LEUKEMIA & LYMPHOMA SOCIETY®

PROVIDING THE LATEST INFORMATION
FOR PATIENTS & CAREGIVERS

Myelodysplastic Syndromes

Revised **2024**

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

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

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

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

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

Contents

Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by:

Rafael Bejar, MD, PhD
Associate Professor of Medicine
Medical Oncologist/Hematologist
Moores Cancer Center
UC San Diego Health
La Jolla, CA

Support for this publication provided by Bristol Myers Squibb and Taiho Oncology, Inc.

Introduction

Myelodysplastic syndromes (MDS) are a group of blood cancers in which the bone marrow does not make enough healthy blood cells. They are also known as "myelodysplastic neoplasms."

Myelodysplastic syndromes are rare. In the United States, an average of 15,529 new cases of MDS were diagnosed each year between 2015 and 2019.* As of 2019, the latest year for which statistics are available, an estimated 58,835 people were living with MDS.

This booklet provides information about MDS for patients and families. It also includes brief descriptions of blood and bone marrow as well as definitions of health terms related to MDS.

The more you know about your disease, the better you can take care of yourself. We hope you will keep this booklet handy, and should you ever feel alone when confronting problems, you will turn to it for information and guidance to find the support and resources that you need. You can also contact us directly at (800) 955-4572.

We are here to help.

All LLS publications mentioned in this booklet are free and can be viewed, downloaded or ordered online at www.LLS.org/booklets.

Feedback. Visit www.LLS.org/PublicationFeedback to give suggestions about this booklet.

*Source: Facts 2022-2023. The Leukemia & Lymphoma Society. April 2023.

New treatments may have been approved since this booklet was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4752.

Myelodysplastic Syndromes

"Cancer" is a term for a group of diseases in which abnormal cells grow uncontrollably in the body. As cancer cells multiply, they can crowd out normal cells and make it hard for your body to work as it should. Cancer can start almost anywhere in the body.

Myelodysplastic syndromes (MDS) are a group of blood cancers. They begin in the bone marrow in cells that would normally develop into blood cells.

There are three main types of blood cells: red blood cells, white blood cells and platelets. Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clotting (clumping together) at the site of an injury.

Most blood cells are made in the bone marrow. Bone marrow is the spongy tissue in the center of bones. Inside the bone marrow, there are blood stem cells, called "hematopoietic" stem cells, which are immature cells that can develop into red blood cells, white blood cells and platelets. A blood stem cell may become a myeloid stem cell or a lymphoid stem cell. Myeloid stem cells develop into immature cells called "blasts" that go through many changes before they eventually develop into red blood cells, platelets, and certain types of white blood cells (basophils, eosinophils, monocytes and neutrophils). For an illustration of how blood cells develop, see **Figure 4** on page 40.

In MDS, a mutation or a series of mutations in the DNA (genetic material) of a single myeloid stem cell results in the formation of an abnormal myeloblast. This abnormal myeloblast does not develop into a healthy functioning blood cell. Instead, it becomes a cancer cell (also referred to as a "blast," "blast cell" or "MDS blast cell").

When a mutated blast cell starts to make copies of itself, it produces clones that have the same mutated DNA. MDS blast cells are often abnormal in shape and size. This condition is called "dysplasia." Abnormal cells may not function properly because of their dysplasia.

As the abnormal blast cells multiply and accumulate in the bone marrow, they take up space. This leaves less room for the production of normal, healthy red blood cells, white blood cells and platelets; there are too many immature blast cells and not enough healthy blood cells. In addition, these abnormal blast cells often die in the bone marrow or soon after entering the bloodstream. As a result, people with MDS have too few heathy blood cells and low blood cell counts.

When this happens, the body's organs and tissues may not receive enough oxygen to work properly due to decreased red blood cells. Also, the body may

not be able to fight infections, due to decreased white blood cells, or form blood clots when they are needed, due to decreased platelets.

Medical Term	Definition
Anemia	Low number of red blood cells
Thrombocytopenia	Low number of platelets ("thrombocyte" is another word for platelet)
Neutropenia	Low number of neutrophils (a neutrophil is a type of white blood cell)

There are several types of MDS. Some types progress slowly and may cause mild-to-moderate anemia or decreases in white blood cells and/or platelets. Other types of MDS may cause more severe low blood cell counts.

Some people with MDS go on to develop another type of blood cancer called acute myeloid leukemia (AML), a fast-growing cancer of the blood and bone marrow. MDS used to be called “smoldering leukemia” or “pre-leukemia,” but only about 30 percent of cases of MDS actually progress to AML. Even if MDS does not develop into AML, it can still be a life-threatening condition.

For more information on acute myeloid leukemia, see the free LLS booklets *Acute Myeloid Leukemia in Adults* and *Acute Myeloid Leukemia in Children and Teens*.

