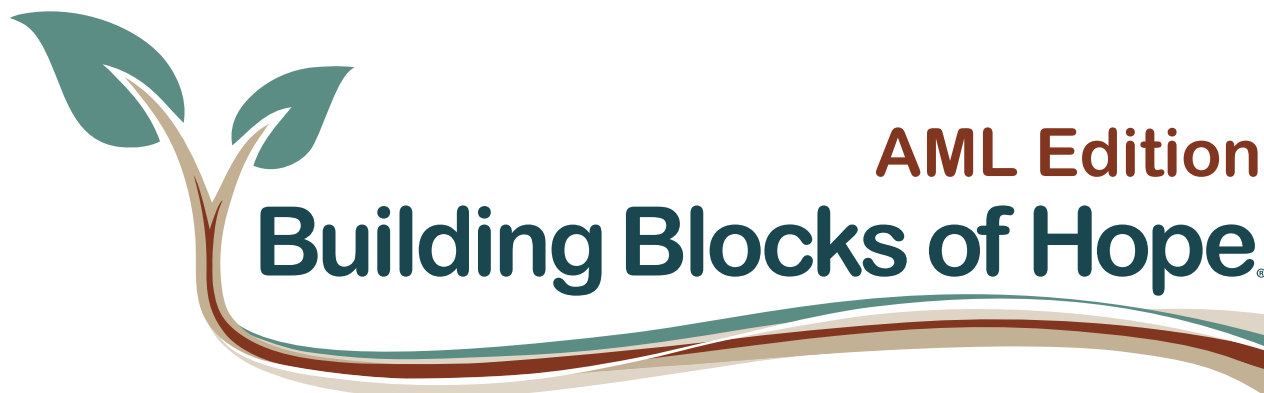


English Edition
(USA)



AML Edition Building Blocks of Hope®

Strategies for
Patients & Caregivers
LIVING with **AML**
Acute Myeloid Leukemia (AML) Edition

by Sandra Kurtin

A global MDS Foundation print and online patient advocacy initiative, providing a personalized educational program for the patient and caregiver to prepare, participate, and **LIVE** with AML.



Published by the Myelodysplastic Syndromes Foundation, Inc.

You or someone you know has been diagnosed with AML. Hearing the words Acute Myeloid Leukemia or AML can be frightening. The diagnosis of AML is often unexpected and filled with both immediate and long-term challenges. You probably have many questions. We are pleased that you have requested a copy of the **Building Blocks of Hope® AML Edition**. It is designed to help get you the information that you are looking for and take an active part in your AML journey.

There are four chapters and a glossary of AML terms included in the **Building Blocks of Hope® – AML Edition**:

- **Chapter 1 — Understanding Acute Myeloid Leukemia:** A complete description of the disease process of AML and answers to common questions.
- **Chapter 2 — Seeking Treatment:** The treatment of AML can vary based on the type of AML you have and how severe it is. This section will provide details about the various approaches to treatment.
- **Chapter 3 — General Resources for Living with AML:** This chapter will provide you with strategies for staying well, managing your health and your AML. Quick-Tips are provided to help you recognize and manage common symptoms or problems experienced by patients and caregivers living with AML. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary of terms that will help you to understand the complex language used to describe myeloid diseases.
- **Chapter 4 — The MDS Foundation:** The MDS Foundation is an international publicly supported organization dedicated to improving the lives of patients and caregivers living with MDS and other myeloid diseases. The MDS Foundation provides a number of resources which support the Building Blocks of Hope® program.

There are several components to the Building Blocks of Hope® program. You have received the printed version. These printed materials, along with digital materials, links to online resources, and a number of very practical tools, can be accessed online on the MDS Foundation website www.mds-foundation.org. You can also view the complete handbook in a beautiful page-turning format at <http://buildingblocksofhope.com>. This includes a search feature and thumbnail views that will help you quickly find the information that you are looking for. This is a great way to share this information with family and friends. You can visit the MDS Foundation website or contact the MDS Foundation directly to learn more and check for any new information (see contact information below).

Allow yourself time to adjust to the diagnosis of AML. Take time to explore the **Building Blocks of Hope®**. We wish you the best in your journey and hope that the **Building Blocks of Hope®** program will provide you and your caregivers with tools and strategies for LIVING with AML.

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UNDERSTANDING AML

*Acute Myeloid Leukemia (AML) is a group of myeloid malignancies (cancers). There are several types of AML. Each type of AML has a variable onset, prognosis, and options for treatment. Understanding AML, the first chapter in the **Building Blocks of Hope® - AML Edition**, provides a description of what happens to the normal bone marrow when AML develops and what symptoms you may have as a result. Details about how AML is diagnosed with an explanation of each subtype of AML is provided. Understanding your AML diagnosis will help you and your caregiver(s) take an active part in your individual treatment plan.*

UNDERSTANDING AML

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What Does Bone Marrow Do

What does bone marrow do?

All blood cells begin as hematopoietic (*hee-muh-toh-poi-et-ik*) stem cells in the bone marrow. The bone marrow is the factory for these stem cells. In healthy persons, hematopoietic stem cells develop and mature (differentiate) in the bone marrow to form all the different blood cells that can be found in the bloodstream.

In the initial stage, the hematopoietic stem cell differentiates into a multipotent stem cell. These cells can form new blood cells. Hematopoietic stem cell transplantation uses these cells to repopulate the bone marrow with cells that can produce all the elements of blood.

The multipotent stem cell further differentiates to form either a lymphoid progenitor cell or a myeloid progenitor cell (progenitor cells).

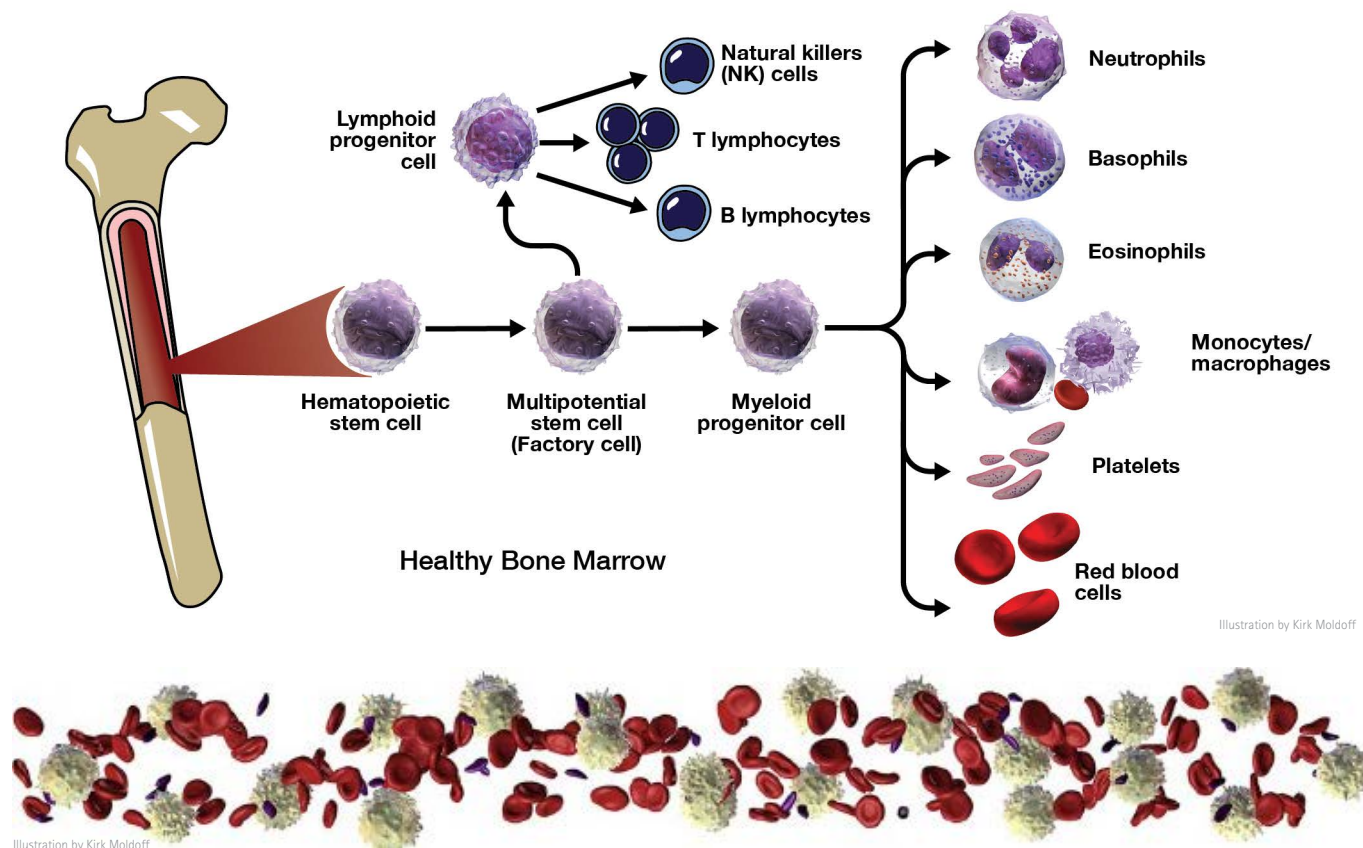
The myeloid progenitor cell gives rise to white blood cells, platelets, and red blood cells

White blood cells (WBCs) – (neutrophils, basophils, eosinophils, monocytes, macrophages)– help to fight infection

Platelets (Plts) – help to clot blood, stop bleeding

Red blood cells (RBCs) – carry oxygen to all the cells in the body

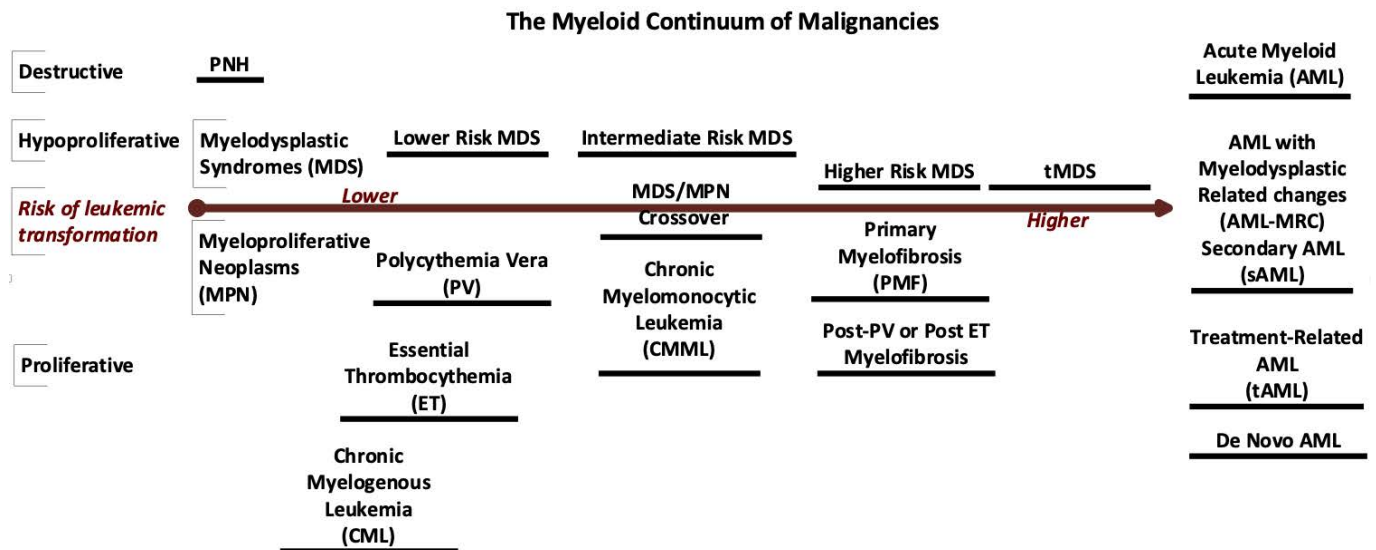
The lymphoid progenitor cell gives rise to T lymphocytes, B lymphocytes, and natural killer cells. These cells provide important immune functions that help to fight common bacterial or viral infections.



Normal Hematopoiesis (the formation and development of blood cells)

The Myeloid Continuum of Diseases

Myeloid malignancies include diseases that may decrease production of blood cells or increase production of blood cells. Each disease has specific criteria for diagnosis, estimated prognosis and options for treatment. All of these diseases have the potential to evolve into acute leukemia. The focus of this issue of the Building Blocks of Hope® is on Acute Myeloid Leukemia (AML).



The Bone Marrow Biopsy and Aspirate

When blood tests indicate the presence of low blood counts (cytopenias), your physician may recommend a bone marrow examination. A bone marrow examination can reveal abnormalities in the cells of the marrow (e.g., dysplastic cells) and will allow evaluation of the chromosomes (cytogenetics). These tests provide additional information that can help in establishing a diagnosis. There are two parts to a bone marrow examination: the aspirate and the core biopsy. Both the aspiration and biopsy are usually performed at the same time.

The bone marrow aspirate

The bone marrow aspirate is a sample of the liquid portion of the bone marrow. Spicules of the bone marrow contain small collections of blood forming cells. This provides information about the shape of the cells (morphology), how the cells are maturing (differentiation) and the number of blasts (immature cells) in the bone marrow. The aspirate may also be used for additional testing that may help to determine the cause of the cytopenias, such as cytogenetics.

The bone marrow biopsy

The bone marrow biopsy is a small core (the shape and size of a medium pencil lead) of the spongy center of the bone marrow. The bone marrow core is usually 1.5–2.0 cm in length. It provides information about the cellularity of the bone marrow (crowded=hypercellular, empty=hypocellular). It will also provide useful information about iron storage, scarring (fibrosis), and the presence of any other abnormal cells.

Processing the sample

The bone marrow biopsy and aspirate samples are placed on glass slides and in various laboratory tubes. These are sent to a Hematopathologist—a physician trained to evaluate blood and bone marrow samples to diagnosis diseases. The physician uses a microscope to examine the cells in the bone marrow aspirate and biopsy samples. The results of a bone marrow biopsy and aspirate generally take 2–4 days. Cytogenetic studies and other special studies may require up to 2 weeks.

The bone marrow and biopsy procedure

A bone marrow examination can be performed in the physician's office usually in about twenty minutes. It can be performed with local anesthesia or, in some cases, mild sedation or analgesia.

1. The patient is placed either on their side or on their abdomen. It is always useful to empty your bladder prior to the procedure. It is important to continue to breathe slowly throughout the procedure to help relax the muscles.
2. The healthcare provider performing the procedure will prepare a sterile field, including cleaning the skin over the posterior iliac crest, a bony protrusion on the right or left back side of the hip (near where your back pocket might be on a pair of jeans).
3. The skin above the site will be anesthetized (numbing the skin) using a form of lidocaine (numbing medicine). You may feel a pin prick from the needle and a very brief sting from the lidocaine.
4. A second needle is then inserted to numb the surface of the bone (periosteum)—this is where all of the nerve endings are. You may feel a brief stinging sensation with the first injection, similar to having the gums numbed for a dental procedure.

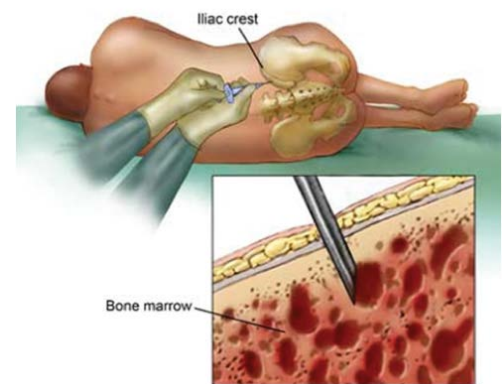


Illustration by Kirk Moldoff

The Bone Marrow Biopsy and Aspirate



5. Once the skin and bone has been anesthetized, a small incision may be made on the surface of the skin to allow insertion of the bone marrow needle. There are a variety of needles being used today. Most allow for both the aspirate and the biopsy to be obtained during the same procedure.
6. The larger bone marrow needle allows for penetration through the hard outer layer of the bone (cortical bone). It is roughly the size of a meat thermometer with a hollow core. You will feel pressure. Some patients have very hard bones requiring more pressure to be used to penetrate the bone. Be sure to let your provider know if you are experiencing sharp pain at the site or pain that is traveling down your leg.
7. Once the needle reaches the spongy bone marrow (red marrow), the inner portion of the needle is removed, and the aspirate is obtained. You may experience a brief (few seconds) quick pressure sensation, almost like a cramp, with the first draw of the bone marrow. It will help to take a deep breath when the aspirate is being drawn. The number of samples drawn will be determined by the tests being ordered by your physician.
8. The same needle is then used to obtain the core biopsy. The inner sheath is removed once the cortical bone has been penetrated. The hollow needle is then inserted into the bone marrow. Your provider will twist and shake the needle gently to loosen the bone core to help remove it in one piece. You will feel pressure and some shaking very briefly. There is sometimes a quick sting when the bone is removed.
9. After the procedure, the provider will apply pressure to the site to prevent any bleeding. A pressure dressing is generally applied.
10. You should not shower for 24 hours. No soaking in water (bath, swimming, hot tubs) for 48-72 hours.
11. Ask your provider for instructions on how to care for the biopsy site.
12. Some patients may develop a bruise or swelling under the skin, particularly patients with a low platelet count or patients taking medication to thin the blood. Be sure to let your healthcare provider know if you are taking aspirin or other medications that thin the blood.
13. Mild pain or discomfort may be experienced at the procedure site for two to three days after the bone marrow exam.
14. For safety reasons, the patient should have a friend, family member, or caregiver travel home with them. The patient should not drive.

What are Acute Myeloid Leukemias

Leukemias are forms of cancer that begin in cells within the bone marrow. The bone marrow is the spongy material inside of bones that is responsible for production of large numbers of healthy blood cells (see: *What Does Bone Marrow Do?*).

Cancer is a consequence of disordered cells in the body that have acquired (gained) mutations (changes) in their DNA that cause the cells grow out of control, without normal checks and balances on their growth to grow out of control. As a result, the normal checks and balances are ineffective. Cancer can begin in any organ or area of the body.

There are several different types of leukemia. These are classified based on whether the leukemia typically grows rapidly ("acute") or more slowly ("chronic"), as well as the type of blood cell that is involved.

"Myeloid" blood cells are distinguished from **"lymphoid"** blood cells, and these cells give rise to different types of white blood cells with distinct roles in the immune system.

Leukemias that develop in myeloid cells include chronic myeloid leukemia (CML) and **acute myeloid leukemia (AML)**.

Normal white blood cell development begins with a seed cell called a **stem cell**. Normally, stem cells give rise to cells that progress through various stages to make healthy mature blood cells. One of the stages is called the **blast cell stage**. This early stage is a normal part of blood cell development, and most healthy people have 1-2% blast cells in their bone marrow.

In acute leukemias, cancerous stem cells become stuck at the blast stage. When more than 20% of cells in the bone marrow or blood (or both) are blast cells, and these blast cells are of the myeloid type rather than lymphoid, it is called AML. If a cancer evolves in the bone marrow which the cells are the myeloid type but less than 20% of the cells are blasts, this might be called myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN), or another term. Over time, MDS or MPN can evolve to AML (see: the Myeloid Continuum of Diseases).

The abnormal cells in AML are produced in the bone marrow, but they often spill out into the blood. Sometimes AML involves other parts of the body besides the marrow and blood, such as the central nervous system (i.e., the brain and spinal cord), lymph nodes, spleen, liver, or testes. This is called **"extramedullary leukemia"**; extramedullary means "outside the bone marrow."

Because the malignant cells in AML circulate in the blood, they are sometimes called **"liquid tumors"** or "hematologic malignancies", in contrast to a "solid tumor" like breast cancer or lung cancer that grows as a local mass and usually does not circulate in the blood. As such, AML is not staged the way a solid tumor would be (i.e., there is no Stage 1, 2, 3 or 4). The severity of the disease is based on other factors.

AML is a result of changes in the DNA of normal bone marrow stem cells. DNA, which makes up our genes, controls the function of our cells. DNA is packaged into long strands called chromosomes.

Many changes that are acquired in the DNA during life in bone marrow stem cells have no consequence. But occasionally, a particular gene or chromosome will become changed in a way that the behavior of the cell is altered. Some of these changes result in the development of cancer.

In AML, changes may involve single DNA letters, but often changes will occur involving whole chromosomes. These changes may involve deletions, additions, translocations, or inversions.

- **Chromosome deletions** mean that a part of a chromosome is lost or a whole chromosome is lost.
- **Chromosome additions** mean that an extra chromosome is present, or a chromosome has gained some additional genetic material.
- **Chromosome translocations** are the most common type of chromosome change in AML. Translocations occur when a piece of one chromosome breaks off and becomes attached to a different chromosome, which affects the behavior of genes near the breakpoint.
- Finally, **chromosome inversions** occur when a piece of a chromosome gets flipped so that it is in a reverse configuration from what it would normally be.
- The specific types of DNA and chromosome changes often have prognostic implications or may influence the behavior of AML cells and the recommended treatment approach to AML.

What Happens to the Bone Marrow in AML

In patients with AML, the development and maturation (differentiation) of the factory cells in the bone marrow (hematopoietic stem cells) is impaired.

This leads to an accumulation of immature cells (blasts) in the bone marrow or peripheral blood, and results in the inability of the bone marrow to make normal blood cells that come from the myeloid factory cell causing low blood counts (cytopenias).

Most patients with **de Novo AML** have a crowded bone marrow, known as a hypercellular bone marrow. Patients with **secondary AML** may have either a hypercellular or hypocellular (empty) bone marrow.

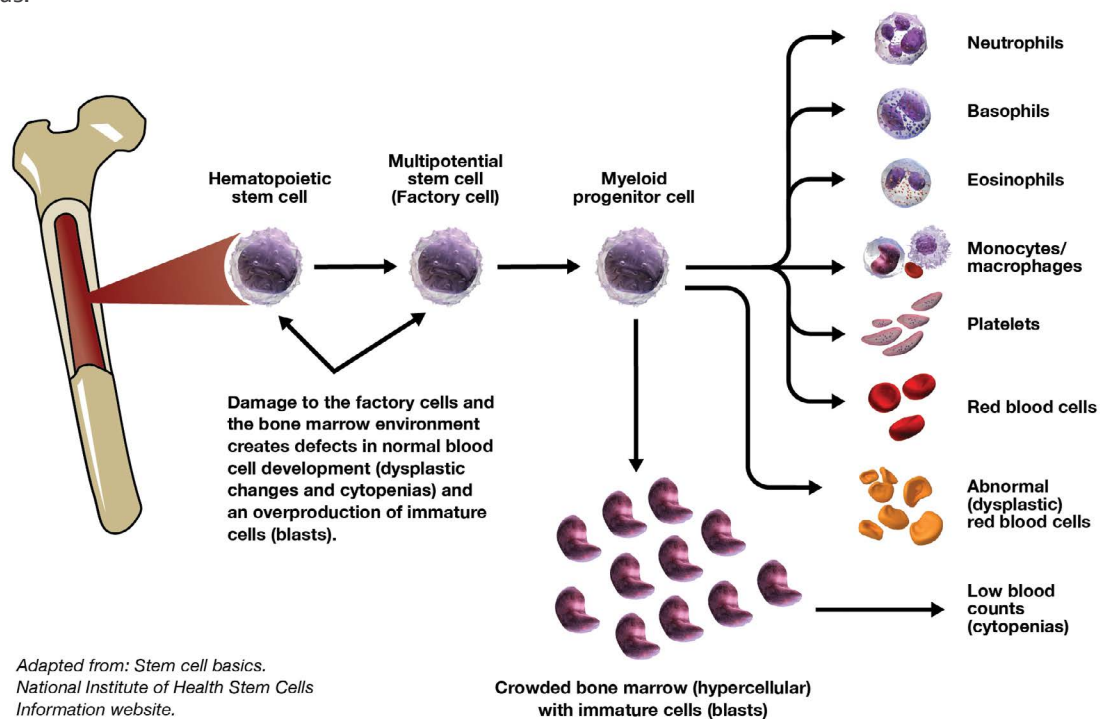
Red blood cells, white blood cells, and platelets all come from the same myeloid factory cell (progenitor cell). These are the cells that we can measure in the peripheral blood. In de Novo AML, the white blood cells may be extremely high with low platelets and red blood cells. In secondary AML, most patients have low WBCs (neutropenia), platelets (thrombocytopenia) and/or red blood cells (anemia) due to a damaged bone marrow from previous treatments or pre-existing myeloid diseases.

The causes of the damage to the myeloid factory cells are thought to result from changes within the cell and changes in the bone marrow environment, known as the microenvironment.

The most common changes within the myeloid factory cells that are thought to cause AML include changes in DNA (chromosome changes) and epigenetic changes (changes outside the DNA).

