemia & Lymphoma Society offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist throughout the entire clinical-trial process. **Visit www.LLS.org/CTSC for more information.**
- **Re-treatment with the same induction regimen that produced the patient's first remission.** This is an option if a relapse occurs 12 months or more after remission.
- **Chemotherapy followed by Allogeneic Stem Cell Transplantation.** In fit patients, salvage chemotherapy can be used to induce a remission before stem cell transplantation. This is an option for patients younger than 60 years of age and patients older than 60 years who are physically fit.
- **Targeted Therapy.** Below are some targeted therapies recommended by the National Comprehensive Care Network (NCC) Guidelines:
  - Therapy for AML with *FLT3*-ITD mutation
    - Gilteritinib
    - Hypomethylating agents (azacitidine [Vidaza®] or decitabine) + sorafenib
    - Quizartinib

- Therapy for AML with *FLT3*-TKD mutation
  - Gilteritinib
- Therapy for AML with *IDH1* mutation
  - Ivosidenib
  - Olutasidenib
- Therapy for AML with an *IDH2* mutation
  - Enasidenib
- Therapy for CD33-positive AML
  - Gemtuzumab ozogamicin
- Therapy for AML with lysine methyltransferase 2A gene (*KMT2A*) rearrangement
  - Revumenib (Revuforj®)

- **Intensive Treatment Options.** Intensive treatments for fit patients, suggested by the NCCN Guidelines, include:
  - Cladribine + cytarabine + granulocyte colony-stimulating factor (G-CSF) ± (mitoxantrone or idarubicin)
  - Cytarabine ± (daunorubicin or idarubicin or mitoxantrone)
  - Fludarabine + cytarabine + G-CSF ± idarubicin ± venetoclax
  - Etoposide + cytarabine ± mitoxantrone
  - Clofarabine ± cytarabine ± idarubicin
  - CLIA (cladribine + idarubicin + cytarabine) + venetoclax
- **Less Intensive Treatment Options.** Less intensive treatments, suggested by the NCCN Guidelines, include:
  - Hypomethylating agents (azacitidine [Vidaza®] or decitabine)
  - Low-dose cytarabine
  - Venetoclax plus hypomethylating agents (azacitidine [Vidaza®] or decitabine) or low-dose cytarabine

Research is ongoing to determine optimal drug combinations, doses and administration schedules.

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for each drug's prescribing information.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called "clinical trials." Researchers use them to find better ways to care for and treat people with cancer. In the United States, the FDA requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer. Researchers use cancer clinical trials to study new ways to

- Treat cancer using:
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug (by mouth, intravenously (IV), etc)
- Manage cancer symptoms and treat side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term treatment side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients who have been willing to join clinical trials. Anyone interested in participating in a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions)
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process.

Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals

- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as past treatments, treatment responses, and your cancer genetic profile), your current health and your medical history. This information is taken into account and may factor into your eligibility to participate in certain clinical trials
- Help you to understand how your finances, insurance coverage, and support network, as well as your ability and willingness to travel might impact your choice of a clinical trial
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you participate in a trial
- Support you throughout the clinical-trial process

Call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Clinical Trials for Blood Cancers.*

Related Diseases

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN). BPDCN is a very rare, fast-growing blood cancer. It is similar to AML. But, unlike AML, BPDCN can affect other organs such as the lymph nodes, spleen, central nervous system and skin in addition to the blood and bone marrow. In fact, most patients with BPDCN have skin lesions, and the disease is often diagnosed through a skin biopsy. It may also be diagnosed through a bone marrow or lymph node biopsy.

Most patients with BPDCN are older, with a median age of 65 to 67 years at diagnosis, and it is more common in men than women. A diagnosis of BPDCN requires a finding of at least 4 of the following 6 antigens on the cancer cells: CD123, CD4, CD56, TCL-1, CD2AP and CD303/BDCA-2. In addition, recurrent mutations in the following genes have been described: *ASXL1, ETV6, IDH1, IDH2, IKZF1, IKZF2, IKZF3, NPM1, NRAS, TET1, TET2, SRSF2, TP53, U2AF, ZEB2* and *ZRSR2*.

Patients with BPDCN should seek treatment at a cancer center with doctors who have experience treating patients with this disease. Treatment may include the drug tagraxofusp-erzs (Elzonris®). Tagraxofusp-erzs targets the CD123 protein on the surface of BPDCN cells and leads to cancer cell death.

See **Table 4**, *Drug Classes and Drug Mechanisms* on page 47; and **Table 5**, *Some Drugs Used in the Treatment of AML* on page 48, for prescribing information.

Patients in first remission may undergo allogeneic stem cell transplantation, if appropriate. Other treatment options include induction regimens used for AML, acute lymphoblastic leukemia (ALL), or lymphoma. Recent clinical trials with agents targeting some of the BPDCN cell surface markers have shown great promise.

Mixed Phenotype Acute Leukemia (MPAL). MPAL is a subtype of acute leukemia (also known as "biphenotypic leukemia" or "mixed lineage leukemia") and has an ambiguous lineage. It has features of two forms of leukemia: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). It accounts for 2 to 5 percent of all acute leukemia cases, affecting patients of all ages. There are several different subtypes of MPAL.

Since MPAL is rare, patients with MPAL should seek treatment at a cancer center that has experience treating patients who have this disease. The best treatment approach for MPAL has not yet been determined, and it is associated with a poor prognosis. This is due to the difficulty in correctly identifying this type of leukemia, its low incidence, the lack of experience in treating it and its tendency to be resistant to both ALL and AML therapies. The reasons for this resistance are not yet clear but may be related to the high percentage of high-risk chromosomal abnormalities found in patients with MPAL. Some studies have shown that ALL therapy may be the preferred approach. Currently there is no standard therapy for MPAL, but clinical trials are underway.

A variety of factors are involved in determining the best treatment for patients with MPAL. These include the patient's age, medical history (and other relevant medical conditions) and the characteristics of the leukemia cells as determined by immunophenotyping and genetic tests. It is also important to determine whether the patient has the Philadelphia chromosome-positive (Ph+) subtype, which accounts for about 25 percent of all cases of MPAL. Treatment for Ph+ MPAL usually consists of a chemotherapy regimen for ALL, based on the patient's age, in combination with a tyrosine kinase inhibitor (TKI). This may be followed by allogeneic stem cell transplantation.

For patients with a Philadelphia chromosome-negative (Ph-) subtype of MPAL, treatment often consists of an ALL-induction regimen followed by allogeneic stem cell transplantation. For patients for whom an ALL regimen does not result in remission, treatment can be switched to an AML-like regimen followed by consolidation therapy with an allogeneic stem cell transplant.

Visit www.LLS.org/CTSC to work with Clinical Trial Nurse Navigators to search for clinical trials for people diagnosed with MPAL.

Side Effects and Complications

AML and its treatment often cause side effects. In addition to treating the cancer, an important part of care is relieving a person's symptoms and side effects. Most side effects in patients with AML are temporary and subside once the body adjusts to therapy or when therapy is completed. If side effects become severe, patients may need to be hospitalized.