Signs and Symptoms

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

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

Some people are diagnosed with MDS before they have any symptoms. Low blood cell counts from a routine blood test may be the earliest signs of the disease.

For people with symptoms, it is common not to feel good because of the lack of normal, healthy blood cells. This happens when the MDS blast cells in the bone marrow crowd out the normal blood-making cells. As a result, people with MDS may not have enough mature red blood cells, white blood cells and/or platelets, so they often have symptoms related to low blood cell counts.

- Symptoms of anemia (low red blood cell count) include:
  - Fatigue
  - Dizziness
  - Weakness
  - Shortness of breath during normal physical activity
  - Headache
  - Palpitations (noticeably rapid or irregular heartbeat)
  - Pale skin
- Symptoms of neutropenia (low number of neutrophils, a type of white blood important in fighting infections) include:
  - Frequent infections, or infections that do not go away
  - Fever
- Symptoms of thrombocytopenia (low platelet count) include:
  - Bruising easily
  - Prolonged bleeding from minor cuts
  - Pinhead-sized red spots on the skin, called “petechiae”
  - Frequent and/or severe nosebleeds
  - Bleeding gums

It is important to note that symptoms of MDS may be similar to those of other blood disorders or medical conditions. Speak with your doctor if you have any of these symptoms to ensure proper diagnosis and treatment.

Testing for MDS

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

- Determine the MDS subtype
- Estimate how the disease will progress
- Decide on the most appropriate treatment

MDS can sometimes be mistaken for other blood disorders, so repeated blood and bone marrow tests may be needed to establish a definitive diagnosis. It is also important for an experienced hematopathologist to examine laboratory samples under a microscope. A “hematopathologist” is a doctor who has special training in diagnosing diseases of the blood, bone marrow and lymphatic system.

Talk to your doctor about:

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

Some of the tests may be repeated both during and after treatment to find out if treatment is working.

Medical History. Your doctor will take a thorough medical history. This may include asking about your past illnesses, injuries, medications and other treatments. It is also important to tell your doctor if you have had in the past:

- Frequent infections
- Tendency to bruise or bleeding episodes
- Blood transfusions
- Treatment with chemotherapy or radiation
- Exposure to benzene or pesticides

Some illnesses run in families, so the doctor may ask about the health of your blood relatives. Your doctor will ask if you have a family history of blood cancer. In some cases, certain gene mutations present at birth may increase a person's risk of developing MDS or another cancer called acute myeloid leukemia (AML). Patients with a family history of leukemia and/or other cancers occurring in two or more closely related relatives or generations should be evaluated for an inherited predisposition syndrome to help better manage treatment.

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

Complete Blood Count (CBC) With Differential. This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of blood. It also measures the amount of hemoglobin, a protein inside red blood cells that carries oxygen from the lungs to tissues in the body.

The CBC should include a "differential," which measures the numbers of the different types of white blood cells in the sample. There are many types of white blood cells and each help the body fight infection and other diseases. One

important infection-fighting white blood cell is the neutrophil. An "absolute neutrophil count" is a measure of the number of neutrophils in the blood. The absolute neutrophil count is one of the factors incorporated into the most common prognostic scoring systems for MDS. See page 16 for more information on prognostic scoring systems.

Most patients with MDS have low blood cell counts. A low blood cell count is called a "cytopenia." Most often, patients have too few red blood cells. They may also have a low white blood cell count and/or a low platelet count. If there is a low red blood cell count, additional blood tests are done to look for the cause. Low red blood cell counts may be caused by thyroid disease, kidney disease, low vitamin levels (folate or B12) or iron deficiency.

Reticulocyte Count. Reticulocytes are newly produced, relatively immature red blood cells that are still developing. A reticulocyte count measures the level of reticulocytes in the blood. This test is done to determine if the bone marrow is creating red blood cells at an appropriate rate. The body's normal response to anemia is for the bone marrow to produce and release more reticulocytes into the blood. In people with MDS, the reticulocyte count is often low, indicating that the bone marrow is not able to produce enough red blood cells to respond to the anemia.

Peripheral Blood Smear. In this test, a single drop of blood is spread on a glass slide, dried and then stained with a special dye. The sample is viewed under a microscope to examine the number, size, shape, appearance and maturity of various blood cells. In MDS, some blood cells exhibit "dysplasia" (an abnormal shape or size). A peripheral blood smear also checks for blast cells in the blood, which are normally found only in the bone marrow.

Serum Erythropoietin (EPO). This test measures the level of erythropoietin (EPO) in the blood. EPO is a hormone primarily made in the kidneys to stimulate the bone marrow to produce new red blood cells. The kidneys produce and release EPO into the blood in response to low blood oxygen levels. Your doctor may order this test to help determine the cause of anemia that does not appear to be the result of an iron deficiency, vitamin deficiency or internal bleeding. Most patients with MDS-related anemia have an EPO level that is higher than normal, yet lower than it should be for their degree of anemia.