Changes in the bone marrow microenvironment that promote AML

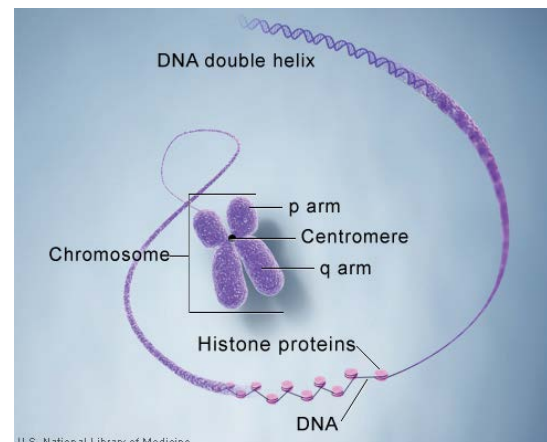
There are several changes in the bone marrow microenvironment that are thought to promote the development of AML. Some of the changes in the bone marrow microenvironment also help to explain the abnormal or ineffective development of the components of blood. Several of the current medications used to treat AML target one or more of these areas.



Chromosomes, Genes and Genetic Changes in AML

Cells are the fundamental working units of every living system. The instructions needed to direct cellular development and activity are contained within the DNA and RNA. DNA is found in the nucleus of every cell in the body (except red blood cells which have no nucleus). The 4 letters of DNA are arranged into genes; humans have about 30,000 genes, which are organized into long strands called **chromosomes**, of which we have 46.

The number of chromosomes in human cells is 46 with 22 autosomal pairs (one of each type contributed by the mother and one of each type from the father) and 2 sex chromosomes, 2 X chromosomes for females (one from father and one from mother) or an X and a Y chromosome for males (the X from the mother and the Y from the father). Each chromosome has a narrow center called the **centromere**, which divides the chromosome 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.



Normal male chromosome profile (karyotype) = 46XY [20]

Normal female chromosome profile (karyotype) = 46XX [20]

Cytogenetic abnormalities are common in all myeloid malignancies, including AML. The changes are described based on the actual structural changes seen when evaluating the chromosomes. These include **deletions** (missing a portion of the chromosome); **additions** (parts added to a chromosome), and **translocations** (switching parts of chromosomes).

Genetic mutations

Genes serve as blueprints for proteins. Proteins are the primary component of all living cells. They contain information that is required for the structure, function, and regulation of the body's tissues and organs. When a cell needs a protein, it activates the corresponding gene. Mutation in genes may be hereditary and occur as a result of damage to one or more cell lines (clone).

There are two primary types of mutations:

- **Germline mutations** – mutations present at birth (inherited, hereditary)
- **Somatic mutations** – these are mutations that acquired after birth due to life events, the most common of these is aging. As cells divide, they must copy all of the information coded in the DNA to replace older cells. As we age, cells trying to repair themselves are not able to complete the process effectively, resulting in random errors in DNA or chromosomes, resulting in somatic mutations.

Over time, other events can accelerate acquired mutations due to further clonal damage, including lifestyle (tobacco use, obesity), and exposure to toxins or radiation. Most patients with AML have experienced several different DNA changes prior to the diagnosis of AML, these are known as clonal events.

Epigenetic Changes in AML

Epigenetic marks are chemical groups of various sorts that decorate the histones (proteins) and DNA (genetic material made of a series of proteins, usually in organized patterns). Epigenetic marks can be added or subtracted to turn a gene on or off. In this way, they can either help to transmit the code (signals that tell the cell to act normally) or block it (cell will not behave normally).

In MDS and in AML, methyl groups (chemical complexes) may be abnormally attached to the genes needed for normal hematopoiesis (the development of the components of blood). When too many of these compounds attach to the gene it is known as hypermethylation. Hypermethylation turns off the genes that are needed for normal blood cell development. Hypermethylation is common in MDS and in AML. It is a constant process and is associated with disease progression and the development of leukemia.

Recent discoveries have shown that abnormal epigenetic mechanisms are largely secondary to mutations (changes) in several genes. Some treatments for MDS and AML, known as hypomethylating agents, block the methyl groups to allow the transfer of information needed for normal blood cell development.

Research continues to identify mutations that contribute to the development and progression of AML, including ways to target those mutations for therapeutic benefit.

Individual Factors

Age • Chemical Exposure • Radiation Exposure
Immune Dysfunction • Unknown Factors



Cytogenetic abnormalities • Clonal evolution
Molecular abnormalities • Epigenetic changes

Bone Marrow Factors

Is AML Hereditary



Most AML does not run in families and is not hereditary. It is currently thought that about 5 to 10% of AML arises in individuals with hereditary predisposition.

However, there are exceptions. In order to understand how hereditary leukemia might occur, it is important to know how AML usually arises (see: [What Causes AML](#) and [Understanding Cytogenetic and Molecular Features of AML](#)).

There are certain inborn syndromes which make acquisition of subsequent mutations and cancer development more likely.

Some of these inborn syndromes, such as **Down syndrome** (an inborn extra copy of chromosome 21), are a result of an accident in chromosome division in the egg cell prior to conception. Others are a result of changes at the single gene level, such as **Fanconi anemia** or **dyskeratosis congenita**. These hereditary (germline mutations) predispose patients to impaired DNA repair or integrity and accelerated acquisition of mutations. Individuals with these syndromes typically have other health problems besides a predisposition to leukemia.

Inborn mutations in a gene called TP53 may result in predisposition to many types of cancer, including breast cancer and other cancers as well as AML; this condition is called **Li-Fraumeni syndrome**.

It is now recognized that there are also familial syndromes in which there are no other manifestations besides an increased risk of AML or closely related blood cancers. One example of this is an inborn mutation in the gene called **RUNX1**. Patients with this abnormality typically present with a chronically low platelet count prior to developing leukemia, which may be erroneously attributed to another cause.

Germline mutations in a gene called **DDX41** can cause AML later in life without any predisposition.

The Signs and Symptoms of AML

The signs and symptoms experienced by patients with AML vary according to the type of AML and the time to onset.

- Signs are physical findings or laboratory changes that the clinician or the patient can detect. It is important for you to describe any new physical changes to your clinical team to help in determining the possible causes of each new physical finding.
- Symptoms are things experienced by the patient as a result of the changes in the blood, bone marrow, and other organs as a result of the underlying AML or other causes. In some cases, symptoms may be a result of other illnesses, medications, or unknown causes. It is important for you to describe any new symptoms to your clinical team to help in determining the cause of each symptom.

For some patients, the time to onset of signs and symptoms is very abrupt and symptoms may occur suddenly (within days to weeks). Patients who develop AML after having another myeloid malignancy such as MDS or an MPN or other types of cancer, generally develop signs or symptoms more gradually (weeks to months). In both cases, the signs and symptoms are related to changes in the bone marrow, blood, and certain organ systems in the body and require specific testing to determine the underlying cause.

Changes in the blood and associated symptoms:

Patient with newly diagnosed AML may have either low blood counts (cytopenias) or high blood counts, in particular very high white blood cells (leukocytosis). Each of these blood changes may be associated with specific signs or symptoms.

- Low red blood cells (anemia): fatigue, shortness of breath, heart skipping a beat (palpitations)
- Low white blood cells (neutropenia): fever, recurrent or prolonged infections
- High white blood cells (leukocytosis): headache, bone pain, skin lesions, fatigue, fevers
- Low platelets (thrombocytopenia): bruising, petechiae, or bleeding

Changes in the bone marrow and associated symptoms:

- **Hypercellular bone marrow:** Too many cells in the bone marrow (hypercellular) is common in MDS, but may also be present in AML with an acute onset. Blast cells (immature myeloid cells) greater than 20% is diagnostic for AML. Symptoms of a hypercellular bone marrow may include bone pain, low-grade fevers, itching, and symptoms associated with thrombocytopenia or anemia.
- **Hypocellular bone marrow:** Too few blood cells in the bone marrow (hypocellular) are common in MDS and late-stage myelofibrosis. Cytopenias in one or more cell lines is common, even with the presence of too many blast cells (greater than 20%).

Organ specific changes and associated symptoms:

- **Skin:** Changes in the skin that may indicate AML include bruising or petechiae (pinpoint red dots on the skin) due to thrombocytopenia, raised red or purplish lesions as a result of leukemia involvement of the skin (leukemia cutis), and itching.
- **Liver and Spleen:** Both the liver and the spleen may become enlarged as a result of too many blood cells, particularly in patients with AML after diagnosis of a MPN. Symptoms may include abdominal pain, getting full fast (early satiety), pain with a deep breath, and fatigue.
 - Changes in liver function (LFTs) may be tested in the blood.
 - Radiology imaging (methods for getting pictures of organs/parts of the body) can be used to look at the liver, the spleen, and other organs of the body. These may include ultrasound, CT or MRI.
- **Brain:** When the blood becomes very thick due to too many cells in circulation, patients may experience headaches, confusion, trouble walking, or other neurological (function controlled by the brain or nerves) changes. Samples of the fluid circulating through the brain and spinal cord, the cerebrospinal fluid (CSF), may be obtained by performing a lumbar puncture to determine if leukemia cells are present in the CSF. Imaging of the brain with a CT or MRI may also be obtained to detect involvement of the brain by leukemia
- **Other organs:** Although rare, leukemic cells may accumulate in other organs in the body or along nerves causing pain, fevers, or neurological changes. These leukemia cell clusters are known as chloromas.

What tests might you need to make the diagnosis of AML?

The Diagnosis of AML

The diagnosis of AML requires a careful review of the patient history and presenting signs and symptoms as well as evaluation of blood and bone marrow samples (see: *Signs and symptoms of AML*).

Patient history

The patient history will assist the clinical team in making the diagnosis of AML and determining the subtype. It is important to provide details of your history including:

- Any active or historic medical or surgical diagnoses
- Any history of other cancers and the details of treatment (chemotherapy, radiation therapy, surgery), including dates
- Any relevant family history
- Current medications and who and why they are prescribed
- Historic laboratory and imaging results

Blood and Bone Marrow Results

The diagnosis of AML requires evaluation of both peripheral blood and bone marrow. The presence of at least 20% myeloid blasts (immature cells) in the blood or bone marrow is required for the diagnosis of AML. The process used for diagnosis is like the process used to diagnose MDS. Three rare subtypes of AML can be diagnosed with <20% blasts. These are: AML with inv(16) or t(16;16), AML with t(8;21) and Acute promyelocytic leukemia [t(15;17)], all of which carry a more favorable prognosis.

The disease is then categorized based on the way the cells look on a slide (morphology) when reviewed by a pathologist, and the genetic signature of the disease. AML is a complex dynamic disease, characterized by multiple genetic abnormalities. There can be more than one genetic abnormality present at any time during the disease and these abnormalities may change over time.

Other testing

- **Selected** radiology imaging studies may be obtained based on presenting **signs** and symptoms
 - **Imaging for pulmonary (lung) function:** Chest X-ray, Computed Tomography (CT) of the chest
 - **Imaging for evaluated the liver, spleen, and kidneys:** CT of the abdomen and pelvis, Ultrasound of the abdomen, Magnetic resonance imaging (MRI) of the **abdomen**.
- **Testing for cardiovascular (heart) function:** Echocardiogram, Electrocardiogram (EKG/ECG)
- **Testing for Neurological (brain and cerebrospinal fluid) function or disease:** MRI or CT of the brain, lumbar puncture to evaluate cerebrospinal fluid (CSF) for possible leukemic involvement.

References:

Kurtin, S. (2018). In Yarbro C, Wujick D., Gobel B.H., Eds. *Cancer Nursing, Principles and Practice, 8th Edition*. Jones Et Bartlett, Burlington, MA.

There are two main categories of AML, de Novo AML and secondary AML

De Novo AML: De-novo (or 'at the start') AML occurs in patients of all ages. Most of the time AML arises abruptly or "out of the blue", without any predisposing condition or risk factors; this is called "**de novo AML**." Most patients present with fever, infections, bruising or bleeding, fatigue, bone pain, and in some cases skin nodules. This type of AML is uncommon in patients with MDS, MPNs or CMML. Some may have a favorable chromosomal karyotype and respond well to standard chemotherapy.

Hereditary pre-disposition to AML: Secondary AML may also arise in someone with a familial or hereditary syndrome that can predispose to AML, or with an inborn genetic condition such as Down Syndrome, as described in the section on hereditary AML.

Secondary AML: This type of AML comes after either being exposed to treatment for another type of cancer or as a part of the natural evolution of a pre-existing myeloid malignancy. The risk of developing secondary AML is variable and is largely related to the risk of the underlying myeloid malignancy and the complexity of genetic changes, or the intensity and type of treatment for other cancers. Genetic abnormalities (including loss of one chromosome 7 [-7], or deletion of a portion of a chromosome [7q-,5q-] are present in more than 90% of patients with these subtypes of AML. Secondary AML carries a less favorable prognosis.

- **Therapy related AML (tAML)** may arise in someone who has been treated with chemotherapy or radiation for another type of cancer such as non-Hodgkin lymphoma, Myeloma, breast cancer, ovarian cancer, or other cancer type. This type of AML occurs as a results of damage to the bone marrow cells and microenvironment that pre-dispose them to the development of AML. The time to onset is highly variable and is largely dependent on the specific drugs and doses used or the amount and of location of radiation.
 - Early onset (3 years):
 - » topoisomerase II inhibitors – etoposide, teniposide, topotecan, doxorubicin
 - » MLL gene (11q23) most common, t(8;21), t(15;17), AML1 (21q;22)
 - Late onset (5-10 years):
 - » therapeutic alkylators – Cytosan, melphalan or radiation
 - » chromosome 5 or 7 abnormalities most common, 17p, del(3p)

Patients can present with a high grade MDS or AML. You can learn more about tAML at www.youandaml.com.

- **AML with myelodysplastic related changes (AML-MRC)** may arise in someone who has been diagnosed with another disorder such as myelodysplastic syndromes (MDS) or a myeloproliferative neoplasm (MPN) as a natural progression of disease. All patients with a myeloid malignancy carry some risk of developing AML-MRC. This risk is related to the subtype of MDS or MPN, the genetic profile of the disease and the risk category. Patients with higher-risk MDS or primary myelofibrosis are at an increased risk of developing AML-MRC. The time to onset is highly variable. Some patients may present with what appears to be De Novo AML based on the number of blasts (>20%) in the peripheral blood or bone marrow and are later found to have AML-MRC.

There are specific criteria for the diagnosis of AML-MRC.

Clinical History	<i>Prior history of a myeloid malignancy MDS, CMML, or an MPN</i>	
Morphology	Multilineage dysplasia: dysgranulopoiesis, dyserythropoiesis, and/or dysmegakaryopoiesis in > 50% of ≥2 cell lineages in the absence of genetic abnormalities defining the category of recurrent genetic abnormalities	
Genetic Abnormalities	≥3 unrelated abnormalities, not including the recurrent genetic abnormalities encountered in AML	
	Unbalanced abnormalities: deletions, additions, inversions	
	-7/del(7q)	
	del(5q)/t(5q)	
	i(17q)/t(17p)	
	-13/del(13q)	
	Balanced abnormalities: translocations	
	t(11;16)(q23.3;p13.3)	t(5;7)(q32;q11.2)
	t(3;21)(q26.2;q22.1)	t(5;17)(q32;p13.2)
	t(1;3)(p36.3;q21.2)	t(5;10)(q32;q21.2)
	t(2;11)(p21;q23.3)	t(3;5)(q25.3;q35.1)
	t(5;12)(q32;p13.2)	

You can learn more about AML-MRC at www.youandaml.com.

References:

Dohner et al. Blood (2017) 129 (4): 424–447
 Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–2405

2016 World Health Organization (WHO) diagnostic criteria for AML

As you can see the diagnosis of AML has become increasingly complex.

Myeloid neoplasms with germline predisposition without a preexisting disorder or organ dysfunction

- AML with germline CEBPA mutation
- Myeloid neoplasms with germline DDX41 mutation

Myeloid neoplasms with germline predisposition and preexisting platelet disorders

- Myeloid neoplasms with germline RUNX1 mutation
- Myeloid neoplasms with germline ANKRD26 mutation
- Myeloid neoplasms with germline ETV6 mutation

Myeloid neoplasms with germline predisposition and other organ dysfunction

- Myeloid neoplasms with germline GATA2 mutation
- Myeloid neoplasms associated with bone marrow failure syndromes
- Juvenile myelomonocytic leukemia associated with neurofibromatosis, Noonan syndrome, or Noonan syndrome-like disorders
- Myeloid neoplasms associated with Noonan syndrome
- Myeloid neoplasms associated with Down syndrome

AML with recurrent genetic abnormalities

- AML with t(8;21)(q22;q22.1); RUNX1-RUNX1T1
- AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11

- APL with PML-RARA
- AML with t(9;11)(p21.3;q23.3); MLLT3-KMT2A
- AML with t(6;9)(p23;q34.1); DEK-NUP214
- AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM
- AML (megakaryoblastic) with t(1;22)(p13.3;q13.3); RBM15-MKL1
- Provisional entity: AML with BCR-ABL1
- AML with mutated NPM1
- AML with biallelic mutations of CEBPA
- Provisional entity: AML with mutated RUNX1

AML with myelodysplasia-related changes (AML-MRC)

- Therapy-related myeloid neoplasms (tAML)
- Secondary AML (sAML)
- AML, not otherwise specified
- AML with minimal differentiation
- AML without maturation
- AML with maturation
- Acute myelomonocytic leukemia
- Acute monoblastic/monocytic leukemia
- Pure erythroid leukemia
- Acute megakaryoblastic leukemia
- Acute basophilic leukemia
- Acute panmyelosis with myelofibrosis

2017 European Leukemia Network Risk Stratification by Genetic Profile for AML

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 or with FLT3-ITD ^{Low}
	Biallelic mutated CEBPA
Intermediate	Mutated NPM1 and FLT3-ITD ^{High}
	Wild type NPM1 without FLT3-ITD or with FLT3-ITD ^{Low} (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); MLLT3-KMT2A
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); DEK-NUP214
	t(v;11q23.3); KMT2A rearranged
	t(9;22)(q34.1;q11.2); BCR-ABL1
	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM (EVI1)
	-5 or del(5q); -7; -17/ abnormal (17p)
	Complex karyotype; monosomal karyotype
	Wild type NPM1 and FLT3-ITD ^{High}
	Mutated RUNX1
	Mutated ASXL1
	Mutated TP53

References:

Dohner et al. Blood (2017) 129 (4): 424-447

Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391-2405

SEEKING TREATMENT FOR ACUTE MYELOID LEUKEMIA

*Acute Myeloid Leukemia (AML) includes a group of myeloid malignancies (cancers). There are several subtypes of AML. Each type of AML has a variable time to onset, prognosis, and options for treatment. Seeking Treatment for AML, the second chapter in the **Building Blocks of Hope® - AML Edition**, provides an overview of the currently available treatment options for each subtype of AML and how these treatments are selected.*

Treatment selection is based on each patients' individual AML profile as well as general health status (fitness) and personal goals for treatment. Understanding your AML diagnosis and available options for treatment will help you and your caregiver(s) ask important questions about each treatment option, expectations for treatment outcomes and how each treatment may affect your quality of life and daily routines. Preparing for each visit (discussed in Quick Tips) will help you prepare and take an active part in treatment decisions.

SEEKING TREATMENT FOR AML

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The goals of treatment for all types of AML are to eradicate the myeloid blasts to the lowest level possible (remission requires <5% blasts) with no evidence of residual genetic mutations (minimal residual disease or MRD). Like MDS, allogeneic stem cell transplantation is the only potential for cure in patients with AML, with a few exceptions. Determining transplant eligibility (see: Am I a candidate for a stem cell transplant/bone marrow transplant) and fitness for treatment is the first step.

The type of treatment selected and the goals of treatment for AML are based on a number of factors including:

1. Your general health and ability to be independent in the activities of daily living
2. Other illnesses, how well they are controlled and what medications are needed to manage them
3. Your individual social and emotional profile
4. Insurance coverage and finances
5. The characteristics of your AML – higher risk vs. lower risk and the presence of certain genetic markers
6. Currently available treatment options including clinical trials (these may be based on geographical location)
7. Eligibility for a stem cell transplant
8. The availability of a caregiver
9. Proximity to the healthcare setting
10. Your personal goals and how the individual treatment may affect your quality of life and lifestyle
11. Your age, although the factors listed above will supersede chronological age in most cases when considering treatment

It is important to understand the treatment recommendations suggested by your oncology provider, how they may affect you on a day-to-day basis, and what the goals of treatment are so you can make an informed choice.

Treatment Intensity

High-intensity treatment

Patients must be deemed “fit” for this type of treatment which most often includes a stem cell transplant. Patients eligible for high intensity treatment receive chemotherapy, usually in phases. Induction, consolidation, stem cell transplant, and in some cases maintenance therapy. Many of these treatments require intermittent hospitalization.

Low-intensity treatment

Patients who may not be fit enough for high-intensity treatment may receive less aggressive therapy. Patients receiving low-intensity treatment may continue treatment indefinitely if they are benefitting and do not experience serious side effects. Low-intensity treatments are not curative. Most of these treatments are administered in the outpatient setting.

There are several phases to the treatment of AML. Depending on the subtype of AML, the type of treatment and duration of therapy will vary. The only potential cure for AML, regardless of subtype, is an allogeneic stem cell transplant. Therefore, transplant eligibility is evaluated at the time of diagnosis for all patients with AML (see: [Bone Marrow Transplant](#)).

Several procedures will be performed as soon as AML is suspected (see: [How is AML diagnosed?](#)). You will also likely have a central venous catheter or peripherally inserted catheter (PICC) placed to allow for frequent testing of blood and administration of treatment and supportive care.

Induction Therapy or Initial Treatment

Initial treatment of AML is generally called induction therapy. The goals of induction therapy are to control the aggressive and uncontrolled growth of leukemia (blast) cells, restore bone marrow function, and correct any associated effects on other organs. Depending on the subtype of AML and the severity of the disease, induction therapy may require hospitalization.

Patients with de Novo AML treated with **high-intensity therapy** require hospitalization due to the potentially life-threatening effects of the disease and treatment. In the majority of cases, these potential risks can be effectively managed, but may require hospitalization for several weeks. A repeat bone marrow biopsy is generally performed at specified intervals after induction therapy to confirm the clearing of blasts cells and then again to confirm that the leukemia is in remission.

Patients with secondary AML with a lower blast count and no serious health problems, may be considered for outpatient induction therapy. This is usually **lower-intensity therapy**. There are several criteria for outpatient induction therapy including:

- availability of a reliable caregiver and driver around the clock
- proximity to the treatment center (usually within 45 minutes)
- no uncontrolled co-morbidities (other illnesses)

Because secondary AML is often associated with low blood counts at the time of diagnosis, frequent visits to the clinic will be required to administer treatment, monitor labs, and administer transfusions or other supportive care. Repeat bone marrow biopsies may or may not be required immediately after induction therapy depending on the disease and goals of treatment.

Induction therapy most often includes chemotherapy but may also include hypomethylating agents +/-targeted agents in patients who are eligible for this type of treatment.

When to Start Induction Treatment

Treatment of AML is generally started immediately and may include supportive care measures to control disease related effects on the patient, including bleeding, infection, and neurological changes. For patients with presenting signs and symptoms that do not require immediate intervention, disease-directed treatment may be delayed up to a week to allow results of the bone marrow biopsy to become available to guide treatment selection.

Consolidation

Once the bone marrow has recovered from induction therapy (normal or near normal blood counts), a bone marrow biopsy is performed to confirm the patient is in remission (<5% blasts). Approximately two thirds of patients who undergo intensive induction chemotherapy treatment for AML will achieve remission. Additional cycles of chemotherapy are administered to improve the depth of response and reduce the chance that the AML will come back (relapse). The number of cycles is determined by the type of AML, the age and fitness of the patient, and whether the patient is eligible for an allogeneic stem cell transplant. Consolidation therapy can be administered in the outpatient setting in patient who meet criteria (see above).

Similar to the process used for selection of induction, many factors figure into the process of selecting the best/most appropriate consolidation regimen for each patient. Some of these factors include but are not limited to the following:

- the number of cycles of induction chemotherapy needed to induce remission
- the risk of relapse or leukemia cells coming back
- the availability of an acceptable stem cell donor
- the presence or absence of prognostic factors/genetic mutations (previously discussed)
- the patient's age and overall fitness
- the patient's wishes

Allogeneic Stem-Cell Transplant remains the only potential curative treatment for most types of AML (see: *Bone Marrow Transplant* for detailed discussion)

Maintenance

Selected patients may receive additional treatment following an allogeneic stem cell transplant to reduce the risk of post-transplant relapse.

Continuous Therapy

Patients not eligible for a stem cell transplant may continue treatment indefinitely if they are benefitting and do not experience serious side effects.

Relapse

When a patient achieves a remission and the leukemia returns, this is considered a relapse. Relapse is common in many patients with AML, even after an allogeneic stem cell transplant. The characteristics of the AML, including the molecular and genetic profile may change with each relapse. Multiple relapses may occur with increasing difficulty getting the disease back into remission after each relapse.

Progression

Progression of disease is defined as increasing blasts counts or new extramedullary disease (leukemia involvement outside the bone marrow). This occurs in patients who have not achieved a remission and may vary in the tempo of the changes. For some cases, progression may be abrupt and change rapidly requiring immediate change in treatment. In other cases, the progression may be slow and adjustments in the current treatment may be made before changing therapy.