Low Blood Cell Counts. Cancer and cancer treatments often cause drops in blood cell counts. This can result in a severe deficiency in a patient's number of red blood cells, white blood cells and platelets. Patients almost always need transfusions of red blood cells and platelets for several weeks during treatment. After that, blood cell counts usually return to normal levels.

White blood cell transfusions are generally not used for people with AML, so doctors sometimes use growth factors to help increase a patient's white blood cell count. Growth factors stimulate the bone marrow to make new white blood cells. Granulocyte colony-stimulating factors (G-CSFs), such as filgrastim (Neupogen®) and pegfilgrastim (Neulasta®), stimulate the production and release of neutrophils into the bloodstream. Granulocyte-macrophage colony-stimulating factors (GMCSFs), such as sargramostim (Leukine®), stimulate the production of different types of white blood cells including neutrophils and macrophages.

However, growth factors are used only in special circumstances and routine use of these agents is not recommended. For patients with acute promyelocytic leukemia (APL), growth factors are also not recommended during induction therapy because they can increase the risk of differentiation syndrome. Patients with this condition may experience symptoms such as unexplained fever, weight gain, labored breathing, pleuropericardial effusion (fluid around the lungs and heart), hypotension (low blood pressure) and renal (kidney) failure. (For more information on differentiation syndrome, see page 40).

Infections. During treatment for AML, the deficiency of white blood cells can lead to infections from bacteria, viruses and fungi that are normally present in the environment, on the skin, in the nose and mouth, on the gums or in the colon. The risk of infection may be increased because chemotherapy damages the cells lining the mouth and intestines, making it easier for bacteria to enter the bloodstream. After starting a course of chemotherapy, patients commonly receive antibiotics to prevent bacterial infection, as well as other drugs that prevent fungal and viral infections.

Because of the increased risk of infection, medical staff and all family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents. Caregivers of patients who have central lines or ports need to be meticulous when cleaning insertion sites and catheters.

Patients at home should seek medical attention immediately if any signs of infection develop. A temperature of 100.4°F or higher or the onset of chills may be the only sign of infection in a patient who has a very low white blood cell count. Other signs and/or symptoms of infection may include persistent coughing, sore throat, pain during urination or diarrhea.

Patients with AML are advised to receive certain vaccinations. For adult patients, these include vaccinations for influenza, pneumococcal pneumonia, COVID-19 and shingles. If a family member or friend of the patient receives a live vaccine, they should not go near the patient for a period of time. Speak to your doctor for more information.

Visit www.LLS.org/booklets to view the free LLS booklet *Side Effect Management: Reducing Your Risk of Infection.*

Tumor Lysis Syndrome (TLS). Patients with AML may be at high risk of developing TLS. This condition occurs when a large number of cancer cells die within a short period of time, releasing their contents into the bloodstream. TLS can be a severe complication during the early phases of AML treatment, especially for patients who have very high white blood cell counts before they start induction therapy.

Uric acid is one of the chemicals released by the dying cancer cells. Very high levels of uric acid and other chemicals can cause severe damage to the kidneys and heart. If untreated, TLS can lead to heart arrhythmias, seizures, loss of muscle control, acute kidney failure and even death.

Patients with AML are constantly monitored for the development of TLS and are given drugs such as allopurinol (Zyloprim®) to prevent TLS or rasburicase (Elitek®) to treat existing TLS and reduce its effects.

Differentiation Syndrome. This is a potentially life-threatening side effect of treatment with differentiating agents, such as all-trans retinoic acid (ATRA), arsenic trioxide, enasidenib, ivosidenib and revumenib. It usually occurs within 1 to 2 weeks after the patient starts treatment, but it can occur earlier or later. It is caused by a large, fast release of cytokines (immune proteins) from leukemia cells that are affected by the anti-cancer drugs.

Signs and symptoms of differentiation syndrome include fever, swelling in the limbs and trouble breathing. Patients may also experience a drop in blood pressure and have fluid build-up around the lungs or heart. Treatment must begin as soon as the patient experiences the very first signs and/or symptoms. Treatment consists of corticosteroid therapy or the administration of the chemotherapy drug hydroxyurea and other chemotherapy drugs to decrease the number of white blood cells, which are the source of differentiation effects. In severe cases, use of differentiating agents is stopped.

Other Side Effects. Chemotherapy drugs affect cells that divide quickly, which is why they work against cancer cells. But they also affect healthy cells in the body that also divide quickly, such as cells in the skin, hair follicles and lining of the intestines. Common side effects of chemotherapy may include:

- Mouth ulcers
- Diarrhea
- Hair thinning/loss
- Rashes
- Itchy skin
- Nausea and vomiting
- Loss of appetite and weight loss
- Fatigue
- Neuropathy (pain, numbness, tingling or muscle weakness, usually in the hands or feet)

Inform your doctor about any side effects you experience. Your doctor may prescribe medications that will prevent or relieve your side effects, change dosages of the medicines you are taking or adjust treatment schedules to prevent side effects from getting worse. Your doctor may also suggest other ways to prevent or minimize them.

Visit www.LLS.org/booklets to view the free LLS series *Side Effects Management* (filter for Side Effect Management) for more information.

Sometimes drugs or drug combinations cause side effects that continue for a period of time after treatment ends. Some of these effects may be long-lasting (see *Long-term and Late Effects of Treatment* on page 44 for more information).

Nutrition and Cancer

Eating well is important for patients receiving treatment for blood cancer. Proper nutrition plays a key roll in keeping the body strong, supporting the immune system and reducing the risk for diseases. Patients who eat well and maintain a healthy weight usually manage treatment and its side effects better. It is also important for patients with weakened immune systems to follow all food safety guidelines to reduce the risk of foodborne illness. Speak to your healthcare team about food and nutrition and for a referral to an oncology registered dietitian (RD) for specific nutrition advice and guidance.

LLS registered dietitians have expertise in oncology nutrition and provide patients, parents and caregivers with free nutrition consultations by phone. Call 877-467-1936 or visit www.LLSnutrition.org/consult to schedule.

Visit www.LLS.org/booklets to view the free LLS booklets *Food and Nutrition During Cancer Treatment and Nutrition Handbook: Feeding your family from meal planning to meal time.*

Financial Concerns

Paying for healthcare is a major concern for many people who are living with blood cancer. The high cost of cancer can lead to significant financial and emotional stress for both patients and their families. Even if you have health insurance, cancer can still take a toll on your finances. You may have new expenses such as co-payments or travel for treatment. You may also have less income if you need to take time off from work.

Speak with your healthcare team if you have any concerns about being able to afford your treatment. They may be able to provide information and resources that can help. Health insurance plans may not cover all the costs of cancer care, but there are many resources available to help with prescription drug payment. In addition, several major drug manufacturers currently provide patient assistance or prescription assistance programs. These programs can provide both insured and uninsured patients free or reduced-cost medications.

We offer financial assistance programs and medical debt case management for eligible patients. You can call our Information Specialists at (800) 955-4572 for more information.