Lactate dehydrogenase (LDH). This test measures the level of lactate dehydrogenase (LDH) in the blood. LDH is a protein found in most cells. When a cell is damaged, LDH is released into the bloodstream. High levels of LDH in the blood may be caused by cancer and may also be a sign that the cancer is widespread. Increased LDH levels can also be caused by damaged red blood cells, indicating that red blood cells are being destroyed in the body more rapidly than they should be.

Human Leukocyte Antigen (HLA) Typing. "HLA typing" is a blood test done to identify certain proteins, called human leukocyte antigens (HLAs) found on the surface of most cells in the body. These proteins make up the body's tissue type, which varies from person to person. They also play an important role in the body's immune response to foreign substances by helping the body distinguish its own cells from foreign cells. An HLA test is done before allogeneic stem cell transplantation to find out if there is a tissue match between a potential donor and the patient receiving the transplant. HLA typing is not used to diagnose MDS; however, it is an important test for newly diagnosed MDS patients if allogeneic stem cell transplantation is being considered as a treatment option. See page 28, *Candidate for Allogeneic Stem Cell Transplantation* for more information on allogeneic stem cell transplantation.

Bone Marrow Aspiration and Biopsy. MDS starts in the bone marrow, the spongy tissue inside the center of most bones. When blood tests show low blood cell counts or the presence of blast cells, your doctor may recommend a test of the bone marrow to see whether your bone marrow is healthy and making normal amounts of blood cells. Doctors use the results from these tests to diagnose and monitor blood and bone marrow diseases, including MDS.

Bone marrow has both a liquid and a solid component.

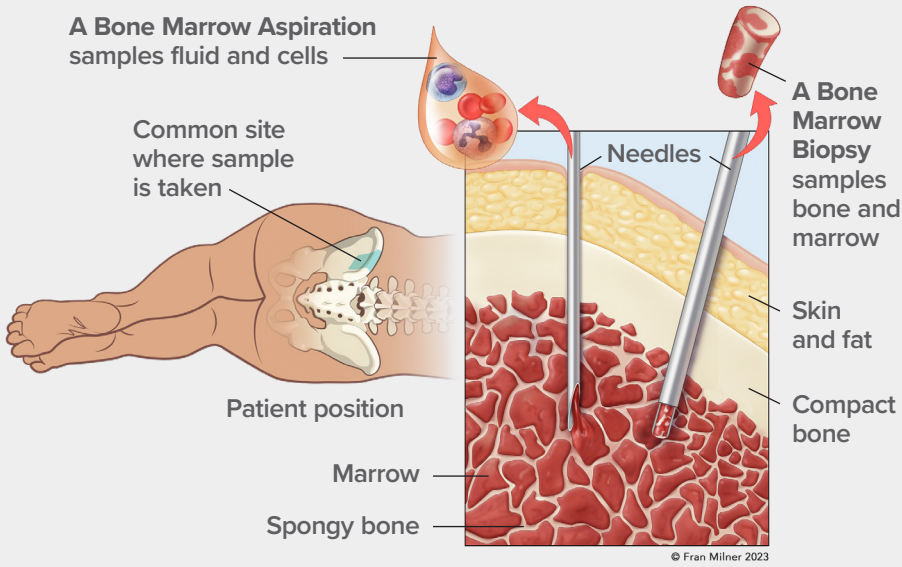
- A bone marrow aspiration is a procedure to remove a sample of the liquid part of the bone marrow.
- A bone marrow biopsy is a procedure to remove a small sample of the solid, spongy part of the bone marrow.

Both tests are frequently done at the same time, either at the doctor's office or in a hospital. Both samples are usually taken from the large hip bone in the lower back. You will likely lie on your stomach or side.

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

For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both needles are inserted through the skin, generally in the same area. Both bone marrow samples are sent to the laboratory where they are examined under a microscope. See **Figure 1** on page 9 for an illustration of the bone marrow tests.

Figure 1. Bone Marrow Aspiration and Biopsy



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

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

Cell Assessment. At the laboratory, a hematopathologist examines the blood and bone marrow cells under a microscope to determine their size, shape and type, and to identify other cell features. As part of this assessment, the hematopathologist will note any signs of MDS, such as one or more of the following:

- Dysplasia (cells that are abnormal in size or shape)
- An abnormal number of any type of blood cells (either too many or too few)
- The percentage of blast cells in the bone marrow
- An abnormally low or high number of cells in the bone marrow
- Presence or absence of ring sideroblasts (red blood cells containing rings of iron deposits)
- The extent of bone marrow fibrosis (scarring) if present
- Presence of blast cells in the blood (blast cells are normally not found in the blood)

The hematopathologist then performs additional tests to see if there are abnormalities in the chromosomes and genes of the cancer cells. These tests help in the diagnosis and treatment of MDS.