Refractory AML

Although rare, some patients with AML have disease that does not respond to the best available therapies. For these patients, a clinical trial should be considered. Salvage therapy (treatment used with the intent to achieve a temporary improvement in disease) may be administered with the goal of getting the patient ready for a stem cell transplant or a clinical trial.

Unacceptable Toxicity

All treatments for AML are associated with selected side effects. All patients receiving active therapy for the treatment of AML should also receive concurrent supportive care to prevent and mitigate expected or unexpected side effects. If side effects cannot be effectively managed, a change in treatment is indicated.

The treatment of AML includes the use of chemotherapy agents, targeted therapies, and concurrent supportive and palliative care, and is some patients emergent treatment.

Emergent cytoreductive therapy

Patients presenting with extremely high white blood cell counts (leukocytosis) with a high percentage of blasts (blast crisis) may require initial measures to quickly reduce the number of circulating cells to avoid life threatening blood clots (thrombosis) or severe bleeding (hemorrhage). Measure to emergently reduce leukocytosis include cytoreductive therapy and in some cases leukapheresis.

The most common agent used for cytoreduction is Hydroxyurea. Doses are tailored to the level of the white blood cell count and blast percentage.

Leukapheresis, the removal of excess white blood cells from the circulating blood, is a special procedure that placement of a special indwelling catheter and a process that is similar to dialysis. Although rare, this process is necessary in patients with advanced disease.

Prevention of emergent metabolic processes that may occur as a result of circulating blast cells and their breakdown require aggressive supportive care at the time of diagnosis and through the induction process.

Tumor lysis syndrome, a metabolic syndrome that is a result of rapid break down of blast cells and release of electrolytes and other cellular chemicals into the circulating blood may result in kidney or heart failure. In addition to cytoreductive therapy, patients may require specialty drugs to avoid kidney failure and in rare cases short-term dialysis may be required.

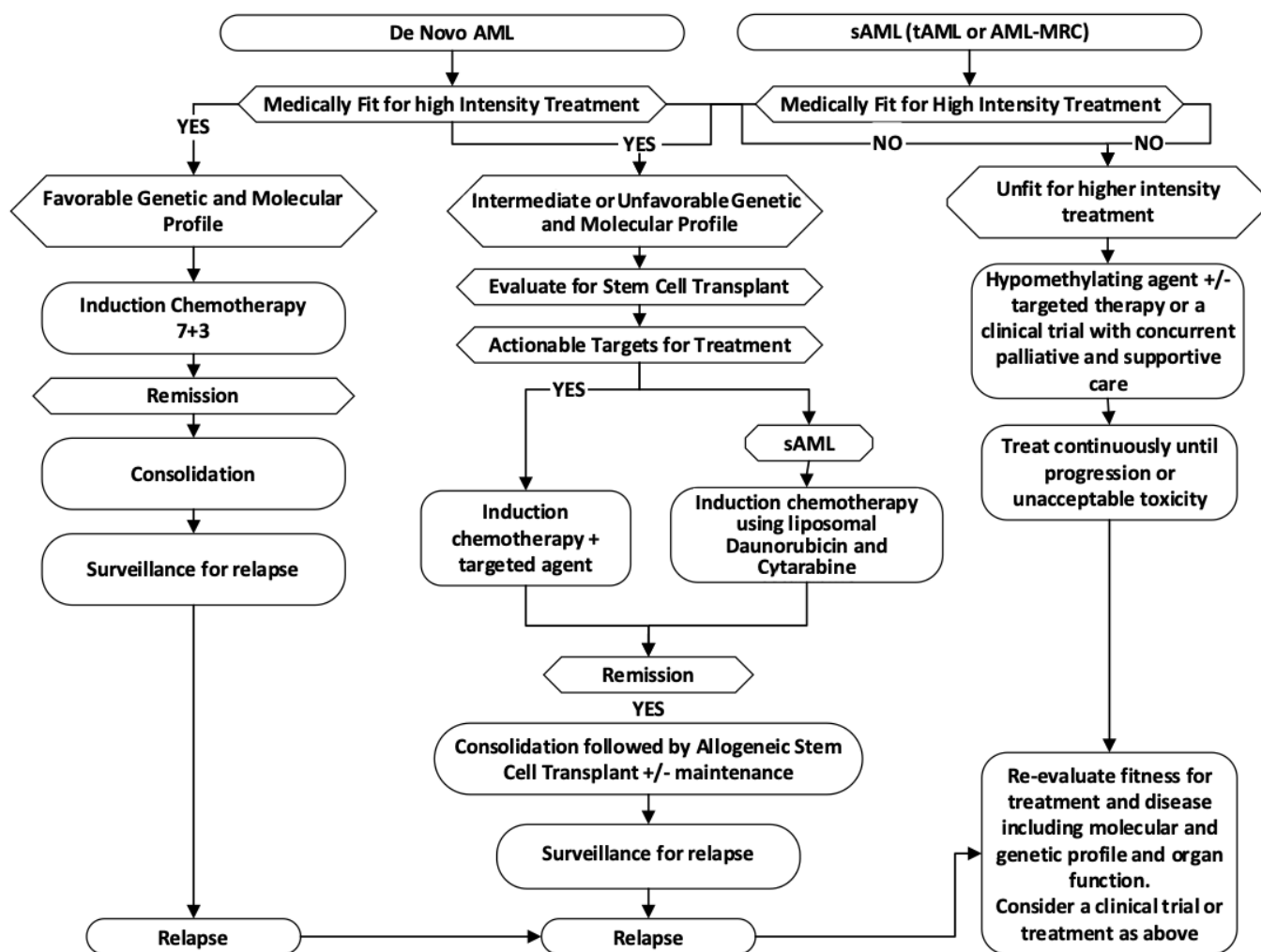
Chemotherapy

Drugs that affect proteins, including the building blocks of DNA and RNA provide the backbone for treatment of AML. Most are given in the vein, intravenously.

Targeted Therapies

In some subtypes of AML, mutated genes can be targeted using specific drugs to interrupt the abnormal production of leukemia cells and the bone marrow microenvironment. Genetic mutations are currently identified by sequencing the DNA, commonly using a technique called "next generation sequencing" (NGS) using the material from a bone marrow sample. Importantly, the genetic profile may change over time. This is why it is important to re-characterize AML at points of progression. The majority of targeted agents used to treat AML are pills taken orally.

General Approach to Treatment of AML



Currently Available Treatments for AML

Currently Available Treatments for AML: Chemotherapy

CHEMOTHERAPY			
Agent	Class	Indication and route of administration	Link to Drug Information
Azacitidine (Vidaza®)	Hypomethylating agent	Low-intensity treatment for de Novo AML, or sAML	http://chemocare.com/chemotherapy/drug-info/azacitidine.aspx
Azacitidine (Onureg®)	Hypomethylating agent	Oral formulation agent may also be used for maintenance therapy after a stem cell transplant.	www.onureg.com http://chemocare.com/chemotherapy/drug-info/azacitidine.aspx
Clofarabine (Leustatin®)	Anti-metabolite	High-intensity alternative induction or consolidation regimens for relapsed AM	http://chemocare.com/chemotherapy/drug-info/clofarabine.aspx
Cytarabine (Cytosar-U®)	Anti-metabolite	May be used for high intensity or low-intensity treatment for newly diagnosed or relapsed AML. Doses, schedules, and route of administration vary. May be used to treat the CSF (intrathecal)	http://chemocare.com/chemotherapy/drug-info/cytarabine.aspx
Daunorubicin (Cerubidine®)	Anthracycline	High-intensity therapy combinations in newly diagnosed de Novo AML or sAML	http://chemocare.com/chemotherapy/drug-info/daunorubicin.aspx
Decitabine (Dacogen®)	Hypomethylating agent	Low-intensity treatment for de Novo AML, or sAML	http://chemocare.com/chemotherapy/drug-info/decitabine.aspx
Decitabine + cedazuridine (Inqovi®)	Hypomethylating agent	Low-intensity treatment for high risk MDS	www.inqovi.com/
Etoposide (Vespid)	podophyllotoxin derivatives	High-intensity alternative induction regimens for AML	http://chemocare.com/chemotherapy/drug-info/etoposide.aspx
Hydroxyurea	Alkylating agent	May be used to reduce very high white blood counts in newly diagnosed AML while waiting to confirm the diagnosis	http://chemocare.com/chemotherapy/drug-info/hydroxyurea.aspx
Fludarabine	Anti-metabolite	High-intensity alternative induction regimens for relapsed AML	http://chemocare.com/chemotherapy/drug-info/fludarabine.aspx
Idarubicin	Anthracycline	High-intensity treatment for newly diagnosed AML	http://chemocare.com/chemotherapy/drug-info/idarubicin.aspx
Liposomal Cytarabine + Daunorubicin (Vyxeos®)	Anthracycline + Anti-metabolite	High-intensity therapy combinations in newly diagnosed de Novo AML or sAML	http://chemocare.com/chemotherapy/drug-info/daunorubicin-and-cytarabine-liposomal.aspx www.vyxeos.com
Methotrexate	Anti-metabolite	May be used to treat the CSF (Intrathecal)	http://chemocare.com/chemotherapy/drug-info/methotrexate.aspx

Currently Available Treatments for AML

Currently Available Treatments for AML: Targeted Therapies

TARGETED AGENTS			
Agent	Class	Indication and route of administration	Link to Drug Information
Enasidenib (Idhifa®)	IDH2 inhibitor	Oral agent used for low-intensity treatment	http://chemocare.com/chemotherapy/drug-info/enasidenib.aspx https://www.idhifa.com/
Gemtuzumab ozogamicin (Mylotarg™, GO)	Monoclonal antibody	Injectable agent used as monotherapy or in combination for relapsed AML as salvage therapy	http://chemocare.com/chemotherapy/drug-info/gemtuzumab-ozogamicin.aspx
Gilteritinib (Xospata®)	FLT3 inhibitor	Oral agent used in combination with high-intensity chemotherapy during induction and consolidation for AML	http://chemocare.com/chemotherapy/drug-info/gilteritinib.aspx www.xospata.com/
Ivosidenib (Tibsovo®)	IDH1 inhibitor	Oral agent used for low-intensity treatment	http://chemocare.com/chemotherapy/drug-info/ivosidenib.aspx
Midostaurin (Rydapt®)	FLT 3 inhibitor	Oral agent used in combination with high intensity chemotherapy during induction and consolidation for AML	http://chemocare.com/chemotherapy/drug-info/midostaurin.aspx www.us.rydapt.com
Sorafenib (Nexavar®)	FLT3 inhibitor	Oral agent used in combination with high intensity chemotherapy during induction and consolidation for AML	http://chemocare.com/chemotherapy/drug-info/Sorafenib.aspx www.nexavar-us.com
Venetoclax (Venclexta®)	BCL2 inhibitor	Oral agent used in combination with low-intensity chemotherapy during induction and consolidation for AML	http://chemocare.com/chemotherapy/drug-info/venetoclax.aspx www.venetoclax.com

7+3 (Standard formulation of Cytarabine + Daunorubicin)

Cytarabine and Daunorubicin (7+3) is the most common induction chemotherapy regimen used to treat de Novo AML. This combination is administered in the inpatient setting and requires placement of a central venous catheter.

The 7+3 regimen gets its name from the number of days each chemotherapy agent is administered/delivered.

- **Cytarabine** (an anti-metabolite) is given daily as a continuous infusion into an implanted venous catheter for seven days (7).
- **Daunorubicin** (an anthracycline) is given daily for three days (3) as a short infusion.
- **Idarubicin** (an anthracycline) may be substituted for daunorubicin and is given for 3 days as a short infusion.

Side effects may vary by patient and may occur within the first few days of treatment or in the days or weeks following treatment. Laboratory testing is obtained frequently during the induction phase of treatment to evaluate response and to identify any side effects that require treatment. Imaging studies may also be obtained based on individual signs and symptoms. The majority of patients will require transfusion support for red blood cells and platelets, intravenous fluids, and antibiotics during this time.

Side effects that may occur immediately (during treatment):

- Low blood counts (cytopenias, including anemia, thrombocytopenia, or neutropenia) – these cytopenias may last weeks following induction or consolidation therapy and will require transfusion support.
- Nausea, vomiting, diarrhea
- Tumor lysis syndrome – this is a rare but potentially life-threatening metabolic syndrome that is a result of the rapid break down of the leukemia cells (see: Quick-Tips)
- Infections, including pneumonia, urinary tract infections and more serious infections including febrile neutropenia and sepsis
- Embryo-fetal toxicity – fertility discussions and confirmation that any women of child-bearing age is not pregnant prior to starting treatment is essential.

Other side effects that may occur in the first few weeks of treatment

- Hair loss
- Muscle or joint pain
- Skin Rashes
- Acral erythema (redness and tenderness of the hands and feet, sometimes with blistering) (cytarabine – dose related)
- Neurological symptoms (cytarabine) – dose related
- Keratoconjunctivitis (irritation of the lining of the eye) – dose related and required steroid eye drops during drug administration
- Typhlitis (inflammation of the rectum and sigmoid colon) or rectal abscess
- Decreased appetite
- Cardiomyopathy (damage to the heart muscle causing heart failure) related to total dose over time and pre-existing heart disease.

Evaluating the response to Induction Therapy

Two weeks following treatment (day 14) a bone marrow sample will be obtained to determine treatment efficacy. The sample is expected to be empty (hypoplasia) with <5% blasts. If the bone marrow is empty, the patient will continue to receive supportive care until the blood counts recover (generally between 21–28 days after the start of treatment). A bone marrow biopsy will be performed once blood counts recover to ensure that there are no longer leukemia cells present and less than 5% blasts (remission). If the bone marrow shows persistent leukemia, the patient will undergo a second induction with alternative drugs or may have another bone marrow biopsy to evaluate a possible delayed response to the first induction.

Patients in remission will move on to consolidation therapy with continued evaluation for a stem-cell transplant, including initiating a donor search.

Monitoring cumulative doses of Anthracyclines

Anthracyclines are known to cause cardiomyopathy (damage to the heart muscle) in higher doses administered over time (cumulative doses). The maximum dose of daunorubicin is 550 mg/m²; 450 mg/m² in patients who have received prior mediastinal radiation and the maximum lifetime dose of idarubicin is 150 mg/m². Patients must undergo an echocardiogram or MUGA scan prior to initiating treatment with these medications and should be monitored throughout the course of treatment for any cardiac symptoms (Venkatesh and Kasi, 2020).

Consolidation following standard 7+3

Although the 7+3 regimen can be modified to a 5+2 regimen for consolidation, cardiac toxicity (damage to the heart) may occur with cumulative (repeated) doses of anthracyclines. Alternative regimens may be considered for consolidation using age adjusted doses and schedules of cytarabine.

The number of cycles of consolidation will depend on eligibility for stem cell transplant and the availability of a stem cell donor. Patients with favorable risk AML who are fit for intensive treatment and do not require a stem cell transplant, generally receive 4 cycles of consolidation.

High-dose Cytarabine (HiDAC) or Intermediate dose Cytarabine (IDAC):

Cytarabine used for consolidation is given in varied doses and scheduled based on age and fitness.

HiDAC

Higher doses are generally given twice a day (10–12 hours apart), every other day (days 1, 3, 5), for a total of 6 doses, or days 1–3 in divided doses. HiDAC may require hospitalization.

IDAC

The IDAC regimen is used for patients who cannot tolerate the intensity of HiDAC consolidation. The dose of cytarabine is reduced and may be given in the same sequence as HiDAC or may be given daily for 3–5 consecutive days.

Liposomal Cytarabine + Daunorubicin (CPX-351; Vyxeos®)

Vyxeos®, a liposomal formulation combining Cytarabine and Daunorubicin and is approved for induction and consolidation therapy for tMDS and MDS-MRC. You can learn more about the treatment of tAML and AML-MRC at www.youandaml.com.

Importantly, although Vyxeos® combines cytarabine and daunorubicin, similar to the standard 7+3 regimen, the liposomal formulation requires different dosing and administration. It is a very dark purple color and may cause some discoloration of the urine when excreted.

The treatment schedule for induction is Vyxeos® 44mg/100mg per m², given as a 90-minute infusion on days 1, 3, and 5.

The treatment schedule for re-induction in patients who do not achieve a remission following the first cycle of induction is Vyxeos® 44mg/100mg per m², was administered as a 90-minute infusion on days 1 and 3.

The treatment schedule for consolidation is Vyxeos® 29mg/65mg per m² on days 1 and 3.

Vyxeos® induction therapy is administered most often in the inpatient setting. Outpatient administration of Vyxeos® induction therapy is available at selected specialty centers that have expanded hours, availability of same day transfusion and supportive care, and the ability to transfer the patient to an inpatient setting when needed.

The toxicity profile for Vyxeos® is very similar to that of the standard 7+3 regimen with the exception of prolonged time to recovery of the bone marrow. As a result, repeat bone marrow biopsies may be delayed and consolidation therapy may not be administered for up to 6 weeks after induction therapy. Pre-treatment evaluation of the heart and monitoring for any cardiac symptoms is required and the drug may cause tissue damage if it leaks outside of the vein. Most patients have indwelling catheters for this reason.

You can learn more about Vyxeos® at www.vyxeos.com/about-vyxeos or <http://chemocare.com/chemotherapy/drug-info/daunorubicin-and-cytarabine-liposomal.aspx>

Patients that can tolerate high intensity therapy but may not be candidates for cytarabine and daunorubicin or idarubicin regimens due to underlying diseases, may benefit from alternative induction therapies. These same treatments may also be considered as salvage therapies in patients who do not achieve a remission following standard induction therapy or who relapse after achieving an initial remission.

Pre-existing heart disease

One specific contraindication to traditional 7+3 induction chemotherapy is poor cardiac function. Patients who have pre-existing heart conditions may not be able to receive the anthracycline agents (daunorubicin, idarubicin or mitoxantrone).

Anthracycline free regimens may be considered for patients who otherwise qualify for high intensity treatment, although in most cases, these patients will not qualify for a stem cell transplant and the long-term goals of therapy will shift to long-term remission or continued response.

Agents used for alternative induction regimens or relapsed or refractory AML

Clofarabine is an antimetabolite that may be used in combination with other chemotherapy agents for relapsed or refractory AML. It is given in varied sequences based on the regimen and the overall health of the patient. The side effect profile is very similar to that of cytarabine.

You can learn more about Clofarabine at <http://chemocare.com/chemotherapy/drug-info/clofarabine.aspx>

Etoposide is a podophyllotoxin derivative that works by slowing or stopping the growth of cancer cells. It can be used in a number of regimens and may be given either intravenously or by mouth (oral tablet).

You can learn more about Etoposide at <http://chemocare.com/chemotherapy/drug-info/etoposide.aspx>

Fludarabine is an antimetabolite used for alternative induction regimens for patient with relapsed or refractory AML.

You can learn more about Fludarabine at <http://chemocare.com/chemotherapy/drug-info/fludarabine.aspx>

Agents used to treat or prevent leukemic infiltration of the cerebrospinal fluid (CSF) or the brain.

There are only a few drugs that can be given to treat or prevent leukemic infiltration of the brain or cerebrospinal fluid. Cytarabine and Methotrexate are the most commonly used agents. They may be given through an Ommaya Reservoir (an implanted port placed in the scalp) or by lumbar puncture.

Enasidenib (Idhifa®)

Drug Class: IDH2 (isocitrate dehydrogenase 2) Inhibitor and differentiation agent

FDA Approved Indication: Relapsed or refractory AML that is IDH2 mutated

Background Information: Enasidenib is a selective inhibitor of mutant-IDH2 enzymes. A Phase 1/2 study established the clinical activity of enasidenib in patients with mutant-IDH2 advanced myeloid malignancies. Enasidenib 100 mg once daily demonstrated efficacy. Among patients with relapsed or refractory AML, overall response rate was 40.3%, with a median response duration of 5.8 months. Median overall survival among relapsed/refractory patients was 9.3 months, and for the 34 patients (19.3%) who attained complete remission, overall survival was 19.7 months. This trial was registered at www.clinicaltrials.gov as #NCT01915498.

How Administered: Oral tablet, 100 mg once daily with or without food at approximately the same time each day. Swallow tablets whole with a full glass of water. Do not split or crush the tablets.

Common Side Effects:

- Nausea and vomiting
- Diarrhea
- Decreased appetite or taste changes
- Changes in blood tests including liver studies (bilirubin) and electrolytes (phosphorous)

Potentially serious side effects

- Differentiation Syndrome: A rare, but potentially serious or fatal complication that may occur 1 day to 5 months after starting enasidenib. Symptoms of differentiation syndrome may include:
 - Fever
 - Cough
 - Shortness of breath
 - Swelling of the arms or legs, neck often with rapid weight gain of more than 10 pounds in a week.
 - Bone pain

It is important to report any of the symptoms immediately for rapid treatment with steroids, and other supportive care.

- Embryo-fetal toxicity

Resources: You can learn more about Enasidenib (Idhifa) at:

<http://chemocare.com/chemotherapy/drug-info/enasidenib.aspx>
www.idhifa.com

Gemtuzumab ozogamicin (Mylotarg™)

Drug Class: Anti CD33 Monoclonal antibody

Gemtuzumab ozogamicin is a monoclonal antibody used to treat AML that expresses CD33, a protein expressed on some leukemia cells.

FDA Approved Indication: Newly diagnosed or relapsed/refractory CD33-positive acute myeloid leukemia (AML) in adults and pediatric patients 1 month and older.

Background Information: Gemtuzumab ozogamicin has been approved either as a single agent or in combination with other drugs based on two key studies:

ALFA-0701 (NCT00927498), a multicenter, randomized, open-label Phase 3 study of 271 patients with newly-diagnosed de novo AML ages 50 to 70 years. Patients were randomized (1:1) to receive induction therapy consisting of standard 7+3 (see 7+3) with (n=135) or without (n=136) MYLOTARG 3 mg/m² (up to maximum of one vial) on Days 1, 4, and 7. Median event free survival was 17.3 months in the MYLOTARG arm versus 9.5 months in the control arm; hazard ratio (HR) 0.56 (95% CI: 0.42–0.76); 2-sided p less than 0.001 by log-rank test. Patients who did not achieve remission with first induction were eligible to receive additional treatment. EFS was not as favorable.

AML-19 (NCT00091234), a multicenter, randomized, open-label Phase 3 study comparing MYLOTARG to best supportive care for patients with newly diagnosed AML who were a) greater than 75 years of age or b) 61 to 75 years of age with adequate performance status or were unwilling to receive intensive chemotherapy received induction therapy. The efficacy of MYLOTARG was established on the basis of improvement in overall survival (OS). Median OS was 4.9 months in the MYLOTARG arm versus 3.6 months in the control arm.

How Administered: Intravenously

Common Side Effects:

- Low blood counts (cytopenias)
- Rash
- Headache
- Nausea and vomiting
- Changes in blood tests for liver function
- Swelling of the hands or feet
- Diarrhea or constipation

Less common, but more serious side effects

- Infusion related reactions are not uncommon in monoclonal antibody treatment. You will receive medications ahead of the infusion to reduce the risk of a reaction that may include fever, shaking chills, a rash, tightness in the throat, and in rare cases difficulty breathing. Reaction may be treated with additional medications.
- Veno-occlusive disease (VOD) is a rare complication in patients treated with Mylotarg™ who have relapsed after an allogeneic stem cell transplant. Your clinical team will monitor your blood work before and after treatment to prevent more severe cases of VOD.
- Tumor Lysis Syndrome – the breakdown of leukemia cells leading to the release of and shifting of electrolytes and urine acid that may cause serious heart and kidney damage. Symptoms may include:
 - Fever
 - Confusion
 - Dark or cloudy urine
 - Chills
 - Shortness of breath
 - Unusual tiredness
 - Nausea
 - Seizures
 - Muscle or joint pain
 - Vomiting
 - Irregular heartbeat

Resources: You can learn more about Gemtuzumab ozogamicin at:

<http://chemocare.com/chemotherapy/drug-info/gemtuzumab-ozogamicin.aspx>

Ivosidenib (Tibsovo®)

Drug Class: IDH 1 (isocitrate dehydrogenase-1) Inhibitor

FDA Approved Indication:

- adults with newly diagnosed AML who are 75 years or older or who have health problems that prevent the use of certain chemotherapy treatments.
- adults with AML when the disease has come back or has not improved after previous treatment(s).

Background Information: Newly Diagnosed: Ivosidenib blocks the IDH 1 pathway of the mutant isocitrate dehydrogenase 1 (IDH1; mIDH1) enzyme. A Phase 1 study of 258 patients with the IDH 1 mutation was conducted and complete remission 30.3%. Median overall survival was 12.6 months. Ivosidenib was well-tolerated and induced durable remissions and transfusion independence in patients with newly diagnosed AML.

Relapsed/Refractory: Phase 1 trial in IDH1-mutated AML patients with relapsed or refractory AML receiving 500 mg of ivosidenib daily. 125 patients were enrolled. The overall response rate was 41.6%. The median durations of these responses were 6.5 months. This trial was registered at www.clinicaltrials.gov as #NCT02074839.

How Administered: oral tablet; 500 mg once daily. May be taken with or without food. Do not take with high fat meal. Avoid grapefruit and grapefruit juice.