Visit www.LLS.org/booklets to view the free LLS booklet *Cancer and Your Finances.*

Follow-up Care

Your medical care for AML does not stop once active treatment has finished. Your doctor will continue to check on you to make sure your leukemia has not returned, manage side effects and monitor you for late effects of treatment. This is called “follow-up care.”

Monitoring for Recurrence of AML. After a patient completes treatment for AML and is in remission, follow-up tests are done to check how well the treatment worked and to look for signs of relapse. Tests are also done to check how well the patient’s organs are working.

Patients undergo frequent follow-up tests during the first year after treatment, but tests are done less often during the second and third years. Testing and checkups may be required less often as times goes on, but scheduled follow-up visits should continue indefinitely.

The National Comprehensive Cancer Network (NCCN) recommends patients with AML should have a complete blood count every 1 to 3 months for the first 2 years after completing consolidation therapy, then every 3 to 6 months thereafter up to 5 years. Bone marrow tests should be performed only if blood test results are abnormal.

If you have been treated for AML you are encouraged to:

- Maintain your regular follow-up appointments with your hematologist-oncologist. Your doctor will monitor you for any signs and/or symptoms of disease relapse. Your doctor will also be able to detect any side effects from treatment or the onset of other medical problems.
- Keep a record of your cancer diagnosis, treatment and follow-up care needs. This is often called a "survivorship care plan." Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The plan should include the following information:
  - A list of all your healthcare providers
  - A diagnosis summary with specifics such as the subtype and/or genetic markers
  - A treatment summary with specifics such as the names, dates and dosages of chemotherapy or other drugs; site of radiation treatment, surgery and/or transplantation information; response to treatment; and side effects
  - Maintenance treatment information, if applicable
  - A list of possible late effects
  - A schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
  - Health and wellness recommendations, such as nutrition guidelines and suggested exercises regimens
  - Records of other disease screenings and vaccinations
- Receive periodic screening and monitoring for skin, gastrointestinal, kidney, blood, bladder, prostate, breast, lung, head and neck cancers, as well as other types of cancer because of the increased risk of a second cancer that is associated with AML and its treatment.
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as stopping smoking, skin protection against prolonged sun exposure, healthy eating and exercising.

You may experience difficulties when you return to your daily routines after a long period of treatment. Getting support throughout this time, and using it for as long as needed, is important.

Long-term and Late Effects of Treatment. Some treatments for AML can cause significant long-term or late effects. Long-term effects of cancer treatment are medical problems that last for months or years after treatment ends. Late effects are medical problems that do not appear until years, or even decades, after treatment ends.

People who have been treated for AML may be at increased risk for heart damage, other cancers and neurologic or cognitive problems. They should be seen by a primary care doctor for general health examinations at least once a year and should also be examined regularly by an oncologist.

It is important to know about the potential for long-term effects of treatment so any problems can be identified early and managed. Various factors can influence the patient's risk of developing long-term or late effects, including their:

- Type and duration of treatment
- Age at the time of treatment
- Gender
- Overall health

Many people with AML are treated with an anthracycline, such as daunorubicin. Anthracyclines have been associated with increased risk for heart muscle injury or chronic heart failure. However, heart disease may not become apparent until many years after treatment ends.

Certain long-term and late effects have also been associated with stem cell transplantation. These include infertility, thyroid dysfunction, chronic fatigue and risk for developing a secondary cancer (although the number of patients who develop a secondary cancer is small).

These and other possible long-term and late effects can be managed.

Talk to your doctor about:

- Possible long-term and late effects follow-up care.

Visit www.LLS.org/SurvivorshipWorkbook to view the free LLS booklet *Navigating Life During and After a Blood Cancer Diagnosis*. There are versions for adults, young adults, and children and adolescents. Each workbook has information about long-term and late effects of blood cancer treatment.

Treatment Outcomes

The outlook and prognosis for AML varies widely. Doctors consider many factors when giving someone a prognosis such as a person's type of AML or age. AML is a difficult disease to cure. Just a few decades ago, almost no adults with AML could

be cured. However, today, advances in understanding of the genetic features of the disease and the use of targeted therapies have resulted in improved remission and cure rates for people with AML.

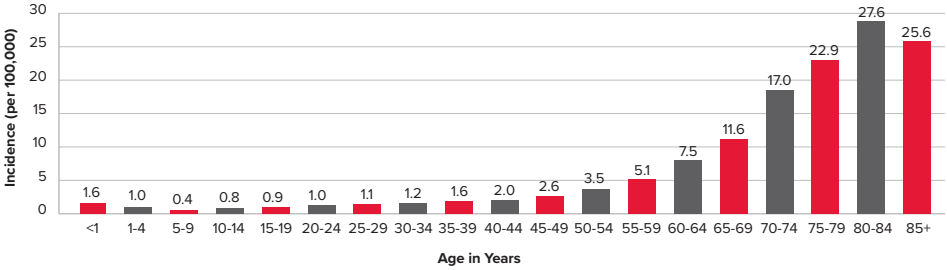
It is also important to remember that survival statistics are only estimates and are based on patients diagnosed with AML some time ago. Since the statistics were collected, new treatments have been approved, and more are being studied in clinical trials. As a result, the outlook may be better for people diagnosed with AML today.

Incidence, Causes and Risk Factors

Incidence. Approximately 20,800 new cases of AML were expected to be diagnosed in the United States in 2024. In 2019, there were an estimated 64,652 people living with or in remission from AML.

AML is the most common type of acute leukemia in adults. Older people are more likely than younger adults or children to develop AML. See **Figure 4** below.

Figure 4. AML: Age-Specific Incidence Rates 2016-2020



The horizontal axis shows 5-year age intervals. The vertical axis shows the frequency of new cases of AML per 100,000 people, by age-group.

Source: SEER*Explorer: An interactive website for SEER cancer statistics [Internet] Surveillance Research Program, National Cancer Institute; 2023 Apr 19 [updated: 2023 Nov 16; cited 2024 Feb 21] Available from: https://seercancergov/statistics-network/explorer/ Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries.

Causes and Risk Factors. Although in most cases it is not clear what causes the genetic changes that lead to AML, there are some known risk factors. A "risk factor" is anything that increases a person's chance of developing a disease. However, having a risk factor does not mean that a person will develop the disease. Some people with several risk factors never develop a disease, while others with no known risk factors may develop the disease. AML is not contagious.

The factors that are associated with an increased risk of developing AML include:

- **Age.** The risk of developing AML increases with age. While AML can occur at any age, it typically affects older adults. The risk for developing AML increases about 9-fold from aged 30 to 34 years (1.3 cases per 100,000 people) to ages 65 to 69 years (about 12.1 cases per 100,000 people). The risk continues increasing with incidence peaking in people between the ages of 80 and 84 years (28.5 cases per 100,000 people). See **Figure 4** above.

- **Sex.** Males are more likely than females to develop AML.
- **Exposure to dangerous chemicals.** Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of AML. Although benzene is found in certain industrial settings, strict regulation of its use has decreased benzene exposure in the workplace.
- **Smoking.** AML is linked to exposure to tobacco smoke, which contains benzene and other cancer-causing substances. According to the Agency for Toxic Substances and Disease Registry, half of the total exposure to benzene in humans in the United States comes from cigarette smoke. This is true despite the fact that petroleum products contribute to most of the benzene in the atmosphere.
- **Previous cancer treatment.** People who received radiation therapy or chemotherapy (especially with platinum drugs, alkylating agents such as cyclophosphamide and busulfan, or topoisomerase II inhibitors such as etoposide and doxorubicin) have an increased risk of developing AML. When AML develops as a result of treatment for another disease in the past, it is often called "treatment-related" or "therapy-related" AML.
- **Exposure to very high doses of radiation.** People exposed to very high levels of radiation are at increased risk of developing AML (for example, survivors of an atomic bomb blast or a nuclear reactor accident).
- **Other blood cancers.** People who have certain blood disorders are at greater risk of developing AML. These include myeloproliferative neoplasms (MPNs) such as polycythemia vera, essential thrombocythemia and myelofibrosis, as well as myelodysplastic syndromes (MDS), which in some people can evolve over time into AML.
- **Genetic disorders.** Certain genetic conditions, present at birth, seem to increase the risk of AML, including:
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome
- **Familial risk/germline predisposition.** Certain gene mutations, present at birth, may increase the risk of developing AML.

Drug Information

Table 4, below, includes information on drug classifications and their functions and mechanisms of action. **Table 5** on page 48 lists some of the medications used to treat AML. For more information, see the package insert and/or the full prescribing information that accompanies each medication available on the internet.

Table 4. Drug Classes and Drug Mechanisms

Anthracycline	A type of chemotherapy drug derived from certain types of *Streptomyces* bacteria. Anthracyclines work by damaging the DNA of cancer cells, which causes them to die before they can multiply.
Antimetabolite	A type of chemotherapy drug that interferes with the normal division and function of cancer cells. Antimetabolites mimic the building blocks of DNA or RNA that cancer cells need to survive and grow. When the cancer cell uses an antimetabolite instead of the natural substances, it cannot produce normal DNA or RNA and the cell dies.
Antineoplastic Agent	A type of chemotherapy drug that uses chemicals to kill cells that rapidly divide such as cancer cells. They interfere with the growth of cancer cells, which are eventually destroyed.
BCL-2 Inhibitor	Some people with AML have leukemia cells that make too much of a protein called BCL-2. This helps the leukemia cells live longer than they should. BCL-2 inhibitors help the body's natural ability to tell cancer cells to die. With fewer cancer cells, there is room for healthy blood cells to grow in the bone marrow.
CD33-Directed Antibody	Most people with AML have leukemia cells that express a protein called CD33. These drugs target and kill cells with the CD33 protein.
CD123-Directed Cytotoxin	Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a very rare fast-growing blood cancer similar to AML. BPDCN cells have a high number of the protein CD123. By targeting the CD123 protein on the surface of BPDCN cells, the drugs can find and kill these cells.
FLT3 Inhibitor	Some people with AML have a mutation in the *FLT3* gene that can increase the growth and division of AML cells. FLT3 inhibitors are drugs that target these gene mutations to help reduce the growth of AML cells.
Hedgehog Pathway Inhibitor	The hedgehog pathway is essential for normal embryonic development. In adults, however, abnormal activation of this pathway is thought to contribute to the development and proliferation of cancer stem cells. Research studies have shown that disruption of this pathway can decrease the number of cancer stem cells in the bone marrow.

Table 4. Drug Classes and Drug Mechanisms (Continued)

Hypomethylating Agent	A type of chemotherapy drug that works by blocking the DNA that helps cancer cells grow. Hypomethylating agents activate genes that help blood cells grow and mature. They may also help improve blood cell counts, which, in turn may lead to fewer blood transfusions and improve quality of life.
IDH Inhibitor	In some people with AML, the leukemia cells have a mutation in the *IDH1* or *IDH2* gene. These mutations cause the leukemia cells to remain immature and multiply too quickly. IDH inhibitors can help leukemia cells mature into normal blood cells.
Menin Inhibitor	Menin is a protein that interacts with abnormal leukemia fusion proteins such as the fusion protein resulting from *KMT2A*-rearranged leukemia and plays a role in maintaining the leukemic state in *NPM1*-mutated AML. This interaction is necessary for the leukemia cells to grow. Menin inhibitors block the interaction of the fusion protein with menin, ultimately causing the leukemia cells to die
Retinoid	Vitamin A or vitamin A-like compounds that may stop the growth of cancer cells.
Topoisomerase Inhibitor	A type of chemotherapy that blocks topoisomerases (enzymes that break and rejoin DNA strands and are needed for cells to divide and grow). Blocking these enzymes may kill cancer cells.

Table 5. Some Drugs Used in the Treatment of AML

For more information, see the package insert and/or the full prescribing information for each medication (available on the internet).

Drug Name **Administration** **Type of Drug**	**Indications**
All-trans retinoic acid (ATRA, Tretinoin, Vesanoid®) Oral Retinoid	Approved for the induction of remission in adults and pediatric patients 1 year of age and older with acute promyelocytic leukemia (APL), characterized by the presence of the t(15;17) translocation or the presence of *PML::RARα* gene expression, and who are refractory to or who have relapsed from anthracycline chemotherapy or for whom anthracycline-based chemotherapy is contraindicated.
Arsenic trioxide (ATO, Trisenox®) Intravenous (IV) Antineoplastic Agent	Approved: ○ In combination with tretinoin for treatment of adults with newly-diagnosed low-risk acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t(15;17) translocation or *PML::RARα* gene expression. ○ For induction of remission and consolidation in patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or *PML::RARα* gene expression.

Table 5. Some Drugs Used in the Treatment of AML (Continued)

Drug Name Administration Type of Drug	Indications
Azacitidine (Onureg®) Oral Hypomethylating Agent	Approved for continued (maintenance) treatment of adult patients with AML who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.
Azacitidine (Vidaza®) Intravenous (IV) or Subcutaneous injection Hypomethylating Agent (This form of azacitidine is not interchangeable with the oral form of azacitidine [Onureg®])	For the treatment of specific subtypes of myelodysplastic syndromes (MDS) but is commonly used as an off-label treatment for AML.
Cladribine (Leustatin®) Intravenous (IV) Antimetabolite	For the treatment of hairy cell leukemia and is sometimes used as an off-label treatment for AML.
Clofarabine (Clolar®) Intravenous (IV) Antimetabolite	For the treatment of pediatric patients with relapsed or refractory acute lymphoblastic leukemia (ALL) and is also being studied in the treatment of other types of cancer.
CPX-351 (Vyxeos®) [daunorubicin and cytarabine] Intravenous (IV) Anthracycline and Antimetabolite	Approved for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older.
Cytarabine (Ara-C; Cytosar-U®) Intravenous (IV) or Subcutaneous Injection Antimetabolite	Approved to be used either alone or with other chemotherapy drugs to treat certain types of leukemia including AML.
Daunorubicin (Cerubidine®) Intravenous (IV) Anthracycline	Approved to be used with other chemotherapy drugs to treat AML.
Decitabine (Dacogen®) Intravenous (IV) Hypomethylating Agent	For the treatment of specific subtypes of myelodysplastic syndromes (MDS) but is commonly used as an off-label treatment for AML.