Common Side Effects:

- | | |
|---|----------------------|
| • fatigue | • rash |
| • joint or muscle pain | • cough |
| • high white blood cell count | • decreased appetite |
| • diarrhea or constipation | • muscle pain |
| • nausea | • fever |
| • pain or sores in your mouth or throat | |

Potentially serious side effects

- Differentiation Syndrome: A rare, but potentially serious or fatal complication that may occur 1 day to 3 months after starting ivosidenib. Symptoms of differentiation syndrome may include:
 - Fever
 - Cough
 - Shortness of breath
 - Swelling of the arms or legs, neck often with rapid weight gain of more than 10 pounds in a week.
 - Bone pain
 - It is important to report any of the symptoms immediately for rapid treatment with steroids and other supportive care.
- QTC prolongation – rare but potential changes in the heart rhythm that may be fatal
- Embryo-fetal toxicity

Resources: You can learn more about Ivosidenib (Tibsovo®) at:

<http://chemocare.com/chemotherapy/drug-info/ivosidenib.aspx>
www.tibsovo.com

Midostaurin (Rydapt®)

Drug class: FLT3 (a gene that may be mutated in patients with AML) Inhibitor

FDA approved indication: 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.

Background information: Approval was based on results of a Phase 3 randomized multi-center trial. A total of 717 patients were randomized according to the subtype of FLT3 mutation (point mutation in the tyrosine kinase domain (TKD) or internal tandem duplication (ITD) mutation), with 360 were assigned to the midostaurin group, and 357 to the placebo group. The FLT3 subtype was ITD (high) in 214 patients, ITD (low) in 341 patients, and TKD in 162 patients. Overall survival was significantly longer in the midostaurin group than in the placebo group across all FLT3 subtypes. The rate of severe adverse events was similar in both groups. This trial was registered at www.clinicaltrials.gov as #NCT00651261.

How administered: oral tablet

- Induction: 50 mg twice daily on days 8 to 21 of each induction cycle (in combination with daunorubicin and cytarabine)
- Consolidation: 50 mg twice daily on days 8 to 21 of each 28-day consolidation cycle (in combination with high-dose cytarabine) for 4 consolidation cycles

Common side effects:

- Low blood counts (cytopenias) including neutropenia, thrombocytopenia, and anemia with an increase risk of infections and bleeding
- Infections including pneumonia
- Nausea and vomiting
- Mouth sores
- Headache
- High blood sugar (hyperglycemia)

Warnings and precautions/Potential severe reactions

- Embryo-fetal toxicity: Midostaurin may cause fetal harm when administered to a pregnant woman. All female patient of childbearing age should be tested for pregnancy prior to treatment and should be provided with counseling for prevention of pregnancy during treatment.
- Pulmonary (lung) toxicity: Serious side effects affecting the lungs may occur including interstitial lung disease or pneumonitis, that may be irreversible. Which may be irreversible. Report any shortness of breath, chest tightness, or a new onset of cough to your clinical team immediately.
- Drug-drug interactions are common. These may either increase the toxicity or reduce the benefit of treatment. Be sure to review all medications you are taking with your clinical team regularly to avoid any potential interactions.

Resources: You can learn more about Midostaurin (Rydapt®) at:

<http://chemocare.com/chemotherapy/drug-info/midostaurin.aspx>
www.us.rydapt.com/acute-myeloid-leukemia

Gliteritinib (Xospata®)

Drug class: FLT 3 (a gene that may be mutated in patients with AML) Inhibitor

FDA approved indication: Adults with AML with a FMS-like tyrosine kinase 3 (FLT3) mutation when the disease has come back or has not improved after previous treatment(s).

Background information: Phase 3, open-label, multicenter, randomized clinical trial in 371 adult patients with relapsed or refractory FLT3m+ AML. Median overall survival of patients who received gliteritinib monotherapy was 9.3 months. 14.2% attained a complete response.

How administered: oral tablet, 120 mg once daily with or without food.

- Induction: 50 mg twice daily on days 8 to 21 of each induction cycle (in combination with daunorubicin and cytarabine)
- Consolidation: 50 mg twice daily on days 8 to 21 of each 28-day consolidation cycle (in combination with high-dose cytarabine) for 4 consolidation cycles

Common side effects:

- Changes in liver function tests
- Joint or muscle pain
- Tiredness
- Fever
- Pain or sores in mouth
- Swelling of arms or legs
- Rash
- Diarrhea or constipation
- Shortness of breath
- Nausea or vomiting
- Cough
- Eye problems
- Headache
- Dizziness
- Low blood pressure
- Decreased urination

Warnings and precautions/Potential severe reactions:

- Differentiation Syndrome: A rare, but potentially serious or fatal complication that may occur 1 day to 5 months after starting enasidenib. Symptoms of differentiation syndrome may include:
 - Fever
 - Cough
 - Shortness of breath
 - Bone pain
 - Swelling of the arms or legs, neck often with rapid weight gain of more than 10 pounds in a week.

It is important to report any of the symptoms immediately for rapid treatment with steroids, and other supportive care.

- Embryo-fetal toxicity
- Pancreatitis: Inflammation of the pancreas. This may be associated with upper abdominal pain, nausea, and laboratory changes.
- QTC prolongation – rare but potential changes in the heart rhythm that may be fatal
- Posterior reversible encephalopathy syndrome (PRES): A rare but potentially lethal process that affects the brain. Symptoms may include:
 - Seizure
 - Headache
 - Decreased alertness
 - Confusion
 - Reduced eyesight, blurred vision, or other visual problems

Resources: You can learn more about Gliteritinib (Xospata®) at:

<http://chemocare.com/chemotherapy/drug-info/gilteritinib.aspx>
www.xospata.com

Venetoclax (Venclexta®)

Drug class: BCL-2 Inhibitor

FDA approved indication: used in combination with azacitidine, or decitabine, or low-dose cytarabine to treat adults with newly diagnosed patients with AML who are 75 years of age or older, or have other medical conditions that prevent the use of standard chemotherapy. It is not known if VENCLEXTA is safe and effective in children.

Background information: A Phase 1 clinical trial included 145 patients and demonstrated efficacy of venetoclax with decitabine or azacitidine. During dose escalation, oral venetoclax was administered at 400, 800, or 1200mg daily in combination with either decitabine (20mg/m², days 1-5, intravenously [IV]) or azacitidine (75mg/m², days 1-7, IV or subcutaneously). In the expansion, 400 or 800 mg venetoclax with a hypomethylating agent was given. 67% of patients achieved complete remission. The median duration of responses was 11.3 months. This trial was registered at www.clinicaltrials.gov as #NCT02203773.

An international phase Ib/II study evaluated the safety and preliminary efficacy of venetoclax, a selective B-cell leukemia/lymphoma-2 inhibitor, together with low-dose cytarabine (LDAC) in older adults with AML. Eighty-two patients were treated at the recommended phase II dose: venetoclax 600 mg per day orally in 28-day cycles, with LDAC (20mg/m² per day) administered subcutaneously on days 1 to 10. 54% of participants achieved complete remission. The median OS was 10.1 months and median duration of response was 8.1 months. This trial was registered at www.clinicaltrials.gov #NCT02287233.

How administered: Adults ≥75 years of age or with comorbidities: Oral (Note: Initiate azacitidine, decitabine, or low-dose cytarabine on day 1). The venetoclax dose depends upon the concomitant chemotherapy agent. WBC should be <25,000/mm³ prior to initiation of venetoclax; cytoreduction prior to treatment may be required.

- Day 1: 100mg once daily
- Day 2: 200mg once daily
- Day 3: 400mg once daily

Venetoclax in combination with azacitidine or decitabine: Day 4 and beyond: 400mg once daily until disease progression or unacceptable toxicity occurs (DiNardo 2019).

Venetoclax in combination with low dose cytarabine: Day 4 and beyond: 600mg once daily until disease progression or unacceptable toxicity occurs (Wei 2019).

In combination regimens, you must consider the possible side effects of each drug.

Common side effects:

- Low blood counts (cytopenias) and potential infections or bleeding
- Diarrhea
- Nausea

More serious side effects:

- Tumor Lysis Syndrome – the breakdown of leukemia cells leading to the release of and shifting of electrolytes and urine acid that may cause serious heart and kidney damage. Symptoms may include:
 - Fever
 - Chills
 - Nausea
 - Vomiting
 - Confusion
 - Shortness of breath
 - Seizures
 - Irregular heartbeat
 - Dark or cloudy urine
 - Unusual tiredness
 - Muscle or joint pain

Resources: You can learn more about Venetoclax (Venclexta) at:

<http://chemocare.com/chemotherapy/drug-info/venetoclax.aspx>
www.venetoclax.com

Low Intensity Treatment: Hypomethylating Agents



Hypermethylation, the accumulation of compounds called methyl groups on portions of DNA, has been identified as one of the contributing factors in the development of MDS and leukemia. These compounds silence or turn off genes that are necessary for the normal development and maturation of blood cells. Hypermethylation is a constant process and has been associated with the development of AML.

Hypomethylating agents, drugs that block the methyl compounds, have been shown to improve normal blood cell development (hematopoiesis) in patients with MDS by allowing the silenced genes to be turned back on.

Azacitidine (Vidaza)

Drug class: Azacitidine is a hypomethylating agent

FDA approved indication(s): Indicated for the treatment of intermediate to high-risk MDS and AML in patients not eligible for aggressive therapy.

Background information: Several clinical trials showed that, compared with patients who did not receive azacitidine, MDS patients treated with azacitidine daily for 7 days every four weeks had durable hematologic improvement: increases in red blood cells and transfusion independence, increase in hemoglobin, increases in white blood cell or platelet numbers, and/ or decrease in bone marrow blast percentage. All patients in the clinical trials received supportive care regardless of whether or not they received azacitidine. In some clinical trials, the time to onset of AML was significantly delayed in azacitidine-treated patients when compared with patients who did not receive azacitidine.

Results of a large phase III study in 358 high-risk MDS patients (IPSS of Intermediate-2 or High) showed that compared with conventional care (either low dose chemotherapy plus supportive care or standard chemotherapy plus supportive care), treatment with azacitidine significantly prolonged overall survival (24.4 months versus 15 months). More convenient dosing schedules (5-days once a month) have also been investigated and may be an option for selected patients.

How administered: Azacitidine is an injectable medicine that can be administered either subcutaneously using a syringe and a small needle inserted under the skin in the stomach or legs, like the technique used to administer insulin or intravenously. Azacitidine is given for 7 days each month for most patients.

The most common side effects include:

- Decreased bone marrow activity (*myelosuppression*)
- Constipation
- Fatigue
- Nausea or diarrhea
- Injection site irritation

Resources: You can learn more about Azacitidine at <http://chemocare.com/chemotherapy/drug-info/azacitidine.aspx>

Decitabine (Dacogen)

Drug class: Decitabine is a hypomethylating agent

FDA approval indication(s): Indicated for the treatment of higher risk MDS or AML in patients not eligible for intensive therapy.

A study of MDS 170 MDS patients with intermediate to high risk disease were treated with Decitabine and experienced responses lasting for about 10 months: 17% response for decitabine-treated patients versus 0% for patients receiving standard of care. Those responding to decitabine became or remained transfusion independent. In addition, patients who had a response (complete or partial) to decitabine had a longer time to progression to AML and extended survival compared with patients receiving supportive care alone.

How administered: Decitabine is administered intravenously for five days once a month. For patients with higher risk disease, such as those with the TP53 mutation, Decitabine may be given for 3-10 consecutive days once every 28 days.

The most common side effects include:

- Decreased bone marrow activity (*myelosuppression*)
- Constipation
- Fatigue
- Nausea or diarrhea

Resources: You can learn more about Decitabine at <http://chemocare.com/chemotherapy/drug-info/decitabine.aspx>

INQOVI (decitabine 35mg and cedazuridine 100mg)

Drug Class: Combination of hypomethylating agent and cytidine deaminase inhibitor

FDA approval indication: Indicated for the treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS, including:

- refractory anemia
- refractory anemia with ringed sideroblasts
- refractory anemia with excess blasts
- chronic myelomonocytic leukemia (CMML)
- intermediate-1, intermediate-2, and high risk IPSS groups.

Background Information: The approval of Inqovi® was based on a phase 3 study evaluating the standard of care Decitabine given intravenously five consecutive days every 28 days, compared to the oral formulation of decitabine and cedazuridine. Among 133 patients treated, at a median follow-up of 5.2 months, 101 patients were available for evaluation. Results of this trial showed similar drug concentrations between intravenous decitabine and Inqovi®. Additionally, about half of the patients who were formerly dependent on transfusions were able to no longer require transfusions during an 8-week period. The safety profile of Inqovi® was also similar to intravenous decitabine.

How administered:

- One tablet orally once daily on day 1-5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity. A complete or partial response may take longer than 4 cycles.
- Should be taken on an empty stomach at the same time each day. Avoid eating 2 hours before and 2 hours after each dose.
- Tablets should not be crushed, cut, or chewed.
- If a dose is missed, take the missed dose as soon as possible within 12 hours. If more than 12 hours from the normal time you are scheduled to take the dose, take the dose on the following day at the usual time.
- If you experience nausea or vomiting after taking a dose, do not repeat that dose on the same day.
- Contact your health care team.

The most common side effects are:

- | | |
|--|-------------------------------------|
| • Low blood counts (cytopenias, including anemia, thrombocytopenia, or neutropenia) | • Nausea |
| • Infections, including pneumonia, urinary tract infections and more serious infections including febrile neutropenia and sepsis | • Elevation of liver function tests |
| • Fatigue/tiredness | • Muscle or joint pain |
| • Constipation or diarrhea | • Embryo-fetal toxicity |
| | • Rash |
| | • Decreased appetite |

Resources: You can learn more about Decitabine and Cedazuridine (Inqovi®) at www.inqovi.com

Onureg

Drug Class: Hypomethylating agent

FDA approval indication: Onureg (azacitidine tablets) is approved for continued treatment of patients with acute myeloid leukemia 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.

Background Information: NCT01757535, a multicenter, randomized, double-blind, placebo-controlled trial, included 472 patients who achieved CR or CRi with intensive induction chemotherapy with or without receiving subsequent consolidation therapy. Patients were randomized 1:1 to receive Onureg® 300 mg (238) or placebo (234) orally on days 1 to 14 of each 28-day cycle. Median overall survival was 24.7 months with Onureg®.

How administered: Oral tablet 300 mg orally once daily with or without food on days 1 through 14 of each 28-day cycle. Continue Onureg® until disease progression or unacceptable toxicity.

It is important to understand that Onureg®, the oral formulation of azacitidine is not equivalent to the injectable formulation and should not be used interchangeably.

The most common side effects are:

- Decreased bone marrow activity (myelosuppression)
- Constipation
- Fatigue
- Nausea or diarrhea
- Infections, including pneumonia
- Decreased appetite
- Dizziness

Resources: You can learn more about Onureg at

<http://chemocare.com/chemotherapy/drug-info/azacitidine.aspx>
www.onureg.com

Allogeneic Hematopoietic Stem Cell Transplant for AML



Allogeneic hematopoietic stem cell transplant is the only treatment that is potentially curative treatment for AML.

What is a bone marrow transplant?

A bone marrow transplant (BMT), also known as a stem cell transplant or hematopoietic stem cell transplant (HSCT) involves treatment with high dose chemotherapy and possibly radiation followed by the infusion of stem cells (progenitor cells). These stem cells have the capacity to restore bone marrow function (see: [What Does Bone Marrow Do](#)).

Allogeneic stem cells are obtained from another individual who is genetically like the AML patient. Donors may be related (brother, sister, child) or may be an unrelated volunteer donor. Human Leukocyte Antigen (HLA) testing is required from the AML patient (recipient) and the donor to find the best match. Transplant is not an option without an identified donor.

There are significant risks associated with this procedure. Therefore, although this procedure offers a potential cure for AML, it is available to only a small proportion of adult AML patients.

Am I a candidate for a bone marrow transplant?

The first step toward a bone marrow transplant is to determine if you are a candidate for this type of treatment. Your provider and healthcare team will evaluate several factors known as eligibility criteria.

The most common eligibility criteria include:

1. Age less than 70 years (some exception may be made at some centers)
2. Availability of a HLA identical matched donor
3. Good heart, lung, liver, and kidney function
4. Physically active and able to perform daily activities independently
5. Consistent availability of a caregiver

There are many resources available to help you understand blood and bone marrow transplantation:

- National Marrow Donor Program (NMDP) Be the Match: www.marrow.org
- Blood and Marrow Transplantation Information Network: www.bmtinfonet.org
- National Coalitions for Cancer Survivorship: www.canceradvocacy.org/toolbox

Long-term survival with an allogeneic transplant is in the range of 40-50%, but factors such as patients age, prognostic risk group, and type of donor, may all impact outcomes. Higher treatment-related mortality is observed in myeloablative compared to reduced intensity conditioning transplants; however, higher rates of relapse are observed in reduced intensity conditioning transplants vs. myeloablative transplants. While transplants are not recommended for patients with lower risk disease, it is a consideration for patients with higher risk AML because the risk of death from the disease may be higher than the treatment-related mortality of transplant.

Palliative and Supportive Care

Palliative care focuses on relieving the pain and suffering of individuals with illness. The benefits of palliative care are recognized and accepted by the American Board of Medical Specialties. AML can affect the body, the mind, and the spirit. Patients with AML, their caregivers, and families may have trouble in one or more of these areas during any stage of the illness. Palliative care for patients with AML can be started as soon as they are diagnosed with the disease.

Palliative care may help with:

- Difficult treatment decisions
- Physical symptoms: for example, pain, nausea and vomiting, diarrhea, constipation, fatigue, nutritional needs, etc.
- Emotional needs such as depression or anxiety
- Social needs
- Financial direction
- Spiritual support

Palliative medicine utilizes a multidisciplinary approach to patient care, relying on input from physicians, pharmacists, nurses, chaplains, social workers, psychologists, and other allied health professionals in formulating a plan of care to relieve suffering in all areas of a patient's life. This multidisciplinary approach allows the palliative care team to address physical, emotional, spiritual, and social concerns that arise with advanced illness or incurable diseases. Some cancer centers or clinics have designated palliative care teams; other centers may have access to trained individuals upon request.

A palliative care team may include one or more of the following:

- | | |
|--|--|
| • Physician(s) | • Pain service |
| • Advanced practice Providers (APP): Nurse Practitioner or Physician Assistant | • Chaplain service or other spiritual support services |
| • Oncology nurse specialist | • Nutritionist |
| • Clinical Pharmacist | • Physical therapist |
| • Social worker | • Financial counselor |

Throughout the disease course, counseling is directed at maintaining or improving quality of life. For example, yoga and regular exercise have been studied and found to help alleviate symptoms, improve fatigue, anxiety, and depression in patients with AML.

Open communication with the healthcare team helps align treatment with patient and family-centered goals for care. It is important to discuss the goals of the proposed treatment, including impact on survival and quality of life.

Supportive Care

Supportive care in AML may include blood transfusions, growth factors, and other treatments aimed at improving symptoms, such as antibiotics for an infection, nutritional support, treatment of transfusion related iron overload, spiritual and emotional support.

Certain types of supportive care are administered based on specific criteria. The benefits of supportive care are generally temporary as these strategies do not affect the underlying disease.

Common forms of supportive care aimed at improving blood counts include:	
Blood transfusion	Packed red blood cells, platelets Regulations for the administration of blood products vary by region.
Red blood cell growth factors	Approved for patients with lower-risk AML in Europe. Approved for use in the United Kingdom, Nordic countries, and Canada. Administered in the United States as part of the APPRISE REMS program.
White blood cell growth factors	Approved for use in Nordic countries. Administered in the United States off-label or under special conditions.

About clinical trials

Clinical trials offer an option for treatment under the guidance of a research protocol. Clinical trials provide several important benefits. In addition to developing new treatments for AML and other diseases, clinical trials may:

1. Help to improve diagnostic techniques
2. Identify new targets for treatment
3. Offer treatment options which are not otherwise available
4. Help to improve side effect management

A clinical trial falls into one of four phases:

Phase I	This is the first time a drug is used in humans. The trial is designed to determine dosage, route of administration (oral, intravenous, or by injection), and schedule of administration (how many times a day or week). In this phase, researchers also begin to determine the drug's safety. The Phase I trial is normally conducted in healthy adults and enrolls only a small number of people (15-30).
Phase II	Patients with the disease receive the drug at dose levels determined in the earlier phase. The Phase II trial begins to determine the effectiveness of the drug and provides more information about its safety. Phase II trials usually include less than 100 people.
Phase III	The drug is tested alone or against an approved standard drug. The typical Phase III trial enrolls a large number of patients (100-thousands). If it is a comparison trial, patients may be randomly assigned to receive either the new drug or the standard intervention.
Phase IV	In Phase IV, the drug, already approved by the FDA and available to the public, undergoes continued evaluation in a large number of patients (several hundreds to several thousands). The Phase IV designation is rare.

Some trials, screening trials, and studies evaluating supportive care or prevention are not conducted in phases. In this type of trial, a group following a certain strategy to combat disease, such as a detection method or a behavioral change, is compared to a control group.

How is a clinical trial conducted?

Clinical trials may be conducted at a specific institution or as a part of a collaborative group. Each trial is assigned a lead researcher, known as the Primary Investigator (PI). You may meet some of the other members of the research team when participating in a clinical trial. They all work to be certain that your treatment follows the guidelines set out by the trial and that your safety is maintained.

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

<https://clinicaltrials.gov>

Members of the research team

1. Lead physician, scientist, or nurse researcher—primary investigator (PI)
2. Other clinicians: physicians, nurse practitioners, or scientists (Sub-Investigators)
3. Statisticians
4. Research nurses
5. Data managers

How are clinical trials monitored?

Clinical trials for cancer treatment are overseen by a number of groups. The primary goals are to ensure patient safety and maintain rigorous scientific standards. These groups will review each clinical trial before the trial can be open for patient enrollment.

- **Institutional Review Boards (IRB):** A group of experts from the institution conducting the trial or representing a cooperative group of institutions who review each trial for patient safety and scientific merit. The IRB will continue to monitor the conduct of the trial until it is completed along with the Primary Investigator and the research team.
- **Scientific Review Panels:** A panel of experts who review clinical trials to ensure that they are based on sound scientific principles.
- **Data and Safety Monitoring Boards:** An independent committee of physicians, researchers, statisticians, and other experts.
- **National Cancer Institute (NCI) and National Institutes of Health (NIH):** Oversee selected clinical trials and maintain a list of registered trials. www.clinicaltrials.gov

Key elements of a clinical trial

Patient protection: Patient safety is a primary focus for all clinical trials. The potential risks and benefits of each trial are reviewed carefully by a number of groups. You will be given a consent form which discusses the risks and benefits of the clinical trial in detail. Patient privacy is also a key component of patient safety. Data collected for the clinical trial will list patients by a study number and will only be shared with members of the research team who have signed a confidentiality agreement.

Informed consent: Before you can participate in a clinical trial, the research team must provide detailed information about the trial including the purpose of the trial, potential benefits and risks, the treatment plan (protocol and schedule), and your right to withdraw from the study at any time. You are encouraged to ask questions during this discussion so that you feel you understand the trial. You will then sign a consent form which provides this information and documents your informed consent.

Am I a candidate for a clinical trial?

Each clinical trial has specific criteria for participation. These criteria ensure the specific research goals of the trial and patient safety criteria are being met. You will be screened for the trial before being enrolled to be sure these criteria are met. Additional testing will be conducted after you have signed the consent form for the trial. In some cases, after these tests are obtained, a patient may not meet the criteria for the trial and cannot proceed to treatment.

What questions should I ask about participating in a clinical trial?

These are most often answered during the informed consent process.

1. Why is the trial being done?
2. What are the potential benefits of the trial?
3. What is the potential risk of the trial?
4. What can I expect from day to day while I am on the trial? (Frequency of visits, types of testing, length of visits)
5. If I experience side effects, whom should I contact?
6. What are the costs of participating in the trial?
7. What other treatment options do I have if I do not participate in the clinical trial?
8. How long will I be in the trial?
9. What happens if the treatment is not working?

Clinical trials and drug approval information

National Cancer Institute, National Institutes of Health

Registry and results database of federally and privately supported clinical trials conducted in the United States and around the world

www.clinicaltrials.gov

National Institute of Health and Clinical Excellence

Guidance for cost effectiveness of treatments for England and Wales

www.nice.org.uk

European Medicines Agency

Decentralized agency of the European Union, located in London; responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union

www.ema.europa.eu

Health Canada

Provides a notice of compliance (NOC) for full approval of a new drug or an NOC with conditions in Canada

www.hc-sc.gc.ca

Pharmaceuticals and Medical Devices Agency

Regulation of drug availability in Japan

www.pmda.go.jp

Therapeutic Goods Administration

Division of the Australian government's Department of Health and Aging; responsible for regulating therapeutic goods including medicines, medical devices, blood, and blood products

www.tga.gov.au

U.S. Food and Drug Administration

Approval required for commercial availability of therapy in the United States

www.fda.gov

GENERAL RESOURCES FOR LIVING WITH AML

This chapter will provide you with strategies for staying well, managing your health and your AML and includes several Quick-Tips to recognize and manage common symptoms or problems experienced by patients and caregivers living with AML. Each Quick-Tip includes links to several digital resources that may help you manage your health. This chapter also includes a glossary terms that will help you to understand the complex language used to describe these diseases.