Table 5. Some Drugs Used in the Treatment of AML (Continued)

Drug Name Administration Type of Drug	Indications
Enasidenib (Idhifa®) Oral IDH Inhibitor	Approved for the treatment of adult patients with relapsed or refractory AML with an *IDH2* mutation as detected by an FDA-approved test.
Etoposide (VP-16 Etopophos®, VePesid®) Intravenous (IV) Topoisomerase Inhibitors	For the treatment of testicular cancer and small cell lung cancer, but is used as an off-label treatment for AML.
Fludarabine (Fludara®) Intravenous (IV) Antimetabolite	For the treatment of B-cell chronic lymphocytic leukemia (CLL) but is used as an off-label treatment for AML.
Gemtuzumab ozogamicin (Mylotarg™) Intravenous (IV) CD33-Directed Antibody	Approved for the treatment of ○ Newly diagnosed CD33-positive AML in adults and pediatric patients 1 month and older ○ Relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older
Gilteritinib (Xospata®) Oral FLT3 inhibitor	Approved for the treatment of adult patients who have relapsed or refractory AML with a *FLT3* mutation as detected by an FDA-approved test.
Glasdegib (Daurismo™) Oral Hedgehog Pathway Inhibitor	Approved, in combination with low-dose cytarabine, for the treatment of newly diagnosed AML in adult patients who are ≥75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.
Idarubicin (Idamycin®) Intravenous (IV) Anthracycline	Approved for the treatment of AML in adults in combination with other approved antileukemia drugs.
Ivosidenib (Tibsovo®) Oral IDH Inhibitor	Approved for patients with a susceptible *IDH1* mutation as detected by an FDA-approved test: ○ For newly diagnosed AML in combination with azacitidine or as a monotherapy for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. ○ For the treatment of adult patients with relapsed or refractory AML.
Methotrexate (Trexall®) Intravenous (IV), Intramuscular (IM), Oral or Intrathecal Antimetabolite	Approved for the prophylaxis and treatment of adult and pediatric patients with meningeal leukemia.

Table 5. Some Drugs Used in the Treatment of AML (Continued)

Drug Name Administration Type of Drug	Indications
Midostaurin (Rydapt®) Oral FLT3 inhibitor	Approved for the treatment of adult patients with newly diagnosed AML that is *FLT3* mutation-positive as detected by an FDA approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
Mitoxantrone (Novantrone®) Intravenous (IV) Anthracycline	Approved for the treatment of AML.
Olutasidenib (Rezlidhia®) Oral IDH Inhibitor	Approved for the treatment of adult patients with relapsed or refractory AML with a susceptible *IDH1* mutation as detected by an FDA-approved test.
Quizartinib (Vanflyta®) Oral FLT3 Inhibitor	Approved in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed AML that is *FLT3* internal tandem duplication (ITD)-positive as detected by an FDA-approved test.
Revumenib (Revuforj®) Oral Menin Inhibitor	Approved for the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene *(KMT2A)* translocation in adult and pediatric patients 1 year and older.
Sorafenib (Nexavar®) Oral FLT3 Inhibitor	Being studied in clinical trials in patients with AML with an *FLT3* mutation.
Tagraxofusp-erzs (Elzonris®) Intravenous (IV) CD123-Directed Cytotoxin	Approved for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPCDN) in adults and pediatric patients 2 years and older.
Venetoclax (Venclexta®) Oral BCL-2 Inhibitor	Approved in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

Plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B_{12}
- Electrolytes, such as calcium, potassium and sodium

Blood Cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis" (see **Figure 5** on page 54). The blood cells are suspended in the plasma.

Once the blood cell is created, it will develop into one of the three types of blood cells.

These are:

1. Red blood cells are the cells that carry oxygen; they
   - Make up a little less than half of the body's total blood volume
   - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.
2. Platelets are cells that help blood clot; they
   - Are small cells (one-tenth the size of red blood cells)
   - Help stop bleeding from an injury or cut
   - Stick to the torn surface of the vessel, clump together and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.

3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:
    - Neutrophils and monocytes. These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
    - Eosinophils and basophils. These WBCs respond to allergens or parasites.
    - Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
        - T lymphocytes (T cells)
        - B lymphocytes (B cells)
        - Natural killer (NK cells)

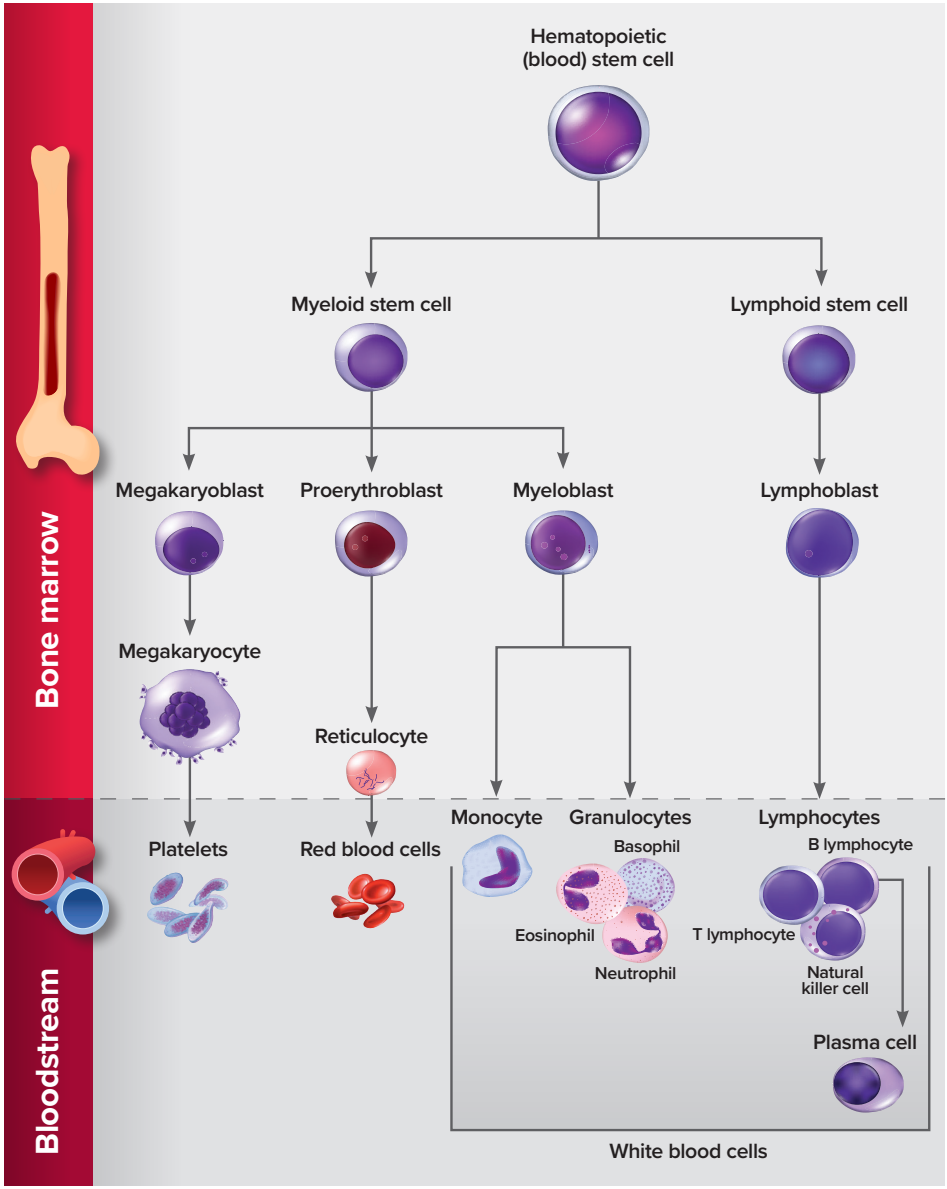
In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the bone marrow and then circulates throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, bone marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the bone marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the bone marrow and have them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can be collected and stored for future use in transplantation.

Figure 5. Blood Cell & Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



Additional Resources

Information for Firefighters. Firefighters are at an increased risk of developing cancer. There are steps firefighters can take to reduce the risk. Please visit www.LLS.org/FireFighters for resources and information.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953-1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs (VA). For more information, please

- Call: the VA (800) 749-8387
- Visit: https://www.va.gov/disability/eligibility/hazardous-materials-exposure/

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Mental Health. Caring for your mental health has benefits for cancer patients. Seek medical advice if you are struggling. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov

If you or your loved one is experiencing a mental health crisis, call 988 to talk to a trained mental health professional. The 988 Suicide and Crisis Lifeline is free, confidential and always available. For the Crisis Text Line, text HOME to 741741.

Other Helpful Organizations. The Leukemia & Lymphoma Society (LLS) offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, visit www.LLS.org/ResourceDirectory to view the directory.

World Trade Center Health Program. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

Health Terms

Alkylating Agent. A type of chemotherapy drug used in cancer treatment. It kills cancer cells by damaging their DNA, which prevents them from dividing (reproducing).

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to restore a patient's bone marrow that is damaged or diseased after receiving intensive chemotherapy and/or radiation therapy. **Visit www.LLS.org/booklets to view the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.**

Anemia. A condition in which the number of red blood cells is below normal. This results in reduced oxygen flow to the body's organs. Severe anemia can cause a pale complexion, weakness, fatigue, dizziness and shortness of breath.

Anthracycline. A type of chemotherapy drug used to treat many types of cancer. It damages the DNA of cancer cells, causing them to die.

Antibody. A type of protein created by blood cells in response to an antigen (a substance that causes the body to mount a specific immune response). Antibodies help the body fight against invaders that make a person sick. They can also be made in the laboratory to help treat cancer.

Antigen. A substance that creates an immune response in the body, especially the production of antibodies. Examples include allergens, chemicals, bacteria and viruses. Cells in the body, including cancer cells, also have antigens on their surfaces that can cause an immune response.

Basophil. A type of white blood cell involved in certain allergic reactions that can be produced in increased numbers in some subtypes of AML.

Biopsy. A procedure to remove a sample of cells or tissue from the body for examination by a pathologist. The pathologist may examine the sample under a microscope or perform other tests on the cells or tissue.

Blast Cell. An immature blood cell.

Blood Cells. There are three major types of blood cells: 1) red blood cells that carry oxygen; 2) white blood cells that fight infections; and 3) platelets that help stop bleeding.

Bone Marrow. A spongy tissue in the hollow central cavity of bones, where blood cells form.

Bone Marrow Aspiration. A procedure in which a liquid sample of bone marrow is removed for examination by a pathologist. The sample is usually taken from the patient's hip bone using a special needle, after a medication

is given to numb the area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are usually done at the same time.

Bone Marrow Biopsy. A procedure in which a sample of bone containing bone marrow is removed for examination by a pathologist. The sample is usually taken from the hip bone, using a special hollow needle, after medication is given to numb the skin and tissue in that area. Bone marrow aspiration and bone marrow biopsy can be done in a doctor's office or in a hospital and are usually done at the same time.

CBC. See Complete Blood Count.

CD. See Cluster of Differentiation.

Central Line. A flexible tube used to deliver medications, fluids or blood products into the body, or to withdraw blood samples from the body. Also called "central venous catheter" or simply "catheter." See Port.

Chemotherapy. Treatment that stops the growth of cancer cells, either by killing them or stopping them from dividing.

Chromosome. Part of a cell that contains genes in a linear order. Human cells have 23 pairs of chromosomes. **Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

Clinical Trial. A research study that is carefully planned and monitored to evaluate how well new medical approaches work in patients. The goal of clinical trials for blood cancers is to develop new treatments, improve quality of life and increase survival time.

Cluster of Differentiation (CD). A term used along with a number to identify a specific protein found on the surface of cells that help differentiate one cell type from another. It is commonly used in its abbreviated form, for example, "CD20." Also referred to as "cluster of designation."

Colony-Stimulating Factor. See Growth Factor.

Comorbidity. The condition of having two or more diseases at the same time.

Complete Blood Count (CBC). A laboratory test that measures the number of red blood cells, white blood cells and platelets in the blood. It also measures the amount of hemoglobin (the substance in the blood that carries oxygen) and the hematocrit (the amount of whole blood that is made up of red blood cells).

Complex Karyotype. Three or more unrelated chromosomal abnormalities in more than one cell.

Computed Tomography (CT) Scan. A procedure in which a series of x-ray images is processed with a computer to create 3-dimensional views of tissues and organs in the body.

Conditioning Therapy. Intensive therapy used to prepare a patient for stem cell transplantation. It may include chemotherapy and/or total body radiation.

Corticosteroid. A class of drugs that is used to reduce inflammation, swelling and pain. In high doses, it can kill leukemia and lymphoma cells.

Cytogenetic Analysis. The process of analyzing the number and size of chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help doctors diagnose specific types of blood cancer, determine which treatment approaches to use and monitor a patient's response to treatment.

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

Deletion (del). In genetics, this refers to a portion of a chromosome that is missing.

Differentiation. The process in which immature cells develop and become mature cells with specific functions. Blood stem cells mature into red blood cells, white blood cells or platelets.

DNA. Abbreviation for deoxyribonucleic acid, the molecules inside cells that carry genetic information. DNA is passed to new cells during the process of cell division. A change or mutation in the DNA can lead to cell death, changes in the cell function and, in some cases, cancer.

Eosinophil. A type of white blood cell that is released during infections and allergic reactions.

Erythrocyte. See Red Blood Cell.