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What can you do to stay healthy?

- Take an active role in managing your health
- Continue to enjoy the things you love – focus on living
- Ask for help when needed
- Be an active participant in your care. Feel empowered.
- Have honest, open discussions with your healthcare team. Ask questions.
- Make your wishes clear
- Share in decision making
- Prepare for each visit
- Learn all you can about your treatment
- Learn to manage and report symptoms
- Take advantage of patient portals to improve communication with your healthcare team and track your results
- Consider participating in a clinical
- Stay well

The Quick tips listed in this section will provide a brief summary of common challenges faced by patients and caregivers living with AML. Links to additional resources are included.

Bleeding and bruising

Bleeding or bruising may be a result of faulty platelet function, acquired bleeding disorders, or too few platelets (thrombocytopenia) in patients with AML. Platelets help stop bleeding by clumping and forming plugs in blood vessel holes (clotting). Platelets also help maintain normal blood vessel health in the body. When a patient develops thrombocytopenia, the risk of bleeding or bruising increases.

The risk of bleeding is related to the severity of the thrombocytopenia. Certain medications may increase the risk of bleeding, such as blood thinners, aspirin, and other anti-inflammatory medications.

Things you can do:

1. Record and track your blood counts, transfusion dates, and any symptoms before and after transfusions. Then bring the results with you to your next health care provider appointment to discuss the results.
2. Keep all your appointments as scheduled.
3. Keep a current list of all of your medications, including over the counter medications. Review this list with your health care team at each visit.
4. Let your health care providers know if you experience unusual bruising, uncontrolled bleeding, or develop petechiae.
5. Avoid excess alcohol, which may contribute to platelet dysfunction.
6. Avoid injuries (falls, cuts, scrapes) and activities that can cause bruising or bleeding, such as contact sports and heavy lifting.
7. Avoid constipation or straining to have a bowel movement.
8. Use a soft tooth brush.
9. Ask for help from family and friends.

Additional Resources:

Cancer.net: Thrombocytopenia [Thrombocytopenia](#)

Oncolink: [Low Platelet Count](#)

Caregiving: Resources for managing each day

Caregivers are an essential part of the healthcare team. They are most often family members or close friends but may also be professionals that assist with organizing and delivering care. There are many distinct roles for caregivers. Many involve everyday activities such as home management, shopping, and running errands. When you are living with a diagnosis of AML either yourself or with your loved one, these daily routines may be more difficult to maintain. In addition, there are several other tasks that will be necessary to accommodate the treatment routine.

Common roles for a caregiver:

- Providing support and encouragement
- Giving medications
- Helping manage symptoms and side effects
- Coordinating medical appointments
- Providing a ride to appointments
- Assisting with meals
- Helping with household chores
- Handling insurance and billing issues

Caring for or being around children

The time spent enjoying the company of family, including children, is important. Most patients with AML can enjoy their family without restrictions. Discuss any recommendations for limiting contact with children with your health care team. Specific recommendations for contact with children are recommended for patients undergoing a stem cell transplant, leukemia therapy, or who have a very low white blood cell counts (neutropenia).

Things you can do:

1. Focus on your needs: ask for help, build a support team
2. Strike a balance each day
3. Maintain a healthy lifestyle: nutrition, exercise, sleep
4. Practice relaxation or meditation
5. Make an appointment to see your health care provider for a wellness check
6. Seek help if you are feeling anxious or depressed
7. Talk with a financial counselor and your certified public accountant for financial guidance

Additional Resources:

Cancer.net: Being a Caregiver www.cancer.net/coping-with-cancer/caring-loved-one

Cancer.net: Sharing Responsibilities: www.cancer.net/coping-with-cancer/caring-loved-one/sharing-responsibilities

Family Caregiver Alliance: Community Resources www.caregiver.org/caregiving-home-guide-community-resources

Be the Match: Caregivers and Bone Marrow Transplant

<https://bethematch.org/for-patients-and-families/caregivers-and-transplant/>

Complementary Therapies

Complementary therapy is treatment used in addition to standard therapy, that is assumed to be safe, and not a risk for causing harm. Common forms of complementary therapies include:

- Acupuncture
- Labyrinth walking
- Prayer and spirituality
- Aromatherapy
- Massage therapy
- Tai chi
- Art therapy
- Meditation
- Yoga
- Biofeedback
- Music therapy

Other alternative treatments

Wheat grass juice has been studied for its ability to remove excess iron in patients with MDS and found to provide a benefit. The study was small, with only 20 patients. The participants drank a tablespoon of fresh wheat grass juice daily for 6 months. There was noted to be a reduction in their ferritin levels, on average from 2,250 to 950 ng/mL. There were no reported negative side effects.

Evening primrose oil has also been found to decrease injection site reactions for patients who are receiving subcutaneous azacitadine. This was tested on ten patients by German researchers. Six of the ten patients experienced a reduction in the injection site redness and irritation. The oil was applied to the injection sites every evening. It is relatively inexpensive and can be purchased in many health food stores. Side effects that were mentioned are headache and stomach upset.

Talk with your healthcare team prior to starting any complementary or alternative therapies to ensure safety.

Additional Resources:

Chemocare is a patient friendly website with a focus on drug information and the management of side effects of chemotherapy. Included are handouts on specific oral and intravenous agents and are updated frequently when new drugs are approved.

www.chemocare.com

Cancer Care: Our comprehensive services include counseling and support groups over the phone, online and in-person, educational workshops, publications, and financial and co-payment assistance. All CancerCare services are provided by oncology social workers and world-leading cancer experts.

www.cancercare.org/about

ASCO People Living with Cancer: Trusted, compassionate information for people with cancer and their families and caregivers, from the American Society of Clinical Oncology (ASCO), the voice of the world's cancer physicians and oncology professionals.

www.cancer.net

<https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs>

Constipation

You may experience either constipation or diarrhea because of your illness(s) or medications. There are several things you can do to prevent or treat changes in bowel function.

Things you can do for Constipation

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Let your doctor know if you have pain with bowel movement, any blood in the stool, severe abdominal pain, persistent nausea, or vomiting.
4. Don't let more than 3 days go by without a normal bowel movement—discuss this with your health care team.
5. Stay active.
6. Drink 2–3 liters of fluid a day.
7. Eat a diet rich in fruits, vegetables, and natural fibers.
8. Soak in a warm bath. Be sure that you feel safe and able to get in and out of the bath on your own.
9. Cleanse after bowel movements or urination.
10. Wash your hands after using the bathroom.

Additional Resources:

Cancer.net: Constipation www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/constipation

Cancer Care: Constipation www.cancercare.org/publications/218-coping_with_constipation

Oncolink: Constipation www.oncolink.org/support/side-effects/gastrointestinal-side-effects/constipation

Depression

Depression is a common consequence of living with cancer, including AML. Adjusting to the diagnosis of AML affects each person differently. While some people can continue to live a full and rewarding life, others may find the stress of coping with AML more challenging. These challenges are real and important. Regardless of the cause, there are things that can help you manage the emotions of Living with AML.

Things you can do for Constipation

1. Recognize some of the common signs of depression:
 - A lack of interest or pleasure in doing things
 - Feeling down, depressed, or hopeless
 - Difficulty sleeping
 - Decreased appetite
 - Tearfulness
2. If you are having any of these symptoms, you may have clinical depression. It may also be helpful to ask someone who knows you well if they think that you may be depressed.
3. Give yourself time to adjust to the diagnosis and changes in your daily routines. While you may not be able to return to as active a lifestyle as you once had, you may be able to substitute those activities with less strenuous ones that are still enjoyable.
4. Set priorities for activities that are necessary to maintain your physical and emotional health.
5. Try to find some activity that you can still enjoy—such as listening to music or watching a ball game.
6. These activities can help you keep a positive outlook.
7. Continue with a diet and exercise routine that will help you to stay healthy. Get enough rest.
8. Avoid alcohol—it can make depression worse.
9. Talk with your healthcare team about resources available to help you.
10. Prayer or meditation may be useful to provide peace.
11. Consider joining a support group—in person, or by computer. Others living with AML may have good suggestions for how to better cope with this disease.
12. Ask your provider about trying an anti-depressant medication. These medications may be helpful in restoring the chemical imbalance in the brain. These medications may take 4–6 weeks before you notice improvement.
13. Anti-depressant medicines should not be stopped suddenly.

Additional Resources:

Cancer.net: Managing emotions: www.cancer.net/coping-with-cancer/managing-emotions

American Cancer Society: <https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/emotional-mood-changes/depression.html>

Oncolink: Managing Practical and Emotional Concerns www.oncolink.org/support/practical-and-emotional

Diarrhea

You may experience either constipation or diarrhea because of your illness(s) or medications. There are several things you can do to prevent or treat changes in bowel function.

Things you can do for Diarrhea:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Report any blood in the stool, severe abdominal cramping, fevers, or symptoms of severe diarrhea to your health care team immediately.
4. Drink 2–3 liters of fluid a day. Avoid caffeine or high sugar drinks.
5. Eat small frequent meals.
6. The BRAT diet is often recommended until more severe symptoms improve: Bananas, Rice, Applesauce, and Toast.
7. Foods to avoid: dietary fiber (brown rice, fruits, vegetables, popcorn, whole grain breads and pasta), alcohol, caffeine, chocolate, greasy foods, dairy products containing lactose.
8. Increase the intake of foods and fluids high in sodium and potassium, such as broths, soups, low-sugar sports drinks, potatoes and crackers.
9. Probiotic supplements or foods containing probiotics (natural gut bacteria) may improve diarrhea.
10. Soak in a warm bath—be sure that you feel safe and able to get in and out of the bath on your own. If you do not feel safe, ask for help.
11. Cleanse after bowel movements or urination.
12. Wash your hands after using the bathroom.

Additional Resources:

Cancer.net: Diarrhea www.cancer.net/navigating-cancer-care/side-effects/diarrhea

Cancer Care: Diarrhea www.cancercare.org/tagged/diarrhea

Oncolink: Diarrhea www.oncolink.org/support/side-effects/diarrhea

Diet, nutrition and Hydration

A balanced diet, daily activity and exercise as tolerated, and participation in activities of enjoyment are important to maintain optimal health and well-being. A balanced diet can help combat fatigue and illness. Adequate intake of food and fluids also helps individuals tolerate treatment.

Fluids are an essential part of a healthy diet. Your body needs fluids to function properly, like a car needs gas to run.

Adequate hydration varies from one person to another. The goal of hydration is to avoid dehydration without drinking too many fluids.

People living with AML may need to follow a special diet if they have a very low white blood cell count or are undergoing a stem cell transplant. Ask your healthcare providers if there are specific restrictions for you.

Things you can do:

1. The Dietary Guidelines for America 2015 (www.dietaryguidelines.gov) provide the basic principles of a healthy diet.
2. Meet with a registered dietician to determine your daily caloric needs and how you might get these in the foods you like to eat.
3. Stay hydrated: Carry fluids with you wherever you go. If drinking a full glass causes bloating, take small sips throughout the day. Drink most of your fluids between meals.
4. Eat a balanced diet:
 - Eat fruits and vegetables. Wash all fruits and vegetables well prior to eating. Eat dark green vegetables like leafy greens or broccoli and orange vegetables like carrots and sweet potatoes.
 - Vary your protein choices with more fish, beans, and peas. Eat at least three ounces of whole-grain cereals, breads, crackers, rice, or pasta every day.
 - Have three servings of low-fat or fat-free dairy (milk, yogurt or cheese) that are fortified with vitamin D to help keep your bones healthy. Consume only pasteurized milk, yogurt, cheese, and other dairy products.
 - Make the fats you eat healthy ones (polyunsaturated and monounsaturated fats).

Additional Resources:

Cancer.net: Nutrition Recommendations During and After Treatment www.cancer.net/survivorship/healthy-living/nutrition-recommendations-during-and-after-treatment

Cancer.net: Food Safety: www.cancer.net/survivorship/healthy-living/food-safety-during-and-after-cancer-treatment

Anxiety

Anxiety is a common reaction to learning that one has a AML. Anxiety can range from a mild and vague feeling that something may be wrong, to an overwhelming feeling that interferes with a person's ability to function. All people experience periods of anxiety in their lives. Uncertainty about the diagnosis of a AML, what treatments might be right for you, how they will work, and what side effects you may experience may contribute to your anxiety.

Things you can do:

There are several resources to help you understand your diagnosis, treatment options, and strategies to take an active part in your journey. Explore the Building Blocks of Hope® www.buildingblocksofhope.com

1. Evaluate other parts of your life where you have been successful in mastering control—use those techniques to help you meet the challenges you face while living with AML.
2. Try to simplify your life. Eliminate or reduce the activities that are not essential to your physical and emotional well-being.
3. Ask for help. This can be from family, friends, or professionals. Counseling from a psychologist or social worker can also be useful.
4. Consider joining a support group—in person, or by computer. Others living with AML or MDS may have good suggestions for how to better cope with this disease. You can contact the MDS Foundation for more information.
5. Explore resources that will help you with relaxation such as meditation, massage, yoga, or listening to relaxing music.
6. Try to eat well and maintain some sort of activity.
7. Avoid excess amounts of alcohol or caffeine.
8. You may find it difficult to remember instructions, or to concentrate when hearing information, so write them down or bring a caregiver or advocate with you to appointments.
9. Talk to your health care team about other options for managing your anxiety. Ask if an anti-anxiety medication might be helpful.

Additional resources:

Cancer.net: Managing emotions: www.cancer.net/coping-with-cancer/managing-emotions

American Cancer Society: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/changes-in-mood-or-thinking/anxiety-and-fear.html

Cancer Care: Anxiety www.cancercare.org/tagged/anxiety

Oncolink: Managing Practical and Emotional Concerns www.oncolink.org/support/practical-and-emotional

Employment

During the initial diagnosis of AML, it may be difficult to continue to work.

Ask your healthcare provider how to plan for the time off you will need to make sure you are receiving your treatment in the safest and most effective way possible. Understand that these recommendations may change unexpectedly due to disease or treatment related factors. It will be important to set up a network of support for these unexpected events.

Ask your healthcare provider to write a letter describing your schedule for treatment or clinic visits.

It is important to ask about your employers' options for sick-leave and family medical leave.

The *Family and Medical Leave Act* (FMLA) provides certain employees with up to 12 weeks of unpaid, job-protected leave per year. It also requires that their group health benefits be maintained during the leave.

For some patients, there may be a need to pursue Social Security Disability. Ask if there is a Social Worker that might help guide you through this process. The process for approval can take several weeks.

Social Security Disability Insurance pays benefits to you and certain members of your family if you are "insured," meaning that you worked long enough and paid Social Security taxes.

Supplemental Security Income pays benefits based on financial need.

When you apply for either program, we will collect medical and other information from you and decide about if you meet *Social Security's definition of disability*.

Use the *Benefits Eligibility Screening Tool* to find out which programs may be able to pay you benefits.

Ask your certified public accountant about options you may have to access any retirement savings early

Additional resources:

Cancer Care: Workplace resources www.cancercare.org/tagged/workplace_issues

Cancer.net: Balancing work and caregiving www.cancer.net/blog/2015-08/balancing-work-and-caregiving

Exercise

The most frequently reported symptom in AML patients is fatigue.

One of the best strategies for fighting fatigue is exercise, so move to improve your fatigue! In several studies, exercise has been shown to decrease fatigue and emotional distress.

Exercise improves functioning and overall quality of life. A variety of exercise interventions have been studied in cancer patients during different phases of treatment, including aerobic exercise, strength training, and stretching.

Examples of studied aerobic exercises are walking and bicycling.

Things you can do:

1. Prior to starting a new exercise program, it is a good idea to discuss your plans with a healthcare provider to make sure that it is safe for your condition.
2. An exercise program can be modified to fit each person based on their age, sex, type of MDS and treatment, and physical fitness level.
3. Ask about a referral to a physical therapist or trainer to develop a tailored program.
4. Strength training can even be done in a chair using resistance bands or light weights.
5. Even light cardio such as walking will add benefit.
6. Blood counts should be considered prior to exercise.
 - If neutropenic, it is best to avoid community swimming pools and hot tubs.
 - If you are severely anemic, you may need to avoid aerobic exercise.
 - Listen to your body, if you experience severe pain or shortness of breath, stop the exercise.
 - When the platelets are less than 50,000 high impact sports should be avoided to prevent problems with bleeding.
 - When in doubt, discuss with your healthcare team.
 - Start slowly and try to make progress by setting realistic goals along the way.
 - Recruit the support of family and friends.

Additional Resources:

Cancer.Net: An Exercise Program for You: 5 Tips for People with Cancer www.cancer.net/blog/2018-09/exercise-program-you-5-tips-people-with-cancer

Cancer.Net: Exercise During Cancer Treatment www.cancer.net/survivorship/healthy-living/exercise-during-cancer-treatment

Onco-Link: Strength Exercises: Minimize the effects of cancer treatment on your muscles www.oncolink.org/support/exercise-cancer/strength-exercises-minimize-the-effects-of-cancer-treatment-on-your-muscles

Fatigue

Fatigue is defined as an unusual tiredness that interferes with normal activities and is not relieved by resting or a good night's sleep. Fatigue may be more severe in patients with AML who also have anemia. Insomnia (difficulty sleeping) is common in older adults and may contribute to fatigue. Other things that can contribute to fatigue include inactivity, pain, emotional distress, poor nutrition, and other illnesses that are not well controlled such as diabetes or thyroid disorders.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your healthcare team.
2. Keep all your appointments as scheduled.
3. Exercise is the best way to treat fatigue. Stay active as much as possible to maintain muscle strength and improve stamina. Consider starting an exercise routine, such as daily walks with a caregiver or friend. Your healthcare provider will provide you with recommendations to maintain or increase your activity safely.
4. List the activities for each day. Set priority activities for the day, and schedule priority activities for periods of highest energy level.
5. Limit naps during the day to less than 1 hour to prevent problems with nighttime sleeping.
6. Talk to your healthcare team if you are having trouble with anxiety or overwhelming sadness.
7. Stay hydrated.
8. Eat small, frequent meals.
9. Ask for help from family and friends.
10. Be sure to discuss any concerns with your healthcare team. Based on your symptoms and how you feel, some changes to your care may be made to ensure safety and make you more comfortable.

Additional resources:

Cancer.net: Fatigue: www.cancer.net/navigating-cancer-care/side-effects/fatigue

Oncolink: Fatigue: www.oncolink.org/support/side-effects/fatigue-and-cancer

American Cancer Society: Fatigue: www.cancer.org/treatment/survivorship-during-and-after-treatment/staying-active/nutrition/nutrition-and-physical-activity-during-and-after-cancer-treatment.html

Fever and infections

Fever may be a result of infections or may be a side effect of certain chemotherapy agents used to treat AML. The Absolute Neutrophil Count (ANC) is used to determine your risk of infection. Guidelines for activities while neutropenic are related to the risk of being exposed to people or things that would increase the chance of developing an infection.

Ask your healthcare providers when you should report a fever, who to call and when you might need emergent treatment. It is essential to treat MDS patients with fevers quickly to avoid the possibility of developing more serious infections.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Record and track your blood counts, including the WBC and Absolute Neutrophil Count (ANC) and any symptoms including fevers, chills, or infections.
3. Keep all your appointments as scheduled.
4. Notify your health care team immediately for any fever $\geq 101.4^{\circ}\text{F}$ or 38.5°C or shaking chills at any body temperature.
5. Have a working thermometer at home. Discuss which type of thermometer is best for you to use with your health care team.
6. Avoid people who are obviously ill, avoid crowded enclosed places when your counts are low, maintain a healthy lifestyle. This does not mean that you can't go out, just avoid close contact with individuals who are ill.
7. Wash your hands frequently. Carry hand sanitizer. Use it in public places.
8. Talk with your health care providers about what immunizations are right for you.
9. Stay hydrated.

Additional resources:

Cancer.net: Neutropenia www.cancer.net/navigating-cancer-care/side-effects/neutropenia

Cancer Care: Infections: www.cancercare.org/publications/216-neutropenia_and_infections_what_you_need_to_know

Cancer.net: Infection: www.cancer.net/navigating-cancer-care/side-effects/infection

Oncolink: Neutropenia: www.oncolink.org/support/side-effects/low-blood-counts/neutropenia

Finances and insurance

Living with any illness and its treatment, including AML, can place a financial burden on you and your family. There are several resources that may be useful in seeking assistance with financial concerns you may have.

The first step is to ask members of your health care team who you can talk to about your financial concerns. There may be a financial counselor or social worker that can assist you. Financial counselors work directly with your providers and your insurance company to obtain authorization for treatments, procedures or certain tests. If you need treatment, the Financial Counselor can discuss your anticipated cost of the treatment prescribed by your provider. A social worker can often identify services and resources within your community to help with transportation, disability or Medicaid enrollment, home care, and other needs.

Drug Assistance Programs

Many of the pharmaceutical companies sponsor drug assistance programs. These programs aim to provide medications used to treat your AML at a reduced fee, or in some cases for free. This is generally based on financial need. Check with your pharmacist or health care team for the availability of these programs.

General Finances

We encourage you to speak to an advisor at your bank and your certified public accountant about things you can do to manage your finances and avoid any penalties.

Additional Financial Resources:

Good Days

877-968-7233 www.mygooddays.org

engine for many of the patient assistance resources that the biopharmaceutical industry offers.

Health Well Foundation

800-675-8416 www.healthwellfoundation.org
Provides aid to underinsured patients who are diagnosed with chronic or life-altering diseases.

Patient Access Network Foundation

866-316-PANF (866-316-7263)
www.panfoundation.org
This foundation assists patients with their coinsurance associated with AML treatments/medications.

National Organization for Rare Diseases Medication Assistance Program

800-999-6673 or 203-744-0100
<https://rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs-2>
This charitable organization offers co-pay assistance for MDS medications.

Patient Advocate Foundation

800-532-5274 www.patientadvocate.org
This program provides direct copayment assistance for pharmaceutical products to insured Americans who financially and medically qualify.

PhRMA's Medicine Assistance Tool (MAT)

<https://medicineassistancetool.org>
A search engine designed to help patients, caregivers and healthcare providers learn more about the resources available through the various biopharmaceutical industry programs. MAT is not its own patient assistance program, but rather a search

Patient Services, Inc.

800-366-7741 www.patientservicesinc.org
A nonprofit charitable organization primarily dedicated to subsidizing the high cost of health insurance premiums and pharmacy copayments for persons with specific chronic illnesses and rare disorders.

Additional Resources:

Cancer.net: www.cancer.net/navigating-cancer-care/financial-considerations

American Cancer Society: www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-health-insurance.html

American Cancer Society: www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-financial-and-legal-matters.html

Home management

Living each day in health or faced with the challenge of illness requires organization and planning. When faced with illness or other unexpected events, it is even more important to organize your resources.

1. We encourage you to build a support team. This can include family, friends, and community resources as well as resources suggested to you by your healthcare team or those included in the Building Blocks of Hope.
2. Consider using online care organization services like **Lotsa Helpings Hands** <http://lotsahelpinghands.com>
3. Make a list of all your service providers such as phone, internet, water, electricity, gas, waste management and any other individuals that provide you with services. If you are experiencing financial difficulties or having trouble managing your bills, this will help you to get in touch with them to alert them to your situation.

Additional resources:

Cancer.net: Coping with Cancer

www.cancer.net/navigating-cancer-care/financial-considerations/tips-organizing-financial-information

Cancer.net: Finding Support and Information www.cancer.net/coping-with-cancer/finding-support-and-information

Cancer Care: Doctor-Patient Communications www.cancercare.org/tagged/doctor-patient_communication

Immunizations

Immunizations are an important strategy in avoiding infections, particularly the flu or pneumonia. The Center for Disease Control (CDC) provides updated guidelines for immunizations on adults who are considered to be immunocompromised due to cancer or cancer treatment.

Things you can do:

1. Get a flu shot every year
2. Pneumonia Vaccine
 - Two pneumococcal vaccines are recommended for adults:
 - 13-valent pneumococcal conjugate vaccine (PCV13, Prevnar13®)
 - 23-valent pneumococcal polysaccharide vaccine (PPSV23, Pneumovax®23)
3. Shingles Vaccines
 - Only attenuated Shingles vaccines are recommended for patients who are immunocompromised – ask your provider before you get a Shingles vaccine
4. Talk with your healthcare provider about which vaccines you should receive (CDC recommendations for age >65, immunocompromised) including the Coronavirus (COVID-19) vaccine

Additional resources:

CDC Immunizations Guidelines by Age: www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

Memory and concentration problems

Problems with attention, thinking and memory are common in patients with cancer. These may vary in severity and I'll often make it hard to complete daily tasks. If you're experiencing any changes in attention, thinking or memory, be sure to discuss this with your healthcare team. We want you to remain safe and encourage you to ask for help.