Extramedullary Disease. Occurs when leukemia cells form tumors outside the bone marrow. See Myeloid Sarcoma.

FDA. The abbreviation used to refer to the United States Food and Drug Administration. The FDA is responsible for assuring the safety, effectiveness and security of drugs, medical devices and the nation's food supply.

FISH. See Fluorescence In Situ Hybridization.

Flow Cytometry. A test that measures certain characteristics of cells in a sample, including their size, shape and the presence of tumor markers on the cell surface. During this test, cells flow through an instrument called a

"flow cytometer." When the cells pass through its laser beam, those with the antibody-specific features light up and can be counted.

FLT3-Mutated AML. A mutation that is present in approximately one-third of people with AML. There are two major classes of activating *FLT3* mutations that have been identified in AML, which include the ITD and TKD point mutations. *FLT3*-mutated AML can be used as a biomarker for treatment. Patients with *FLT3* mutations may be eligible for specific clinical trials or targeted therapies.

Fluorescence In Situ Hybridization (FISH). A technique for studying abnormal chromosomes in cells and tissues. Pieces of DNA that contain fluorescent molecules are added to cells or tissues on a slide. When the pieces of DNA bind to certain genes or chromosomes, they light up when viewed under a specialized "fluorescence" microscope. This test can help to diagnose some types of cancer, plan treatment and monitor the effectiveness of treatment.

Fungal. Referring to a fungus, a single-celled or multicellular organism that is neither a plant nor an animal. Examples of fungi are molds, yeasts and mushrooms. Cancer treatments can weaken the immune system, which can increase a patient's chance of getting a fungal infection.

G-CSF (Granulocyte Colony-Stimulating Factor). See Growth Factor.

GM-CSF (Granulocyte-Macrophage Colony-Stimulating Factor). See Growth Factor.

Germline Mutation. A change in DNA that is inherited from a parent and is present throughout a person's life in virtually every cell in the body.

Graft-Versus-Host Disease (GVHD). A disease that occurs when stem cells transplanted from a donor (the graft) attack the healthy tissues of the transplant recipient (the host). Most often, GVHD affects a patient's skin, liver, stomach and gastrointestinal tract. **Visit www.LLS.org/booklets to view the free LLS booklet *Graft-Versus-Host Disease* for more information.**

Graft-Versus-Leukemia (GVL) Effect. When transplanted blood stem cells from a donor (the graft) perceive leukemia cells in the patient's body as foreign and attack them.

Granulocyte. A type of white blood cell that has many particles (granules). Neutrophils, eosinophils and basophils are types of granulocytes.

Growth Factor. A substance made by the body that stimulates the growth of specific cells. Some growth factors are made in the laboratory for use in cancer treatment. For example, granulocyte-colony stimulating factor (G-CSF) is a substance used to increase the number of neutrophils.

Hematologist. A doctor who specializes in treating blood diseases.

Hematopathologist. A doctor who has special training in identifying blood diseases by examining blood, bone marrow, lymph and other tissue samples under a microscope and performing tests to determine if the blood cells are normal or not.

Hematopoietic Stem Cell. An immature cell that can develop into any type of blood cell, including red blood cells, white blood cells and platelets. Also called "blood stem cell."

Hemoglobin. A protein inside red blood cells that carries oxygen around the body. Hemoglobin concentration decreases when there is a drop in the number of red blood cells.

Human Leukocyte Antigen (HLA). A type of protein on cells that helps the body to distinguish its own cells from foreign cells. A person inherits HLA factors from their mother and father. They make up a person's tissue type, which varies from person to person. They are a critically important factor in allogeneic (donor) stem cell transplantation. Before transplantation takes place, tissue typing is performed in order to determine if the donor's and the recipient's cells are compatible.

Immune System. A complex network of cells, tissues and organs that work together to defend the body against infections.

Immunophenotyping. A process that uses antibodies to identify specific types of cells based on the antigens (markers) on their surfaces.

Immunotherapy. A type of therapy that uses a person's immune system to help fight cancer.

Induction. The first phase of treatment that is given to quickly and significantly reduce the number of leukemia cells in the body.

Inherited Predisposition. An increased risk that a person will develop a disease based on genes they have inherited.

Intrathecal. The term for the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord. In some situations (for example, when leukemia cells are in the central nervous system), drugs are administered directly into the spinal canal. This treatment is called "intrathecal therapy."

Inversion (inv). A genetic abnormality that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted and is now in a different order. **Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

Isochromosome. An abnormal chromosome with two identical arms. Normal chromosomes have one long (q) arm and one short (p) arm, but isochromosomes have either two long arms or two short arms.

Karyotype. An organized profile of a person's chromosomes. It shows the size, shape and number of chromosomes in a sample of cells.

Late Effect. A medical problem that either does not appear or is not noticed until years after treatment ends. Treatment-related cancer and heart disease are examples of late effects.

Leukocyte. See White Blood Cell.

Lumbar Puncture. A procedure in which a thin needle is inserted into the spinal column to collect spinal fluid or to administer anticancer drugs to the central nervous system (CNS). Also called "spinal tap."

Lymph Node. A bean-sized structure that is part of the body's immune system. There are hundreds of lymph nodes throughout the body that contain large numbers of lymphocytes, a type of white blood cell that helps fight infection and disease.

Lymph Node Biopsy. A procedure in which all or part of a lymph node is removed and examined for signs of infection or disease such as cancer.

Lymphocyte. A type of white blood cell that is important to the body's immune system. There are three major types of lymphocytes: 1) B lymphocytes (B cells), which produce antibodies to help combat infections; 2) T lymphocytes (T cells), which have several functions, including assisting B lymphocytes in making antibodies; and 3) natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

Macrophage. A type of white blood cell that surrounds and kills microorganisms, eats dead cells and helps lymphocytes with their immune system functions.

Magnetic Resonance Imaging (MRI). An imaging test that uses magnetic fields and radio waves to create images of the body's organs and tissues.

Maintenance. Treatment that is given to help keep cancer from coming back after it has gone into remission following initial treatment.

Marrow. See Bone Marrow.

Measurable Residual Disease (MRD). The small amount of cancer cells that may remain in the body after treatment, even when the patient's blood and bone marrow may appear to be normal. These residual cancer cells cannot be seen under a microscope and can only be identified by other very sensitive tests. **Visit www.LLS.org/booklets to view the free LLS booklet *Measurable Residual Disease (MRD)* for more information.**

Monocyte/Macrophage. A type of white blood cell that forms in the bone marrow. Some monocytes travel through the blood to tissues in the body, where they become macrophages. Macrophages can combat infection in the body's tissues, ingest dead cells and assist lymphocytes in immune functions.

Monosomal Karyotype. Two or more autosomal monosomies (a monosomy is a condition in which one copy of the chromosome is missing) or one single autosomal monosomy in combination with at least one structural chromosome abnormality.

MRD. See Measurable Residual Disease.

Mutation. A change in the DNA sequence of a cell. A mutation may be caused by an error in cell division or by contact with DNA-damaging substances in the environment.