Organizing health information is important to make decisions about your treatment.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Get enough sleep.
4. Maintain a healthy lifestyle.
5. Stay active.
6. Stay connected to friends and family and community activities.
7. Exercise your mind. Use crossword puzzles, reading, and other mind exercise program such as Luminosity: Memory and Concentration Exercises www.lumosity.com/sign_up
8. Involve as many senses as possible.
9. Reduced background noise during conversations.
10. Register for the patient portal at all of the health care facilities that you receive care.

Additional resources:

Cancer.net: Attention, Thinking or Memory Problems

www.cancer.net/navigating-cancer-care/side-effects/attention-thinking-or-memory-problems

Cancer Care: Chemo Brain www.cancercare.org/publications/72-chemobrain_what_you_need_to_know

Oncolink: Chemo Brain www.oncolink.org/support/side-effects/chemo-brain

Mobility

Out-of-home mobility is necessary for accessing commodities, making use of neighborhood facilities, and participation in meaningful social, cultural, and physical activities. Mobility also promotes healthy aging as it relates to the basic human need of physical movement. You may have limited mobility because of your AML or other illnesses. We want you to remain safe and encourage you to ask for help.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Talk with your health care team about home safety evaluations and other resources to help you maintain or improve your mobility.
4. Ask your health care team if physical therapy might be helpful to improve strength and mobility.
5. Consider installation of assistive devices, such as shower bars, an elevated toilet seat or bars next to the toilet.
6. Make sure there is good lighting in hallways and bathrooms.

Additional resources:

Cancer.net: Nutrition, Physical Activity and You

www.cancercare.org/connect_workshops/256-nutrition_physical_activity_and_you_2011-11-15

American Cancer Society: www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/weakness.html

Mouth sores/mucositis

Sores or swelling in the tissue in the mouth (mucositis) can occur because of cancer treatment, other illnesses, certain medications, or poor dental health. Patients with AML who have had a bone marrow transplant may experience graft-versus-host disease in the mouth that may be painful.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. If you are experiencing pain in the mouth making it difficult to chew or swallow, or if there is any bleeding from the mouth, contact your health care providers immediately. You may need medication.
4. See your dentist regularly, however, speak to your health care team prior to any dental procedures.
5. Rinse with salt water and baking soda and water. You can't make this at home by simply combining a tablespoon of salt to a quart of water in one solution and a tablespoon of baking soda and water in a second solution. Rinse with the saltwater first and then spit it out. Follow-up with a rinse of baking soda and water and spit it out. You can do this several times a day. Avoid alcohol-based mouth washes.
6. Use a soft toothbrush.
7. Stop using dental floss if your mouth is painful. Dental floss can be continued unless your blood counts are too low. Speak to your health care team about when to stop using dental loss.
8. Avoid alcohol.
9. Avoid eating coarse or acidic foods.

Additional resources:

Cancer.net: Mouth sores or mucositis www.cancer.net/navigating-cancer-care/side-effects/mouth-sores-or-mucositis

Cancer Care: Mouth sores www.cancercare.org/tagged/mouth_sores

American Cancer Society: Mouth sores

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/mouth-problems/mouth-sores.html

Oncolink: Mucositis www.oncolink.org/support/side-effects/mucositis

Nausea and vomiting

Nausea is a symptom that is often described as an unpleasant feeling associated with the urge to vomit. Vomiting is a physical phenomenon that involves contraction of the abdomen, chest wall muscles, and movement of the diaphragm followed by expulsion of the stomach contents.

Things you can do:

1. Meeting with a dietician may be helpful in finding a diet that works best for you.
2. Make a note of any symptoms of nausea that you have or episodes of vomiting. Discuss these with your health care provider at your next visit.
3. If you experience vomiting more than 5-6 times in a 24-hour period, notice any blood when you vomit, or are not able to keep food or liquids down, and be sure to contact your health care provider immediately. Talk with your health care provider about when and how to call in case of more severe symptoms.
4. Discuss how many of each type of anti-emetic you can safely use each day and what side effects they may cause. Some of the medications used to treat or prevent nausea and vomiting may increase the risk of developing constipation.
5. Drink 2-3 liters of fluid a day—avoid caffeine or high sugar drinks.
6. Eat small, frequent meals.
7. Avoid: fatty foods, greasy foods, spicy foods, foods that are hard to digest (hard fruits, meats, hard cheese, popcorn), alcohol, caffeine, chocolate, and foods with strong odors.
8. Brush your teeth more frequently and use non-alcohol-based mouth washes to reduce the symptoms of dry mouth and bad taste.
9. Peppermint and ginger supplements have been found to be helpful for some patients.
10. Relaxation, imagery, and meditation may help some patients. Ask your health care team about any resources available.
11. Ask for help from family and friends.

Additional resources:

American Cancer Society: Nausea

<https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting.html>

Cancer Care: Nausea and Vomiting from Chemotherapy

www.cancercare.org/publications/7-coping_with_nausea_and_vomiting_from_chemotherapy

Oncolink: Nausea and Vomiting www.oncolink.org/support/side-effects/gastrointestinal-side-effects/nausea-and-vomiting

Pain

Many patients experience pain during and after cancer treatment. It may help to know that cancer pain can be treated successfully for most patients. It is important to focus on managing pain during all phases of cancer treatment.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. If you are experiencing severe pain contact your health care providers immediately. You may need medication, changes in your medications, or other treatments.
4. If you are experiencing chest pain, contact emergency services (911) immediately.
5. If you are taking pain medication, make sure you are also following a bowel regimen to avoid constipation.
6. There are several other strategies for managing pain including acupuncture, biofeedback, breathing exercises and meditation, massage, and physical therapy. Discussed options for managing your pain with your health care team.

Additional resources:

Cancer.net: Pain www.cancer.net/navigating-cancer-care/side-effects/pain

ASCO Managing Cancer-related Pain: A Guides for Patients, Families and Caregivers
www.cancer.net/sites/cancer.net/files/managing_pain_booklet.pdf

American Cancer Society: Facts About Cancer Pain
www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/pain/facts-about-cancer-pain.html

Cancer Care: Pain www.cancercare.org/tagged/pain

Oncolink: Pain www.oncolink.org/support/side-effects/pain-management

Sexuality and intimacy

Sexuality is an important part of your overall well-being and should be discussed with your healthcare provider. Do not be concerned about bringing up the topic of sexuality to your healthcare provider. There may be some safety precautions necessary if your blood counts are low to prevent infection or bleeding.

Questions you should ask your health care provider:

1. How can AML or the side effects of treatment affect my sexual activity?
2. Describe any changes in your sexual function.
3. What could be causing the change in my sexual ability?
 - Decreased sexual drive: not wanting sex
 - Dryness with intercourse: vaginal dryness
 - Fear of sexual contact: scared to be touched
 - Lack of erection: unable to obtain or maintain penis fullness during sex
 - Lack of orgasm: lack of complete satisfaction
4. Are there any precautions I need to take while on treatment?
5. Pain with intercourse: pain that occurs during sexual activity
6. What referral might be helpful in addressing my sexuality and intimacy concerns?
7. Is it safe to get pregnant?

Additional resources:

Cancer.net: Sexual health <http://cancer.net/blog/2017-03/your-sexual-health-and-cancer-what-know-what-do>

Oncolink: Women's guide to sexuality www.oncolink.org/support/sexuality-fertility/sexuality/women-s-guide-to-sexuality-during-after-cancer-treatment

Oncolink: Men's guide to sexuality www.oncolink.org/support/sexuality-fertility/sexuality/men-s-guide-to-sexuality-during-after-cancer-treatment

Shortness of Breath

The feeling that you are not able to get a good breath or are not getting enough oxygen can be alarming and uncomfortable. Shortness of breath, or dyspnea, may be a result of several underlying problems. In patients with AML, anemia may predispose you to feeling short of breath with activity. Deconditioning due to inactivity may also predispose you to shortness of breath with activity.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Track your blood counts.
3. Discuss when a transfusion may be of benefit to you if you are anemic with your health care team.
4. Keep all your appointments as scheduled.
5. If you experience shortness of breath suddenly and this does not resolve with rest, there may be a more severe problem, and this will need to be reported immediately to your healthcare provider.
6. Stay active.
7. Get enough rest.
8. Practice deep breathing exercises.

Additional resources:

Cancer.net: Shortness of Breath or Dyspnea

<https://www.cancer.net/navigating-cancer-care/side-effects/shortness-breath-or-dyspnea>

American Cancer Society: Shortness of Breath

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/shortness-of-breath.html

Oncolink: Shortness of Breath www.oncolink.org/support/side-effects/shortness-of-breath-dyspnea

Skin Changes including rash and pruritus

The most common skin changes for patients with AML are rashes, petechiae, bruises and in some cases, leukemic infiltrates in the skin.

A rash is a change of the skin which affects its color, appearance, or texture. A rash may be localized in one part of the body or affect all the skin. Rash is generally caused by a skin irritation that can result from chemotherapy, allergy, infection, or skin problem.

Certain skin changes may indicate more severe skin infections, such as shingles

Things you can do:

1. Examine your skin daily.
2. Report changes in your skin to your health care provider as soon as you notice them.
3. Avoid sun exposure and use sunscreens with a sun protection factor of at least 30.
4. Wear hats, sunglasses, and cover skin as much as possible.
5. Use mild, non-perfumed, non-deodorant soaps, such as Dove, Aveeno, or Neutrogena soaps.
6. Take showers or short, cool baths instead of long, hot showers.
7. Use lanolin-based creams, lotions and ointments regularly to keep your skin well hydrated.
8. Avoid perfumes.
9. Talk with your health care team about other supportive medications such as anti-histamines.

Additional resources:

Cancer.net: Rash www.cancer.net/sites/cancer.net/files/asco_answers_rash.pdf

American Cancer Society: Getting help for skin changes

www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/getting-help-for-skin-changes-english.pdf

Cancer Care: Rash: www.cancercare.org/tagged/rash

Oncolink: Nail and Skin Changes: www.oncolink.org/support/side-effects/nail-and-skin-changes

Sleep and insomnia

Wellness begins with a good night's rest, which can be challenging when diagnosed with AML. It may be reassuring to know that you are not alone in having a tough time sleeping. One-third to one-half of cancer patients experience changes in their sleep patterns. Difficulty sleeping has been linked to physical illness, pain, hospitalization, medications, and the psychological impact of being diagnosed with cancer. Poor sleep interferes with your ability to function well and increases the likelihood of depression and anxiety. Sleep deprived states have also been linked with decreased pain tolerance.

How much sleep is enough? The general recommendation is 7-9 hours of sleep per night, according to the National Sleep Foundation. However, like exercise, sleep needs are individual. One person may function well with 7 hours of sleep, while another may need 10 hours.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. Discuss problems sleeping with the healthcare team. Medications for anxiety, depression, and insomnia may be necessary.
4. If sleep is altered by symptoms related to AML, discuss these symptoms with the healthcare team.
5. Keep regular bedtime and awakening hours.
6. Avoid stimulants and caffeine 2 hours prior to bedtime.
7. Eat light before bed
8. Avoid reading a backlit device in bed
9. Create dark, quiet and comfortable sleeping conditions
10. Help your body relax
11. Exercise for 30 minutes three to five times per week.
12. Limit daytime napping to 30 minutes.
13. Spend 30 minutes to an hour of quiet time prior to going to bed.

Additional resources:

Cancer.net: Sleep www.cancer.net/blog/2016-05/8-steps-restful-nights-sleep

American Cancer Society: Sleep Problems

www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/sleep-problems.html

Cancer Care: Sleep www.cancercare.org/tagged/sleep

Oncolink: Sleep disturbances www.oncolink.org/support/side-effects/insomnia

Spirituality

Spirituality is an important aspect of living with cancer, including AML. There is a growing body of evidence indicating that spiritual practices are associated with better health and wellbeing.

Spirituality is a broad concept that is defined in several ways. In general, it includes a sense of connection to something larger than us, and it typically involves a search for meaning in life. As such, it is a universal human experience—something that touches us all.

Some may find that their spiritual life is intricately linked to their association with a church, temple, mosque, or synagogue. Others may pray or find comfort in a personal relationship with God or a higher power. Still others seek meaning through their connections to nature or art or other aspects of their life or environment.

Things you can do:

1. Discuss your spirituality and beliefs with your health care provider. They may direct you to other resources within the care environment to help you.
2. Many cancer centers have programs for supportive care or integrative medicine that include classes for meditation, yoga, and mindfulness.
3. Journaling may help you with reflection.
4. If you are a member of a church, temple, mosque, synagogue or other religious organization, speak to the leaders of your organization about resources available to you.
5. Maintain friendships and activities as much as possible. Connections to others is important to your overall health. This can be by phone, using digital media, or in person.

Additional resources:

American Cancer Society: Sources of Support

www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/sources-of-support

Cancer Care: Spirituality www.cancercare.org/tagged/spirituality

Oncolink: Spirituality www.oncolink.org/support/practical-and-emotional/integrative-therapies-spirituality/tips-in-a-minute-addressing-spiritual-concerns-across-the-cancer-continuum

Transportation resources

Here are organizations that provide transportation resources for individuals affected by cancer.

Air Charity Network

877-621-7177 www.aircharitynetwork.org

Air Charity Network serves all 50 states and provides free flights to people in need of medical treatment.

American Cancer Society's Road to Recovery Program

800-227-2345 www.cancer.org

Some local chapters of the American Cancer Society may offer volunteers to drive patients to and from treatment.

Angel Wheels to Healing

800-768-0238 www.angelwheels.org

Angel Wheels to Healing provides non-emergency, long distance ground transportation to financially disadvantaged patients for treatment.

Cancer Care

www.cancercare.org/publications/303-transportation_resources

CancerCare provides limited financial assistance for treatment-related transportation to people affected by cancer.

Fisher House Foundation

www.fisherhouse.org

Fisher House Foundation operates a network of comfort homes where military and veterans' families can stay at no cost while a loved one is receiving treatment. Their Hero Miles program uses donated frequent flyer miles to bring family members to the bedside of ill service members.

Good Days

877-968-7233 www.mygooddays.org

Good Days helps patients with chronic medical conditions who have limited financial means with transportation.

The Patient Travel Referral Program

www.patienttravel.org

The Patient Travel Referral program, a program of Mercy Medical Angels, provides information about all forms of charitable, long-distance medically-related transportation and provides referrals to all appropriate sources of help available in the national charitable medical transportation network.

Urinary symptoms

The most common urinary symptoms in older adults are incontinence, difficulty urinating or pain with urination. These symptoms may indicate an underlying problem such as infection, or prostate enlargement. In some cases, these are normal changes of aging.

Things you can do:

1. Keep a log of symptoms that you are concerned about. Discuss these with your health care team.
2. Keep all your appointments as scheduled.
3. If you are experiencing severe pain with urination, are unable to urinate, or have blood in your urine, contact your healthcare provider immediately.
4. If you're experiencing urinary incontinence or need to get up frequently during the night to urinate, ask about a referral to a urologist.
5. If you are getting up frequently during the night to urinate, be certain that there is a night light and that hallways are well lit. Make sure there are no throat drugs or other items that you may trip over when getting up to the bathroom.

Additional resources:

Cancer.net: Urinary incontinence www.cancer.net/navigating-cancer-care/side-effects/urinary-incontinence

Oncolink: Incontinence www.oncolink.org/support/side-effects/incontinence

It is very important to talk with your healthcare team about symptoms that require immediate medical care. Ask when you should call, who to call during normal business hours, who to call after business hours, and what symptoms may require emergency medical care.

- Fevers above 101.4°F (38.5°C)
- Shaking chills at any temperature
- Sudden onset of shortness of breath or chest pain (call 911)
- Skin changes including:
 - Unusual bruising
 - Tiny red, pinpoint spots on your skin (petechiae)
 - A new or worsening rash
- Severe headache
- Sudden changes in vision
- Bleeding that does not stop after a few minutes
- Changes in bowel or bladder function:
 - Visible blood or a red to pink color of the urine
 - Uncontrolled diarrhea or constipation
 - Black or bloody stools
- Uncontrolled nausea or vomiting

Acute

Sudden, such as a sudden onset of symptoms or diseases.

Acute Myeloid Leukemia (AML)

A cancer of blood cells. AML happens when very young blood cells (blasts) in the bone marrow fail to mature normally. More blast cells are produced than needed, so there is not enough room within the marrow for other normal blood cells to develop, such as red blood cells or platelets. Some cases of MDS may develop into AML. However, most do not.

Synonyms: acute myeloblastic leukemia, acute myelocytic leukemia

Allogeneic Stem Cell Transplant

A procedure where bone marrow stem cells are taken from a genetically matched donor (a brother, sister, or unrelated donor) and given to the patient through an intravenous (IV) line. Over time, donated stem cells start making new, healthy blood cells.

Anaphylaxis

A very severe allergic reaction to a foreign protein, such as in a bee sting, or to a medicine. This reaction causes the blood pressure to drop and may cause difficulty breathing. Emergency treatment is required to manage these symptoms. If very severe, anaphylaxis can progress to shock.

Synonym: anaphylactic shock

Anemia

A condition in which the number of red blood cells is below normal. This may result in fatigue, generalized weakness and shortness of breath.

Antibiotics

Medications used to treat bacterial infections and other similar microorganisms.

Antibodies

Proteins produced by plasma cells in response to foreign substances in the body.

Anticoagulant

(ant-i-ko-AG-yuh-lunt) See blood thinner.

Anti-thymocyte globulin (ATG)

An extract of the serum of horses and rabbits that have been immunized against certain human cells; used in the treatment of aplastic anemia.

Apheresis

A procedure in which blood is taken from a person, and part of that blood component (such as white blood cells, red blood cells, or plasma) is separated out, and the remaining blood components are reinfused back into the donor.

Aplastic Anemia

A rare and serious condition in which the bone marrow does not make enough blood cells: red blood cells, white blood cells, and platelets. Anemia is a condition that happens when the red blood cell count is low. Most scientists believe that aplastic anemia happens when the immune system attacks the bone marrow stem

cells. Aplastic anemia can be acquired (begin any time in life) or can be hereditary (less common, passed down from parent to child).

Synonyms: acquired aplastic anemia, hereditary aplastic anemia

Apoptosis

Programmed cell death. This means, if cells are no longer needed, they commit suicide by activating an intracellular death program. This is a natural process.

Autoimmune Disease

Any condition that happens when the immune system attacks the body's own normal tissues. The immune system is a complex organization within the body that is designed normally to "seek and destroy" invaders of the body, including infectious agents.

Basic Research

The study of a subject to increase knowledge and understanding about it. The goal of basic research in medicine is to better understand disease. In the laboratory, basic research scientists study changes in cells and molecules linked to disease. Basic research helps lead to better ways of diagnosing, treating, and preventing disease.

Basophil

A type of white blood cell that plays a role in allergic reactions.

Benzene

A chemical that is widely used by the chemical industry to make plastics, resins, nylon and synthetic fibers. Benzene is found in tobacco smoke, vehicle emissions, and gasoline fumes. Exposure to benzene may increase the risk of developing a bone marrow failure disease. Benzene can affect human health by causing bone marrow stem cells not to work correctly.

Bilirubin

(bil-i-ROO-bun) A reddish yellow substance formed when red blood cells break apart. It is found in the bile and in the blood. Yellowing of the skin and eyes can occur with high levels of bilirubin. Also called total bilirubin.

Biologic Agent

A substance made from a living system, such as a virus, and used to prevent or treat disease. Biological drugs include antibodies, globulin, interleukins, serum, and vaccines. Also called a biologic or biological drug.

Synonyms: biologic, biological drug

Blast Cells

Immature blood cells that would normally become fully functional mature red cells, white cells, or platelets. The number of blast cells in the bone marrow helps define how severe MDS is in a person. When 20 or more out of 100 cells in the bone marrow are blasts, this is considered acute myeloid leukemia (AML).

Synonym: precursor cell

Blood Clot

A clot or small cluster of blood cells that forms when platelets stick together. A combination of platelets and fibrin that form a mesh

with the intention of preventing bleeding in response to an injury or illness. The term thrombus describes a blood clot that develops and attaches to a blood vessel. Blood clots are more common in Paroxysmal Nocturnal Hemoglobinuria (PNH) or in people with blood clotting disorders.

Synonym: thrombus

Blood Tests

Blood samples drawn from a vein, usually the arm, that are evaluated for cell counts (red cells, white cells [and their subtypes], and platelets). The blood is also evaluated for the shape and size of the different blood cells and for how various organs are functioning such as the kidneys and liver.

Blood Thinner

A medicine used to treat or prevent blood clots. Also called anticoagulants. Some common blood thinners are enoxaparin or clexaine (Lovenox or Clexane), heparin (Calciparine or Liquaemin), and warfarin (Coumadin).

Synonyms: anticoagulant, anti-clotting

Blood Transfusion

A procedure in which whole blood or one of its components is given to a person through an intravenous (IV) line into the bloodstream. A red blood cell transfusion or a platelet transfusion can provide temporary improvement for some patients with low blood counts.

Bone Marrow

The soft, sponge-like tissue in the center of bones that functions like a factory to produce white blood cells, red blood cells, and platelets.

Bone Marrow Aspirate

The bone marrow aspirate is a sample of the liquid portion of the bone marrow. It is used to obtain spicules — a small collection of blood forming cells. This provides information about the shape of the cells (morphology), how the cells are maturing (differentiation) and the number of blasts (immature cells) in the bone marrow. The aspirate may also be used for additional testing that may help to determine the cause of the cytopenias, such as cytogenetics.

Bone Marrow Aspiration

The process of removing bone marrow from a specific area using a small needle and syringe. Used for diagnostic purposes. Tests may also be run on the bone marrow cells to look for any genetic abnormalities.

Bone Marrow Biopsy

The bone marrow biopsy is a small core (the shape and size of a medium pencil lead) of the spongy center of the bone marrow. It provides information about the cellularity of the bone marrow (crowded=hypercellular, empty=hypocellular). It will also provide useful information about iron storage, scarring (fibrosis), and the presence of any other abnormal cells.

Synonym: Bone Marrow Trephine Biopsy

Bone Marrow Failure

A condition that occurs when the bone marrow stops making enough healthy blood cells. The most common of these rare diseases are myelodysplastic syndromes (MDS), aplastic anemia, and paroxysmal nocturnal hemoglobinuria (PNH). Bone marrow failure can be acquired (begin any time in life) or can be hereditary (less common, passed down from parent to child).

Bone Marrow Transplant (BMT)

A procedure where bone marrow stem cells are collected from the donor and given to the patient through an intravenous (IV) line. In time, donated stem cells start making new, healthy blood cells.

CD 55 and CD 59

Protein antibodies

Cellularity

How much of the bone marrow volume is occupied by various types of blood cells.

Chemotherapy

The use of medicines that kill cells (cytotoxic agents). People with high-risk or intermediate-2 risk myelodysplastic syndrome (MDS) may be given chemotherapy. Chemotherapy may also hurt healthy cells causing side-effects. If chemotherapy works in controlling abnormal cells, then relatively normal blood cells will start to grow again. Chemotherapy agents include: cytarabine (Ara-C) and hydroxyurea (Hydrea), daunorubicin (Cerubidine), idarubicin (Idamycin), and mitoxantrone (Novantrone).

Chronic Illness

A medical condition that lasts a long time. A chronic illness can affect a person's lifestyle, ability to work, physical abilities and independence.

Chromosomes

A structure that contains your genetic information, or DNA. Normally each person has 23 pairs of chromosomes.

Clinical Trial

A type of research study that tests how a drug, medical device, or treatment approach works in people. There are several types of clinical trials. Treatment trials test new treatment options. Diagnostic trials test new ways to diagnose a disease. Screening trials test the best way to detect a disease or health problem. Quality of life (supportive care) trials study ways to improve the comfort of people with chronic illness. Prevention trials look for better ways to prevent disease in people who have never had the disease. Trials are in four phases:

- **Phase I** tests a new drug or treatment in a small group to see if it is safe.
- **Phase II** expands the study to a larger group of people to find out if it works.
- **Phase III** expands the study to an even larger group of people to compare it to the standard treatment for the disease.
- **Phase IV** takes place after the drug or treatment has been licensed and marketed to find out the long-term impact of the new treatment.

Clone

To make copies. Bone marrow stem cells clone themselves all the time. The cloned stem cells become mature blood cells that leave the bone marrow and enter the bloodstream. Abnormal clones are associated with cancers, such as MDS.

Coagulate

To thicken. Normal blood platelets cause the blood to coagulate and stop bleeding.

Combination Chemotherapy

The use of more than one drug during cancer treatments.

Comorbidities

Additional medical conditions beyond MDS.

Complement System

A group of proteins that move freely in the bloodstream. These proteins support (complement) the work of white blood cells by fighting infections.

Complete Blood Count (CBC)

The CBC measures the number of white blood cells (WBC) and the number and size of red blood cells, the total amount of hemoglobin, and the fraction of the blood made up of red blood cells.

Complex Karyotype

Three or more abnormalities in the chromosomes being evaluated.

Conditioning Treatment

Chemotherapy used to kill all remaining cancer cells before stem cell transplantation.

Cytogenetics

Testing that is performed on bonemarrow samples and examines the chromosomes of the cells. Your cytogenetic results are used to identify the type of MDS you have and to calculate the International Prognostic Scoring System (IPSS) and the revised IPSS (IPSS-R) risk category. Common abnormalities include:

- **Deletion 5q** – deletion of chromosome 5
- **Deletion 20** – deletion of chromosome 20
- **Deletion Y** – deletion of the Y chromosome
- **Monosomy 7** – loss of one of the two 7 chromosomes
- **Trisomy 8** – addition of a third chromosome 8

Synonyms: Chromosomes, Karyotype, DNA

Cytogenetic Remission

No sign of previously detected abnormal chromosomes are found. This represents a response to treatment. When a bone marrow test is performed on a patient with 5q deletion MDS, and there are no signs of an abnormal chromosome 5, then that patient has achieved a cytogenetic remission. Also called cytogenetic response.

Cytokines

Proteins

Cytopenia

A deficiency of (or too few) mature cells in the blood. Deficiencies can occur in red cells, white cells, and/or platelets.

Cytotoxic Agent

A medicine that kills certain cells. Chemotherapy for MDS patients often involves the use of cytotoxic agents.

D-dimer

A test that helps doctors find out if a person has a problem with blood clotting.

del(5q)

Deletion in the long (q) arm of chromosome 5.

De Novo

The original source of disease, something present at the start. MDS may be de novo, the original source of disease, or treatment related, caused from chemotherapy or radiation given for other forms of cancer.

Differentiation

The process of cells maturing to become healthy adult cells of a particular type (i.e. red cells, white cells, and platelets).

Dietary Supplement

Vitamins, minerals, herbs and other substances meant to improve your nutritional intake. Dietary supplements are taken by mouth in the form of a pill, capsule, tablet or liquid.

DNA Methylation

A process that helps control gene activity, resulting in blockage of cell growth.

Dysplasia

Abnormal shape and appearance or morphology, of a cell.

Synonym: dysplastic

Embolus

A blood clot or other foreign matter that gets into the bloodstream and gets stuck in a blood vessel.

Engraftment

Refers to how well a graft (donor cells) is accepted by the host (the patient) after a bone marrow or stem cell transplant. Several factors contribute to better engraftment – physical condition of the patient, how severe the disease is, type of donor available, age of patient. Successful engraftment results in new bone marrow that produces healthy blood cells.

Epidemiology

The study of patterns and causes of disease in groups of people. Researchers who study how many people have a disease, how many new cases are diagnosed each year, where patients are located, and environmental or other factors that influence disease, are known as Epidemiologists.

Erythroid Response

- In patients who have not received red blood transfusions—hemoglobin increase of 1.5 g/dl
- In those who have had transfusions—reduction in transfusions by at least four units of packed red blood cells over 8 weeks compared with the 8 weeks before treatment

Erythrocyte

(i-RITH-ruh-site) See red blood cell.

Erythropoietin (EPO)

A protein substance naturally manufactured by the kidneys in response to low oxygen levels in body tissues. Erythropoietin stimulates the production of red blood cells in the bone marrow.

Erythropoietin-stimulating Agent (ESA)

A medicine used to help the bone marrow make more red blood cells. Epoetin alfa (Epogen, Procrit) and darbepoetin alfa (Aranesp) are erythropoiesis-stimulating agents that can help boost the red blood cell count of some bone marrow failure patients. These medicines are given via an injection. Also called red blood cell growth factor.

Eosinophil

A type of white blood cell that kills parasites and plays a role in allergic reactions.

Etiology

The cause or origin of a disease.

FAB Classification

A criteria used for classifying different types of myelodysplastic syndromes (MDS). The FAB (French, American, British) Classification System was developed by a group of French, American and British scientists. This system is based on 2 main factors: the percentage of blast cells in bone marrow, and the percentage of blast cells in the bloodstream. The FAB system is somewhat outdated, but is still used by some doctors today. The World Health Organization (WHO) Classification System has largely replaced the FAB Classification System.

Fanconi Anemia

A rare inherited disorder that happens when the bone marrow does not make enough blood cells: red cells, white cells, and platelets. Fanconi anemia is diagnosed early in life. People with Fanconi anemia have a high likelihood of developing cancer. Genetic testing is used to diagnose Fanconi anemia.

Fatigue

A feeling of low or no energy, general feeling of tiredness with normal activity. Rest does not necessarily resolve fatigue.

Synonyms: tired, exhaustion, lethargy, malaise

Ferritin

A protein inside of cells that stores iron for later use by your body. Sometimes ferritin is released into the blood. The ferritin level in the blood is called serum ferritin.

Fibrosis

Scarring of tissue. Fibrosis of the bone marrow is a feature seen in some types of unclassified myelodysplastic syndrome (MDS).

Flow Cytometry

A laboratory test that gives information about cells, such as size, shape, and percentage of live cells. Flow cytometry is the

test doctors use to assess for specific proteins on the surface of blood cells. It is the standard test for confirming a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH).

Synonyms: Flow, Immunophenotyping, Fluorescence-activated cell sorting (FACS)

Fluorescence In Situ Hybridization (FISH)

An important laboratory test used to help doctors look for chromosomal abnormalities and other genetic mutations. Fluorescence in situ hybridization, also called FISH, directs colored light under a microscope at parts of chromosomes or genes. Missing or rearranged chromosomes are identified using FISH.

Folate

A B-vitamin that is found in fresh or lightly cooked green vegetables. It helps the bone marrow make normal blood cells. Most people get enough folate in their diet. Doctors may have people with paroxysmal nocturnal hema-globinuria (PNH) take a man-made form of folate called folic acid.

Gene Expression

The process that genes use to make their products, such as proteins.

Graft-Versus-Host Disease (GVHD)

Attack by transplanted cells on the recipient's body in which the transplanted cells cause inflammation of some normal tissues.

- **Acute:** within 3 months of transplantation
- **Chronic:** starting more than 3 months after transplantation

Graft-Versus-Leukemia Effect

T cells (part of the immune system) in the donated stem cells can attack the remaining cancer cells.

Granulocyte

Any one of these three types of white blood cells - neutrophils, eosinophils, and basophils. These cells have granules that contain enzymes to help fight infection.

Growth Factor

A substance made by the body that stimulates the bone marrow to produce blood cells. Some growth factors are man-made in the laboratory and used for treating low blood counts. These include red blood cell growth factors called erythropoietin (EPO) and darbepoetin, and white blood cell growth factors called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GM-CSF). Also called cytokines.

Haploidentical Stem Cell Transplantation

The donor's blood markers match half the patient's markers.

Hematocrit (HCT)

Percent of the total blood volume that is made up of red blood cells. In men a normal hematocrit is 40–52% while in women the normal is 36–46%. Hematocrit is part of a complete blood count. Also called HCT, packed cell volume, PCV. (see red blood cells)

Synonyms: packed cell volume, PCV

Hematologist

A doctor who specializes in the diseases and disorders of blood.

Hematopoiesis

The formation and development of blood cells.

Hemochromatosis

A condition that occurs when the body absorbs and stores too much iron. This leads to a condition called iron overload. In the United States, hemochromatosis is usually caused by a genetic disorder. Organ damage, particularly to the liver and heart, can occur if iron overload is not treated.

Hemoglobinuria

(hee-muh-gloe-buh-NYOOR-ee-uh) The presence of hemoglobin in the urine.

Hemolytic Anemia

Anemia due primarily to the excessive hemolysis or destruction of red blood cells.

Hemolysis

The destruction of red blood cells.

HLA

See human leukocyte antigen.

Hormone

A part of the body's system that serves as chemical messengers. Hormones move through the bloodstream to transfer information and instruction from one set of cells to another.

Human Leukocyte Antigen

(LEW-kuh-site ANT-i-jun) One of a group of proteins found on the surface of white blood cells and other cells. These antigens differ from person to person and are responsible for balancing the immune system. A human leukocyte antigen test is done before a stem cell transplant to closely match a donor and a recipient. Also called HLA.

Hypercellular

A condition in which there are too many cells within the bone marrow.

Hypocellular

A condition in which there are too few cells, within the bone marrow. Patients with aplastic anemia have hypocellular bone marrow.

Hypomethylating Agent

A hypomethylating agent is a drug that inhibits DNA methylation. Works by preventing certain genes involved in controlling cancer from being silenced, allowing for the normal functioning of the tumor suppressor genes.

Synonym: demethylating agent

Idiopathic

Usually refers to any condition with no known cause.

Immature Blood Cells

May be called stem cells, progenitor cells or blasts.

Immune Deficiency

A decreased ability of the immune system to fight infection.

Immune System

The complex group of organs and cells that defend the body against infection and disease.

Immunocompromised

Occurs when the immune system is not functioning properly, leaving the patient open to infection. A person can be immunocompromised due to low white blood cell count or due to some medicines.

Synonym: immune compromised

Immunosuppressive Drug

Drugs that lower the body's immune response in autoimmune diseases. These drugs may be used to allow the bone marrow stem cells to grow and make new blood cells. ATG (antithymocyte globulin) or ALG (antilymphocyte globulin) with cyclosporine are used to treat bone marrow failure in aplastic anemia. Immunosuppressive drugs may help some patients with myelodysplastic syndromes (MDS) and paroxysmal nocturnal hemoglobinuria (PNH).

Intravenous Infusion

A method of getting fluids or medicines directly into the bloodstream over a period of time. Also called IV infusion.

Synonym: IV infusion

Investigational New Drug

A new drug, antibiotic drug, or biological drug that is used in a clinical trial. It also includes a biological product used in the laboratory for diagnostic purposes. Also called IND. In the USA these drugs are not approved by the FDA.

IPSS/IPSS-R

International Prognostic Scoring System – system for grading the severity of MDS. The system turns patient information into a score. The score helps predict what may happen with the patient's MDS in the future.

Iron Chelation Therapy

A drug therapy to remove extra iron from the body. Patients with high blood iron (ferritin) levels may receive iron chelation therapy. The U.S. Food and Drug Administration (FDA) has approved two iron chelators to treat iron overload in the U.S.: deferasirox, an oral iron chelator, and deferoxamine, a liquid given by injection, these may differ depending on which country you live in.

Iron Overload

A condition that occurs when too much iron which is acquired from blood transfusions accumulate in the body. Patients who need regular red blood cell transfusions are at risk for iron overload. Organ damage can occur if iron overload is not treated.

Ischemia

Occurs when the blood supply to a specific organ or part of the body is cut off, causing a localized lack of oxygen.

Lactate DeHydrogenase

(LAK-tate dee-high-DROJ-uh-nase) An enzyme found in the blood and in many of the body's organs. High levels of LDH in the blood can mean that red blood cells are breaking apart (hemolysis) or that there is tissue damage in the body. It is important for patients with paroxysmal nocturnal hemoglobinuria (PNH) to have their LDH monitored regularly. Also called lactic dehydrogenase, LDH.

Leukocyte

(LEW-kuh-site) See white blood cell.

Lymphatic System

A network of organs, lymph nodes, lymph ducts, and lymph vessels that help keep the body's fluids in balance and help the body fight infection.

Lymphocyte

A type of white blood cell. B lymphocytes, or B cells, help make special proteins called antibodies that fight bacteria and viruses (immune response). T lymphocytes, or T cells, help kill tumor cells and help the body's immune response.

Matched Related Donor

A bone marrow/stem cell donor that is a sibling or another family member to the patient.

Mean Corpuscular Volume

A measurement of the average size of a person's red blood cells. If the mean corpuscular volume is high, the red blood cells are larger than normal (macrocytic). If the mean corpuscular volume is low, the red blood cells are smaller than normal (microcytic). Also called MCV.

Megakaryocyte

A large bone marrow cell that makes platelets, necessary for normal blood clotting.

Mini Transplant (aka reduced intensity transplant)

A procedure similar to standard bone marrow transplant. The mini transplant uses a reduced form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable to older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant.

Minimal Residual Disease

Small numbers of cancer cells that stay in the body after treatment and can be measured. Also called MRD.

Monosomy 7

Describes the loss of one of the two number 7 chromosomes. "Mono" means one and "somy" comes from the word chromosome. Bone marrow samples are used to detect monosomy 7 and other genetic abnormalities. Monosomy 7 can occur in adult patients with MDS and can occur in childhood bone marrow failure diseases.

Monoclonal Antibody

A type of protein called an antibody that is engineered to look for a specific substance in the body. There are many kinds of monoclonal

antibodies. Each one looks for only one substance. Eculizumab (Soliris) is a monoclonal antibody that may be prescribed to treat patients with paroxysmal nocturnal hemoglobinuria (PNH).

Monocyte

A large white blood cell. Monocytes move through the blood to the tissues where they become macrophages. Macrophages are immune cells that surround and kill germs such as bacteria and viruses.

Morphology

The study of the structure and form of an organism or one of its parts.

Multilineage Dysplasia

Abnormalities in more than one type of blood cell

Mutation

Any change or alteration in a normal gene. A mutation may cause disease or may be a normal variation. Examples of mutations are deletions or additions of genetic material.

Myelo

A Greek word meaning marrow.

Myelodysplastic Syndromes (MDS)

The Myelodysplastic Syndromes (MDS) are a group of bone marrow failure disorders. Myelo refers to the bone marrow. Dysplastic means abnormal looking cells. In MDS, the bone marrow does not make blood cells normally. The result is too few cells or low blood counts (cytopenias) and cells that have an abnormal form and that do not function properly. The most common cytopenias include:

- **Anemia:** low red blood cells (oxygen carrying cells)
- **Thrombocytopenia:** low platelets (cells that help to clot the blood)
- **Leukopenia:** low white blood cells (WBC) (help to fight infection)
- **Neutropenia:** low neutrophils (most important type of WBC for fighting infection)

Natural Killer Cells

A type of cell that lacks B-cell and T-cell receptors and attacks mutant and virus-infected cells.

Neutropenia

A deficiency (below-normal number) of mature white blood cells called neutrophils that assist in fighting bacterial infections.

Neutropenic Diet

A diet that can be recommended for a patient with very low white blood cell count. A neutropenic diet avoids the use of certain foods that can contain bacteria or fungus, such as raw meats, unpasteurized dairy products, aged cheeses, fermented drinks, and unwashed fruits and vegetables. The concern is the food be "safe" for a patient with low WBC count.

Occlusion

Obstruction; blockage.

Off Label Drug

An approved medicine that is prescribed by a licensed healthcare professional for a purpose other than that for which it was approved by the U.S. Food and Drug Administration (FDA).

Oncologist

A doctor who specializes in the treatment and prevention of cancer.

Over-the-Counter (OTC) Medicine

A medicine that is available without a prescription from the doctor. Also called OTC medicine.

Packed RBCs

A concentrated blood product in which most of the plasma, the fluid part of blood, is removed to make red blood cell transfusions easier and faster.

Pancytopenia

A reduced number of all types of blood cells – red blood cells, white blood cells, and platelets.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

A rare and serious blood disease that causes red blood cells to break apart. Paroxysmal means sudden and irregular. Nocturnal means at night. Hemoglobinuria means hemoglobin in the urine. Hemoglobin is the red part of red blood cells. A person with PNH may have episodes of dark urine in the morning, but this symptom is not present in all PNH patients.

Pathophysiology

Abnormal function or processes that cause or are associated with disease or injury.

Pediatric MDS

MDS is rare in children; but it does happen.

Peripheral Blood Stem Cell (PBSC) Transplant

A procedure where stem cells are collected from the donor's circulating (peripheral) blood. These stem cells are then given to the patient through an intravenous (IV) line. In time, donated stem cells start making new, healthy blood cells. Also called PBSC transplant. This is the most common type of stem cell transplantation that occurs.

Petechiae

Small, flat red or purplish spots caused by pinpoint bleeding into the skin. It is often a sign of a low platelet count.

Phagocyte

A type of white blood cell that surrounds and kills microorganisms, such as bacteria and fungi. They also remove dead cells. Monocytes, macrophages, and neutrophils are phagocytes.

Pharmacist

A highly trained and licensed professional whose job concerns the preparation, distribution, and use of prescription drugs. A pharmacist also can advise patients, as well as physicians and other health practitioners, on the selection, dosages, interactions, and side effects of medications.

Placebo

A placebo is an inactive pill, liquid, or powder that has no

treatment value. Placebo use in clinical trials is extremely uncommon today.

Platelets

Irregularly shaped, colorless cells that are present in blood. Their sticky surface lets them, along with other substances, form clots to stop bleeding. Also called thrombocytes.

Platelet Transfusion

A procedure in which platelets are given to a person through an intravenous (IV) line into the blood-stream. Platelets are more likely than red blood cells to cause an immune response, such as chills and fever. The use of platelets from one donor (apheresis) reduces the chance of reaction to transfused platelets. Transfused platelets increase the blood platelet count and help control bruising and bleeding.

Prophylactic

Something that prevents or protects. For example, blood thinners may be given as a prophylactic measure to prevent blood clots in high risk patients.

Protocol

An action plan that describes what will be done in a clinical trial and how it will be carried out. This plan is reviewed and approved by a committee at each place doing the clinical trial. This committee is known as the Institutional Review Board.

Pulmonary Embolism

(PULL-muh-nerr-ee EM-buh-liz-um) A blockage of an artery that carries blood to the lungs. See Embolus.

Pure Red Cell Aplasia (PRCA)

A condition that occurs when the bone marrow stem cells do not make red blood cells. Red blood cell counts are low. White blood cell and platelet counts are normal.

Red Blood Cell

The most numerous type of blood cell in healthy people. Red blood cells contain hemoglobin, a protein that picks up oxygen in the lungs and brings it to cells in all parts of the body. Also called erythrocyte, RBC.

Red Blood Cell Growth Factor

See erythropoietin-stimulating agent.

Red Blood Cell (RBC) Transfusion

A procedure in which packed red blood cells are given to a person through an intravenous (IV) line into the bloodstream. Transfused red blood cells increase the blood count and help improve symptoms of anemia. Before transfused blood is given, donated blood is typed and cross matched to the recipient's blood. Also called RBC transfusion.

Reduced Intensity Transplant

Also called "mini-transplant". A procedure similar to standard stem cell transplant. The mini transplant uses a reduced form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable to older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant.

Refractory

Not responsive to treatment or cure. For example, refractory anemia is a low red blood cell count that doesn't respond to standard treatments.

Reticulocyte

An immature red blood cell. Reticulocytes are normally found in bone marrow. They are present in the bloodstream only in very low numbers.

Remission

Disappearance of the signs and symptoms of cancer. A remission may be complete (CR) or partial (PR).

Revised IPSS (IPSS-R)

More recent MDS scoring system. It uses additional information than the IPSS and categorizes patients into five risk groups instead of four.

Ring Sideroblast

(SID-uh-ruh-blast) A red blood cell that has too much iron. The iron typically forms a ring around the cell's nucleus.

Secondary MDS

A type of MDS that is caused by a previous treatment for another disorder or disease. Treatments typically associated with secondary MDS include radiation therapy and chemotherapy used to treat cancer. Also called therapy-related MDS, T-MDS.

Synonyms: T-MDS, therapy-related MDS

Serum Erythropoietin

Amount of erythropoietin that is present normally in an individual's blood. It can be measured in the blood.

Serum Sickness

An immune system reaction to foreign proteins in certain medicines. Serum sickness can be a side effect of ATG, a medication used in the treatment of aplastic anemia, causing fever, rash, joint pain, and muscle aches.

Single Lineage Dysplasia

Abnormalities in only one type of blood cell.

Social Worker

A licensed professional trained to help people manage their daily lives, understand and adapt to changes in health and lifestyle. A social worker also will help people find appropriate community resources, healthcare, legal resources, and government assistance.

Somatic Mutation

Change in a DNA that happens after conception in a patient's cells, is not inherited, and is not passed on to the patient's children.

Stem Cells

Cells in the body that develop into other cells. Adult stem cells in the body repair and maintain the organ or tissue in which they are found. Blood forming (hemapoietic) stem cells are found in the bone marrow. These cells make copies of themselves and can also develop into red cells, white cells, and platelets. These are the cells used in stem cell transplantation. Embryonic stem cells come from human embryos and may be used in medical research. Embryonic stem cells are not approved for treatment.

Stem Cell Transplant (SCT)

A procedure where blood-forming (hemapoietic) stem cells are taken from a healthy donor. They enter the patient's bloodstream through an intravenous (IV) needle and make their way into the bone marrow. The donor cells are called a graft. There are three sources of stem cells – bone marrow, cord blood, and circulating (peripheral) blood. The most common source for MDS is peripheral blood stem cells.

Subcutaneous Injection

A method of giving medicine in the fatty tissue area under the skin using a short needle.

Synonyms: shot, injection

Supportive Care

Care given to improve the quality of life, or comfort, of a person with a chronic illness. Supportive care treats the symptoms rather than the underlying cause of a disease. The goal is to help the patient feel better. Patients with low blood counts may be given blood transfusions as supportive care to help manage the symptoms of their disease. Also called palliative care, symptom management.

Synonyms: palliative care, symptom management

T cell

See lymphocyte

T lymphocyte

See lymphocyte

Therapy-Related MDS

See Secondary MDS

Thrombus

A blood clot that develops and attaches to a blood vessel.

Thrombosis

The process of forming a blood clot.

Thrombocytopenia

A condition in which the number of mature platelets, or thrombocytes, is below normal. When severe, the tendency to bruise and bleed more easily can occur.

Transfusion

Process by which blood or one of its components (e.g., red blood cells, plasma, platelets) is delivered directly into the bloodstream by vein (intravenous or IV), similar to other IV medications.

Transfusion Independence

No longer needing any type of blood transfusion.

Treatment Failure

Occurs when a patient does not respond to the treatment, responds only temporarily, or has to stop the treatment because of side effects.

Unrelated Donor

A donor that is not a sibling or other familial relation of the patient (recipient).

Venous thrombosis

Blood clot in a vein.

Vitamin B12

A complex vitamin found in animal products. Vitamin B12 helps maintain healthy red blood cells and nerve cells. A shortage of Vitamin B12 and folate can reduce blood cell production in the bone marrow. Also called B complex vitamins. Levels of B12 can be measured in the blood.

White Blood Cells (WBC)

Cells produced in the bone marrow and lymph nodes. White cells are key cells in the immune system that prevent or fight infection.

World Health Organization (WHO) Classification

The most current system for classifying leukemia and myelodysplastic syndromes (MDS), it was developed by the World Health Organization (WHO). This system is based on patient data from around the world and on the most up-to-date knowledge of MDS. WHO Classification of MDS consists of many subtypes based on tests of the blood and bone marrow.

WHITE BLOOD CELLS

ANC (absolute neutrophil count)

A measure of the actual number of mature neutrophils in a given volume of blood.

Basophil

Type of white blood cell that plays a role in allergic reactions and asthma.

Eosinophil

Type of white blood cell that kills parasites and plays a role in allergic reactions.

Granulocyte

A term for any of the white blood cell types that have granules containing enzymes to help fight infection: neutrophils, eosinophils and basophils.

Lymphocytes

Small white blood cells produced in the lymphoid organs (the lymph nodes, spleen, thymus, and tonsils) or bone marrow that are essential for normal function of the immune system.

Monocyte

A white blood cell that helps the body fight infections from some bacteria such as tuberculosis.

Neutrophil

A type of white blood cell that functions to destroy bacteria. When the number of neutrophils is too low, the body is at greater risk for developing an infection.

BONE MARROW BIOPSY

Biopsy

A medical procedure to remove a small piece of solid bone marrow using a needle that goes into the marrow of the hip bone. The solid bone marrow is examined for cell abnormalities, the number of different cells, and checked for scarring of the bone marrow.

Iliac Crest

The hip bone area from which bone marrow samples are most commonly taken.

BONE MARROW TRANSPLANT

Allogeneic Stem Cell Transplantation

A procedure in which matched bone marrow or peripheral blood stem cells from a donor (usually related) are collected, stored, and infused into a patient (recipient) following high dose chemotherapy with or without radiation therapy. In time, donated stem cells given to the patient begin making new, healthy blood cells (known as engraftment).

Allograft

An allogeneic stem cell collection used for transplant.

Autograft

An autologous stem cell collection used for transplant.

Autologous Stem Cell Transplantation

A procedure in which a patient's own stem cells from bone marrow or peripheral blood are collected, stored, and reinfused following high dose chemotherapy or radiation therapy. In time, donated stem cells given to the patient begin making new, healthy blood cells (known as engraftment).

Bone Marrow Transplant

A procedure in which high doses of chemotherapy or radiation therapy are used to eradicate disease in the bone marrow and lymphatic system and then are replaced with healthy bone marrow from a donor or the patient.

Cord Blood Transplant

A procedure where umbilical cord stem cells are given to the patient through an intravenous (IV) line. Stem cells are collected from an umbilical cord right after the birth of a baby. They are kept frozen until needed. In time, donated stem cells given to the patient begin making new, healthy blood cells.

Engraftment

Refers to how well the donor cells (graft) are accepted by the patient's immune system (host) after a bone marrow or stem cell transplant. Several factors contribute to better engraftment: physical condition of the patient, how severe the disease is, type of donor available, age of patient. Successful engraftment results in new bone marrow that produces healthy blood cells (new white blood cells, red blood cells, and platelets).