Myelodysplastic Syndromes (MDS). A group of blood cancers in which the bone marrow does not make enough healthy blood cells and there are abnormal cells in the blood and/or bone marrow.

Myeloid Sarcoma. A mass of myeloid leukemia cells that develops outside the bone marrow. It may occur beneath the skin or other areas of the body and may be the first sign of leukemia. A myeloid sarcoma is different from a true "sarcoma," which refers to a distinct group of cancers arising from connective tissues like muscle, fat, or bone. A myeloid sarcoma is also called "chloroma," "granulocytic sarcoma," "myeloblastoma," "monocytoma" and "extramedullary disease."

Neutropenia. A condition in which the number of neutrophils, a type of white blood cell, is below normal. People with low neutrophil counts are susceptible to infections.

Neutrophil. A type of white blood cell, and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main type of cell that combats infection. People with some forms of blood cancer, or who have received treatment such as chemotherapy for cancer, often have low neutrophil counts. People with low neutrophil counts are very susceptible to infections.

Next-Generation Sequencing (NGS). This refers to a number of different gene sequencing technologies that can rapidly examine stretches of DNA or RNA.

***NPM1*-Mutated AML.** A mutation that is present in approximately 30% of adults with AML. *NPM1*-mutated AML can be used as a biomarker for treatment. Patients with this gene mutation may be eligible for specific clinical trials or targeted therapies.

Off-label. The legal use of a prescription drug to treat a disease for which the drug has not been approved by the FDA.

Oncologist. A doctor who has special training in diagnosing and treating cancer.

Oral Medication. Drugs taken by mouth.

Pathologist. A doctor who has special training in identifying diseases by examining cells and tissue samples under a microscope.

Performance Status. A measure of how well a person is able to perform ordinary tasks and carry out daily activities.

Peripheral Blood. The blood that circulates throughout the body in the arteries, capillaries and veins.

Petechiae. Pinhead-sized red or purple spots under the skin caused by bleeding. Petechiae may be a sign of a low platelet count.

Phagocyte. A type of white blood cell that protects the body from infection by eating and killing microorganisms, such as bacteria and fungi. Neutrophils and monocytes are the two main types of phagocytes. Once an infection occurs, phagocytes enter the infected tissue from the bloodstream.

Plasma. The liquid portion of the blood, in which blood cells, platelets, proteins and various other blood components are suspended. Also called "blood plasma."

Platelet. A small, colorless piece of a cell that helps control bleeding. Platelets are produced from large cells in the bone marrow, called "megakaryocytes." Platelets travel to and then collect at the site of a wound. The platelets' sticky surface helps them form clots at the site of the wound and stop bleeding. Also called "thrombocyte."

Polymerase Chain Reaction (PCR). A very sensitive genetic laboratory test used to detect and measure some genetic mutations and chromosomal changes that cannot be seen with a microscope. It essentially amplifies (increases) small amounts of specific pieces of either DNA or RNA so they are easier to detect and measure. This test can find a single cancer cell among more than approximately 100,000 healthy blood cells.

Port. A small device that facilitates access to a central line (catheter). It is used to withdraw blood and to administer treatments such as intravenous (IV) fluids, drugs and blood transfusions. The port is placed under the skin, usually in the chest. It is attached to a catheter, which is a thin flexible tube that is inserted into a large vein.

Prognosis. The probable outcome or expected course of a disease; the likelihood of recovery or recurrence of the disease.

Radiation Therapy. The use of x-rays and other forms of radiation to treat cancer and other diseases.

Recurrence. The return of a disease after it has been in remission following treatment.

Red Blood Cell. A type of blood cell that contains a protein called "hemoglobin," which carries oxygen from the lungs to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood volume in healthy people. Also called "erythrocyte."

Reduced-Intensity Stem Cell Transplantation. A type of allogeneic stem cell transplantation in which patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. This protocol may be safer than a traditional high-dose conditioning, especially for older patients. **Visit www.LLS.org/booklets to view the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.**

Refractory. The term used to describe a disease that does not go into remission or improve substantially after treatment.

Relapse. The return of a disease after a period of improvement.

Remission. When signs and/or symptoms of a disease disappear, usually following treatment.

Resistance/Resistant (to Treatment). When cancer cells continue to grow even after intensive treatment. The cancer cells may be resistant to the drug at the beginning of treatment or may become resistant after being exposed to the drug over time. Also called "drug resistance."

Risk Factor. A scientifically established factor that increases a person's chance of getting a disease. Risk factors can be classified as either genetic (inherited), lifestyle-related or environmental.

RNA. Abbreviation for ribonucleic acid, a molecule in cells that carries out the DNA instructions for making proteins.

Salvage Therapy. Treatment given when a person's cancer has not responded to other treatments.

Sedative. A drug used to calm a person down, relieve anxiety or help a person sleep.

Spinal Tap. See Lumbar Puncture.

Spleen. An organ in the left upper portion of the abdomen, just under the left side of the diaphragm. The spleen filters blood, stores blood

cells and destroys old blood cells. Enlargement of the spleen is called "splenomegaly."

Standard of Care. Treatment that is accepted by medical experts as a proper treatment for a disease and that is widely used by healthcare professionals.

Stem Cell. A cell from which other types of cells develop. In the bone marrow, blood-forming stem cells mature into red blood cells, white blood cells and platelets. Stem cells can be collected, preserved and used for stem cell therapy. See Hematopoietic Stem Cell.

Stem Cell Transplantation. See Allogeneic Stem Cell Transplantation; Autologous Stem Cell Transplantation; Reduced-Intensity Stem Cell Transplantation.

Subcutaneous Injection. The administration of medication with a needle that goes under the skin into the space between the skin and muscle.

Thrombocytopenia. A condition in which the number of platelets in the blood is below normal.

Toxin. A naturally derived substance that is poisonous to cells. A toxin can be attached to antibodies that then attach to and kill cancer cells.

Transfusion. A procedure in which whole blood or blood components are placed into a patient's bloodstream.

Translocation (t). A genetic abnormality in which a piece of one chromosome breaks off and attaches to another chromosome. Nearby genes in the location at which the break occurs may be affected, which may lead to medical problems. See Mutation. **Visit www.LLS.org/booklets to view the free LLS booklet *Understanding Genetics* for more information.**

White Blood Cell. A type of blood cell that is part of the body's immune system. The five major types of white blood cells are neutrophils, eosinophils, basophils, monocytes and lymphocytes. Also called "leukocyte."

Wild-Type Gene. A term used to describe a gene when it is found in its natural, non-mutated (unchanged) form. Mutated (changed) forms of certain genes have been found in some types of cancer. Knowing whether a person's tumor has a wild-type or mutated gene may help plan cancer treatment.

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NOTES

A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/ happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, and optimism. Finding joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.

Discover what thousands already have at **www.LLS.org/Community**

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find:

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care

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The mission of The Leukemia & Lymphoma Society (LLS) is to cure blood cancer and improve the quality of life of all patients and their families. Find out more at www.LLS.org.

PS32 15M 5/25