Graft-Versus-Host Disease (GVHD)

GVHD is a common complication of allogeneic bone marrow/stem cell transplantation. It is caused when the donor's immune cells, now in the patient, begin to see the patient's body as foreign and mount an immune response. GVHD most commonly affects the recipient's skin, intestines, or liver. Severity can range from mild to very severe. In some cases, GVHD can be prevented or treated with specific drugs to suppress the body's immune cells (immunosuppressive drug therapy).

Human Leukocyte Antigen (HLA)

One of a group of proteins found on the surface of white blood cells and other cells. These antigens differ from person to person. A human leukocyte antigen test is done before a stem cell transplant to closely match a donor and a recipient.

Matched Related Donor

Bone marrow/stem cell donor that is a sibling or another blood relative to the patient.

Mini-Transplant

See Non-Myeloablative Transplant

Myeloablation

The killing of bone marrow by radiation or chemotherapy. This term usually refers to the complete or near-complete destruction of the bone marrow.

Non-Myeloablative Transplant

Type of allogeneic stem cell or bone marrow transplant that uses lower doses of chemotherapy. This reduces side effects caused by chemotherapy, making it more tolerable for older adults. It does not reduce the risk of graft-versus host disease. Also called nonmyeloablative transplant or reduced intensity transplant.

Reduced Intensity Transplant

Procedure similar to standard bone marrow transplant. The reduced intensity transplant uses a mild form of chemotherapy pre-treatment. This reduces side effects caused by chemotherapy, making it more tolerable for older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant.

Unrelated Donor

A donor that is not a sibling or other familial relation of the patient (recipient).

MEDICATIONS

Adverse Event (AE)

Any undesired actions or effects of a drug or treatment.

Synonyms: side effect, toxicity

Antibiotic Therapy (AB)

Used to treat bacterial infections or prevent recurrence of bacterial infections.

Antithymocyte Globulin (ATG)

An immunosuppressive medication that eliminates abnormally proliferating white blood cells called T lymphocytes which disrupt normal blood cell growth. This may restore normal production of red blood cells which may lead to transfusion independence. The three brand-name drugs are Thymoglobulin®, Lymoglobulin®, and Atgam®.

Colony-Stimulating Factor (CSF)

Protein that stimulates the development and growth of blood cells; sometimes called growth factor. Granulocyte colony-stimulating factor is a CSF that is used to stimulate stem cells from the bone marrow into the bloodstream prior to apheresis.

Corticosteroids

Also called "steroids," corticosteroids are powerful anti-inflammatory medicines used to treat many diseases and conditions. They are similar to a protein called cortisol that is made in the adrenal glands. Names of corticosteroids include prednisone and dexamethasone.

Synonym: steroids

Dacogen™ (decitabine)

A medication used in treating some types of MDS and AML. Dacogen works by preventing certain genes involved in controlling cancer from being silenced, allowing for the normal functioning of genes within the body. It is a DNA hypomethylating agent that is administered intravenously (IV).

Desferal® (deferoxamine)

A medication that binds to iron and promotes its removal from the body for treatment transfusion dependent iron overload. It is an iron-chelating drug that is administered subcutaneously (under the skin).

Erythropoietin (EPO)

A "recombinant" form of a natural growth factor used to treat symptoms associated with anemia. It stimulates the bone marrow to produce red blood cells. The three brand-name drugs are Aranesp®, Epogen®, and Procrit®. These drugs are administered intravenously or subcutaneously.

Exjade® (deferasirox)

A medication that binds to iron and promotes its removal from the body for treatment of transfusion-dependent iron overload. It is an iron-chelating drug that is administered orally.

Growth Factors (hematopoietic)

A substance made by the body that stimulates the bone marrow to produce blood cells. Some growth factors are man-made in the laboratory and used for treating low blood counts. These include red blood cell growth factors called erythropoietin (EPO) and darbepoetin, and white blood cell growth factors called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GM-CSF). Also called cytokines.

Synonym: cytokine

Hycamtin® (topotecan hydrochloride)

A chemotherapy agent that may result in remission of MDS. It is administered intravenously.

JADENU™ (deferasirox)

A medication that binds to iron and promotes its removal from the body for treatment of transfusion-dependent iron overload. It is an iron chelating drug that is administered orally. It is a new oral formulation of Exjade tablets. Whereas the Exjade tablet must be mixed in liquid and taken on an empty stomach, Jadenu can be taken in a single step, with or without a light meal, simplifying administration of treatment for chronic iron overload.

Leukine® (sargramostim)

A growth factor, granulocyte macrophage colony-stimulating factor (GM-CSF), used for the treatment of neutropenia. It increases white cell production, which may help to reduce the likelihood of additional infection. It is administered subcutaneously.

Neupogen® (filgrastim)

A growth factor, granulocyte colony-stimulating factor (G-CSF), used for the treatment of neutropenia. It increases white cell production, which may help to reduce the likelihood of additional infection. It is administered subcutaneously.

Prednisone

A corticosteroid that is used for many reasons. It is prescribed when the body is not producing enough of this chemical on its own. It is sometimes prescribed with ATG treatment to reduce the risk of anaphylaxis or serum sickness. It helps by reducing the antibody production of the immune system and in treating various allergic conditions. There are many brand names of prednisone. (See corticosteroid)

Pyridoxine (Vitamin B6)

A vitamin needed to make red blood cells. It can be useful in improving red blood cell counts in sideroblastic anemia by increasing the red blood cell production.

Reblozyl® (luspatercept-aamt)

First erythroid maturation agent (EMA) approved by the FDA for the treatment of anemia in adult patients with myelodysplastic syndromes (MDS) who have been failed an erythropoiesis stimulating agent (ESA) or are unlikely to respond to an ESA, and are requiring transfusions of 2 or more red blood cell (RBC) units over 8 weeks. Luspatercept may restore differentiation and maturation of red blood cells (normal development) in the last phase of erythroid cell (red blood cell) development in some patients with lower risk MDS.

Revlimid® (lenalidomide)

A medication that works by stimulating the immune system, preventing new blood vessel growth, and stimulating cell death. It is categorized as an immunomodulatory agent and is taken orally.

Telintra™ (TLK199)

A medication that inhibits a key enzyme (glutathione S-transferase P1-1 or GST P1-1) involved in cell growth and proliferation; this results in normal blood cell production. It is given intravenously (IV).

Thalomid® (thalidomide)

A medication that reduces the blood supply in the marrow, thereby working to limit the growth of abnormal blood cells. It also acts to interfere with other proteins (cytokines) that promote premature death of cells in the bone marrow. It's taken orally.

Trisenox® (arsenic trioxide)

A medication that inhibits new blood vessel growth and stimulates cell death of abnormal cells. It may increase transfusion independence. It is administered as an intravenous infusion (IV).

Vidaza™ (azacitidine, 5-azacytidine)

A medication that works by preventing a cellular process (methylation) that silences the genes involved in controlling the development of cancer. It may increase red blood cells, transfusion independence, hemoglobin, white blood cells, platelets, and/or decreases the amount of blast cells within the bone marrow. It is categorized as a DNA hypomethylating agent and can be administered intravenously (IV) or subcutaneously (under the skin).

THE MDS FOUNDATION, INC.

The MDS Foundation, Inc. is a global non-profit advocacy organization dedicated to serving the MDS patient, their caregivers, and the professionals that are working to improve the lives of patients living with MDS. The MDS Foundation provides a number of resources which support the Building Blocks of Hope program.

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THE MDS FOUNDATION, INC.

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About the MDS Foundation, Inc.

The MDS Foundation is a non-profit patient advocacy organization that seeks to increase awareness and foster research of the Myelodysplastic Syndromes. The MDS Foundation was established in 1994 by a global group of physicians and researchers. It was the first organization dedicated solely to improving outcomes for patients with MDS.

Every day approximately 238 people worldwide are diagnosed with MDS. The MDS Foundation assists the MDS community by providing awareness, patient and physician education, facilitating global working groups and assisting with clinical research.

Patient Advocacy & Education

The first focus of the Foundation is patient advocacy, support and education. We provide extensive resources to patients and their families about MDS treatment options, upcoming clinical trials, and recent research so that they can make educated decisions about treatment and how to approach the disease. One such program is our Building Blocks of Hope® Patient and Caregiver Resource, which is an extensive print and online patient advocacy initiative that provides a personalized education program for the patient and caregiver to prepare, participate and LIVE with MDS.

We also provide various printed and electronic patient resources and handbooks that are available in multiple languages. In addition to the education component, the MDS Foundation develops patient support groups, hosts Quality-of-Life Patient and Family Forums, and provides access to a full-time Patient Liaison who is available to advise and refer patients to the appropriate resources, studies, and/or specialists.

The Foundation provides patients with preferential referrals to MDS Centers of Excellence to ensure the best possible treatment.

Professional Education

In an effort to advance medical research and improve the quality of healthcare for MDS patients, we disseminate information to professionals about new treatment options and facilitate an informational exchange between healthcare providers. To do this, we host an MDS symposium preceding the annual American Society of Hematology (ASH) Congress Meeting, which allows us to directly educate more than 600 hematologists, with additional access to 20,000 hematologists throughout the full congress meeting.

We also hold a Biennial MDS International Symposium. Since its inception, we have conducted 14 international educational symposia for healthcare professionals in Austria, England, the United States (Chicago, Washington DC), Spain (Barcelona, Valencia), Czech Republic, Sweden, France, Japan, Italy, Greece, Scotland, and Germany. The 15th International Symposium on MDS will be held in Copenhagen, Denmark on May 8-11, 2019. For these symposia, we host an average of 1,000 healthcare professionals and hold three workshops dedicated to specific MDS-related research developments, 10-12 plenary scientific sessions, which consist of abstract presentations, roundtables and debates, as well as an abstract poster viewing. We also offer the opportunity to include corporate satellite symposia, pharmacist and nursing sessions, as well as medical pipeline sessions.

In addition to these programs, the MDS Foundation also maintains an online Clinical Toolbox resource for healthcare professionals and provides educational support for investigators. This clinical toolbox includes a Learning Management System where professionals can earn continuing education credits.

Global Working Groups

International Working Group for Prognosis in MDS (IWG-PM) – The objective of this group is to continue to refine the currently accepted and utilized prognostic scoring systems based on the current research discoveries. (Responsible for continued revisions to the International Prognostic Scoring System (IPSS) for MDS.)

MDS/MPN International Working Group (MDS/MPN IWG) – The overarching goal of this group is to identify key knowledge gaps in the area of MDS/MPNs (Myeloproliferative Neoplasms) and facilitate international, collaborative, translational science geared to rapidly improve our understanding of these neoplasms. (Developed to foster collaboration among translational scientists in the area of myeloid malignancy to better define, risk stratify, and treat patients with overlap syndrome.)

International Nurse Leadership Board (NLB) – Composed of more than 30 members worldwide, and includes 3 subcommittees: *Professional Education, Patient Education, and Quality of Life.*

Research

From 2012–2017, we have awarded more than \$300,000 in grants through our Young Investigator Grant program. These funds have helped to make great strides in research into areas such as aberrant mRNA splicing induced by ZRSR2 mutation in the pathogenesis of myelodysplastic syndromes, unraveling the role of alternative splicing in normal and MDS hematopoietic stem and progenitor cells, HIF-1a as a central pathobiologic mediator of myelodysplastic syndromes, and targeting TP53 gene mutations in myelodysplastic syndromes through functional reconstitution and immune activation. Providing the resources for these research projects directly improves the quality of life of MDS patients and their caregivers.

The Foundation also assists our industry partners through the clinical trial process by raising awareness of these vital trials and incorporating the patient voice into these trials in an effort to increase enrollment of MDS patients. These research related efforts each year bring us closer to a cure for MDS.

The MDS Foundation, Inc. is a 501c3 tax exempt organization.



Contact us

1-800-MDS-0839 (within the US and Canada)
1-609-298-1035 (outside the US)
1-609-298-0590 fax

or write

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Yardville, NJ 08620

Staff

Tracey Iraca **Executive Director**

Tracey joined the MDS Foundation in 2004 as a part-time Patient Coordinator, assisting with patient education programs. As Executive Director, Tracey now oversees all daily business activities, including finances, staffing, and staff projects. She works with the MDSF Board of Directors on strategic planning for meeting the ongoing needs of MDS patients and healthcare professionals. Tracey manages the corporate grants program and is responsible for all corporate relations and new business development. She serves as liaison to the Foundation's International Nurse Leadership Board, International Working Group for Prognosis in MDS (IWG-PM), and MDS/MPN International Working Group (MDS/MPN IWG).

Audrey Hassan **Patient Liaison**

Audrey joined the MDS Foundation in 2002 as the Patient Liaison. She came to the MDS Foundation with over 14 years' experience in patient services working in the Medical Affairs Department of a leading pharmaceutical company. Her primary role is to provide international support to patients, families, and caregivers touched by MDS. Whether it is face-to-face or by telephone or email, Audrey responds to questions regarding MDS, including information on treatment options, clinical trials, financial assistance, as well as providing patients with a priority referral to any MDS Center of Excellence worldwide.

Lea Harrison **Senior Project Manager**

Lea has been associated with the Foundation since 2001. Lea manages all aspects of various CME programs, live symposia and educational meetings for healthcare professionals. She is also responsible for patient educational projects such as the coordination and translation of our Building Blocks of Hope® patient and caregiver resource.

Janice Butchko **Project Manager**

Janice joined the Foundation in 2008. Janice manages our database of patients and healthcare professionals. She is responsible for the coordination, quality control, and production of printed and electronic Foundation materials. Janice is also responsible for patient correspondence, patient programs, and registration for our live patient events.

Deborah (Dee) Murray **Administrative Support**

Dee joined the Foundation in 2005. Dee manages the Foundation's exhibit shipment needs, coordinates mailings, and is responsible for patient information inquiries, ensuring the fulfillment of requests in a timely manner. Dee is also responsible for administrative bookkeeping services.

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The International Nurse Leadership Board (NLB)

The International Nurse Leadership Board (NLB) is composed of more than 30 members worldwide and includes 3 subcommittees: Professional Education, Patient Education, and Quality of Life. It is important to note that all nurse members of this Leadership Board participate on a volunteer basis.

To see a complete list of members, please visit our website at www.mds-foundation.org/nursing-leadership-board-nlb

Mission

The mission of the NLB is to provide an international nursing forum for the development of patient, caregiver and nursing focused initiatives that promote excellence in the comprehensive care of the patient with bone marrow disorders. Members are invited to participate based on demonstrated excellence in nursing practice and research related to patients with bone marrow disorders, including MDS. The NLB represents various regions and practice settings throughout the world.

Accomplishments to date:

- Formalization of the NLB with international representation.
- Facilitation of patient forums in the US and Europe.
- Development of an MDS Nurse Mentorship Program including facilitation/presentation at 6 regional meetings.
- Nursing sessions at international MDSF symposia.
- Poster presentations for QOL data on behalf of the Foundation (at ASH and MDSF symposia).
- Development of Nursing Education Slide Modules for Europe.
- MDS Foundation Newsletter contributions.
- Development and updates of patient and caregiver guides, including our *Building Blocks of Hope: Strategies for Patients and Caregivers LIVING with MDS (BBoH)*.
- Modification of the content for Patient Forums with incorporation of Building Blocks of Hope program information for patients and caregivers – including a new mobile application for patients to track and manage their treatments – MDS Manager.
- ONS Symposia with release of the CJON supplement dedicated to MDS, developed by the NLB.
- MDS Glossary pocket guide to be distributed at patient forums and included in the BBoH.

Goals:

- Expand membership into areas/regions in need.
- Continued translations and cultural adaptations of the Building Blocks of Hope.
- Updates to the Nursing Education Slide Modules – translations and cultural adaptations for various regions.
- Identify new initiatives for nursing education.
- Identify areas that would benefit from development of new materials for patients and caregivers – online and in print.
- Efforts specifically related to quality-of-life:
 - *Age, Comorbidities, Frailty, and Resilience: Strategies to Improve Options for Treatment in MDS* – A wellness and awareness campaign
 - *Transfusions in MDS: When to transfuse and when to initiate disease modifying therapies* – An awareness campaign for providers and patients integrating the most recent transfusion guidelines from ASH
 - *General QOL in MDS: Continued analysis of the patient survey results.*

Patient Services

The MDS Foundation provides a number of patient and caregiver services globally. These include referrals to an MDS Foundation Center of Excellence, referrals to MDS patient and caregiver support services, and a number of print and online patient and caregiver educational materials.

To learn more, contact our Patient Liaison. The Patient Liaison speaks with newly diagnosed patients and their family members daily and can offer support in various forms, including:

- **Referrals to our Centers of Excellence.** Our Patient Liaison will connect newly diagnosed patients and those seeking a second opinion with an MDS specialist in their area of the world and work closely with the patient and referral institution to coordinate a proprietary appointment convenient for the patient.
- **Provide information on current treatment options and available clinical trials.** Our Patient Liaison will answer general questions and offer information regarding current treatment options in MDS and clinical trials open to MDS patients.
- **Provide responses to email and social media inquiries.** Our Patient Liaison will monitor our social media sites and provide timely responses to inquiries submitted on Facebook, Twitter, and via email.
- **Provide a connection between MDS patients.** Our Patient Liaison will maintain a list of patients worldwide that have offered the distribution of their contact information to newly diagnosed patients in need of support and guidance from someone who is currently being treated for MDS.

In-Person patient and caregiver forums

These events are free one-day conferences for MDS patients and their families.

- Registration is required to attend. Learn the latest on the diagnosis and treatment of MDS from leading experts in the field and meet patients and caregivers just like you. Complimentary breakfast and lunch.
- Visit the MDS Foundation website for more information at www.mds-foundation.org/patient-and-family-forums

MDS Foundation Patient Liaison

Audrey Hassan

1-800-MDS-0839 (*within the US*)

1-609-298-1035 (*outside the US*)

1-609-298-0590 fax

email: patientliaison@mds-foundation.org

ahassan@mds-foundation.org

Online patient and caregiver message board

Free online discussion board featuring information exchanged between patients, caregivers, and family members. For more information or to access the forum please go to www.mds-foundation.org/forums/forum/patient-forum

Global patient support groups

The purpose of a support group is to bring individuals together to meet others with similar challenges, discuss feelings, gather information, and socialize.

The MDS Foundation has assisted in establishing over 25 MDS global patient support groups. To view a current listing of support groups, please visit our website at www.mds-foundation.org/global-patient-support-groups.

With your help we can create additional support groups. If you are interested in starting an MDS support group in your area, please contact our Patient Liaison at 609-298-1035 or via email at patientliaison@mds-foundation.org.

MDS Foundation's MDS Centers of Excellence

The MDS Foundation designates MDS Centers of Excellence if the center meets specific criteria in the diagnosis and treatment of MDS. These criteria include:

- An established university (or equivalent) program
- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
- Ongoing research, including Institutional Review Board-approved clinical trials
- Documentation of peer-reviewed publications in the field

Please contact the Foundation for further information.

The MDS Foundation currently has 70 MDS Centers of Excellence throughout the US and 110 MDS Centers of Excellence in 36 countries outside the US. These numbers are continually increasing as more centers are approved.

To see a complete listing, please visit our website at www.mds-foundation.org/mds-centers-of-excellence/



Online Resources

US-Based Resources

MDS Foundation, Inc.

A multidisciplinary, international, nonprofit organization dedicated to the education of professionals, patients, and caregivers; facilitation and support of clinical trials; and development and support of patient advocacy groups.

www.mds-foundation.org

Aplastic Anemia and MDS International Foundation

A nonprofit health organization dedicated to supporting patients and families living with aplastic anemia, MDS, paroxysmal nocturnal hemoglobinuria, and related bone marrow failure disease.

www.aamds.org

Be The Match

A nonprofit organization that's dedicated to helping every patient get the life-saving transplant they need. As trusted leaders in advancing treatments for those facing life-threatening blood cancers, we provide the ground-breaking research, innovative technologies, patient support and education that save lives.

www.bethematch.org

Leukemia and Lymphoma Society

Mission is to cure leukemia, lymphoma, Hodgkin disease, and myeloma and improve the quality of life of patients and their families.

www.lls.org

MDS Alliance

A global health coalition of MDS advocacy groups that aim to provide patients, caregivers and health care professionals with information about MDS.

www.mds-alliance.org

MPN Advocacy and Education International

An organization dedicated to providing the knowledge, support, and resources patients will need as they adjust to living with an MPN through educational symposia in several cities each year, website access, free webcasts of each program, collateral materials, and direction to people, resources and other organizations that can help.

www.mpnadvocacy.com

MPN Research Foundation

Partner. Advocate. Friend. At the MPN Research Foundation, we're committed to standing with you in the fight against polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF) – the group of blood cancers collectively known as myeloproliferative neoplasms.

www.mpnresearchfoundation.org

NCCN Patient and Caregiver Resources

An alliance of leading cancer centers devoted to patient care, research, and education. Our mission is to improve the quality, effectiveness, and efficiency of cancer care so that patients can live better lives. Our vision is to be the world's leader in defining and advancing high-quality, high-value cancer care.

www.nccn.org/patients

Patient Worthy

An online publication that provides relevant information to rare disease patients, caregivers and advocates alike.

www.patientworthy.com

Internationally-Based Resources

AAMAC (Canada)

A leading funder of research into bone marrow failure diseases in Canada. Our volunteer-run organization supports patients and caregivers across the country who are living with aplastic anemia, myelodysplastic syndrome (also called MDS or myelodysplasia) and paroxysmal nocturnal hemoglobinuria (PNH).

www.aamac.ca/e

Denmark MDS Patientstotte Gruppe (Denmark)

This site is for those who have just established the familiarity with the abbreviation MDS, for those who are going to learn to live with MDS and for those who want to keep up with the latest news from the research front.

<http://dkpsg.mds-and-you.info/>

Hematon (The Netherlands)

A patient organization for patients with a haematological-oncological disorder and / or people who have undergone a stem cell transplant. Our goal is to support them in all aspects that life with and after cancer entails. We are also there for relatives and donors of patients. Companion contact, advocacy and information provision are our spearheads. Hematon bundles knowledge and experience.

www.hematon.nl

Leukaemie Hilfe Rhein-Main (Germany)

The Leukemia Aid RHEIN-MAIN is for adult patients with all haematological diseases (concerning the blood and lymphatic system) and their relatives. The LHRM represents its patient interests both regionally and nationally and at European and international level.

www.leukaemihilfe-rhein-main.de

Lyle (Denmark)

A patient association for people affected by lymphoma, leukemia or MDS—directly as patients or indirectly as relatives.

www.lyle.dk

MDS-Patienten Interessengemeinschaft, Deutschland (MDS-PAT-IG) (Germany)

An association that provides education, advocacy, contacts and information.

www.mds-patienten-ig.org

UK MDS Patient Support Group (United Kingdom)

Offers support, information, referral advice, and patient information in the United Kingdom.

www.mdspatientsupport.org.uk

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Building Blocks of Hope is a global print and online patient advocacy initiative providing a personalized educational program for patients and caregivers to prepare, participate, and **LIVE** with Hematological malignancies, including MDS, MPNs and AML. The colors of the Building Blocks of Hope include Tucson Teal, Navajo Red, and Desert Sand. They are reminiscent of a Southwest landscape with the beauty of the night sky over the sand swept deserts and stunning mountain ranges. The colors represent welcoming, warmth, stability, healing, passion, and protection. These colors form the base for the Building Blocks of Hope logo constructed in a wave-like pattern indicating the fluidity of life, health and illness. The single red band which continues up into the plant symbolizes strength and improvement in bone marrow function. The idea of hope for the future and extension of life is emulated in the sprouting plant.

Building Blocks of Hope was created by Sandra Kurtin, Nurse Practitioner and Assistant Professor of Clinical Medicine and Nursing at the University of Arizona Cancer Center, Executive Committee and Board Member of the MDS Foundation, and advocate for patients and caregivers **LIVING** with hematological malignancies. The individual pages have been developed in collaboration with members of the International Nurse Leadership Board of the MDS Foundation, members of the MDS Foundation Board of Directors, and International experts in the diagnosis and treatment of myeloid malignancies. Creative and technical support was provided by Adam Nichols and his team at Markations. Organizational and communications support was provided by Tracey Iraca, Lea Harrison and the MDS Foundation staff. Bone marrow illustrations provided by Kirk Moldoff.

A special thanks to the countless numbers of patients and their caregivers who have participated and continue to participate in clinical trials that have led to a better understanding of and improved treatment strategies for myeloid malignancies. We would not be where we are without your continued involvement. Thank you to our International Colleagues for their work in adapting the Building Blocks of Hope incorporating translation and integration of their culture for regions throughout the world.

We are grateful to all of our supporters; your contributions make the work of the MDS Foundation and support of patients and caregivers **LIVING** with MDS, MPNs and AML possible. A special thanks to my family for understanding my passion for this work.

We hope this project will provide a useful tool for health care professionals working with AML patients. Most importantly, we hope the Building Blocks of Hope will empower AML patients and their caregivers to **LIVE** with AML.



Best regards and best wishes,
Sandy Kurtin

Thank you to Jazz Pharmaceuticals for supporting this resource.



The Building Blocks of Hope is a registered trademark of Sandra Kurtin.
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