Biomarker Testing. These laboratory tests examine the MDS blast cells from the blood and bone marrow to check for certain genes, proteins or other molecules to provide information about a person's cancer. Each person's cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose many types of cancer. It may also be used to help plan treatment, find out how well treatment is working or predict whether cancer will come back or spread to other parts of the body. Biomarker tests for MDS include the following:

Cytogenetic Analysis. Cytogenetic analysis involves testing samples of blood or bone marrow to look for changes in chromosomes. In this test, a hematopathologist uses a microscope to examine the chromosomes inside of cells. Chromosomes are bundles of tightly coiled DNA that contain most of the genetic information in a cell. In patients with MDS, cytogenetic analysis is used to look for abnormal changes in the chromosomes of the cancer cells. Approximately 50 percent of people who have MDS have one or more chromosomal abnormalities, and 10 to 15 percent of patients have complex karyotypes (three or more chromosomal abnormalities).

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

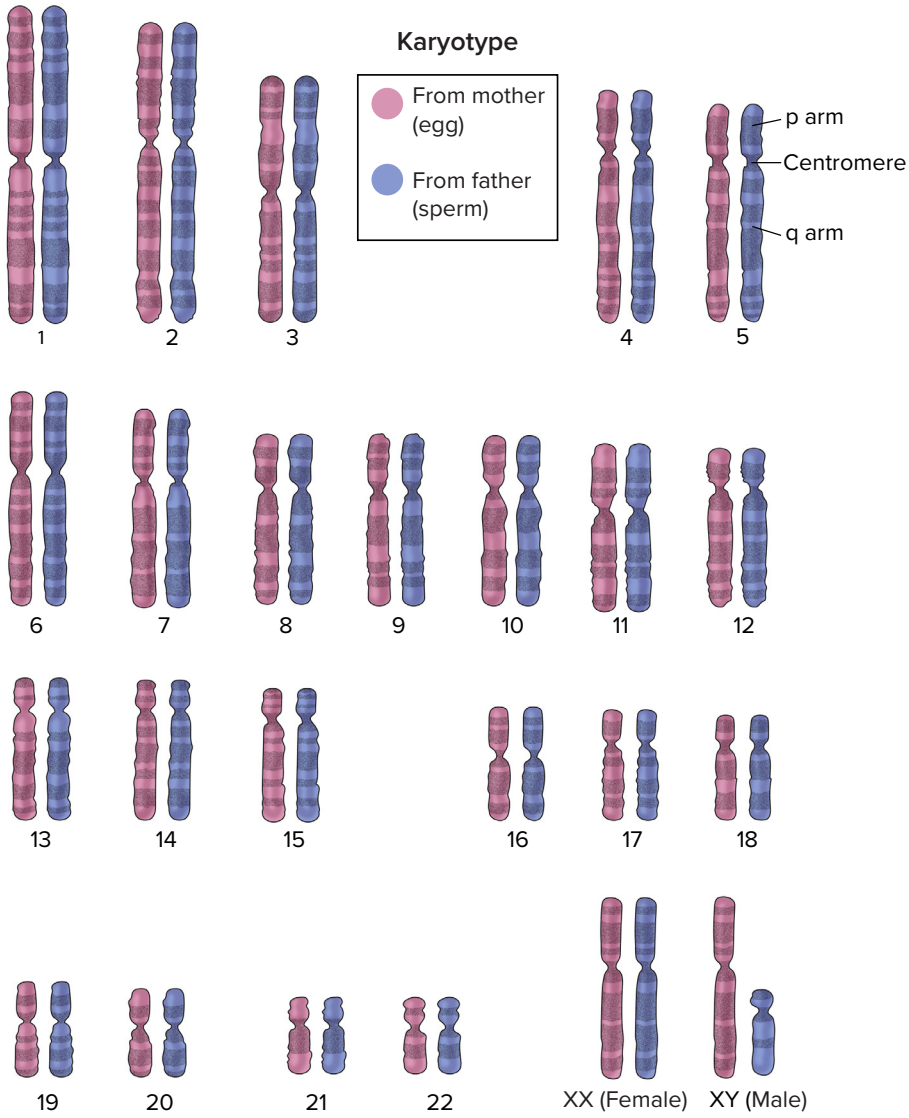
During cytogenetic analysis, the cells in the sample are allowed to grow in the laboratory and then stained to highlight their chromosomes. The chromosomes are then examined under a microscope and photographed to show their arrangement. This is called a "karyotype" (see **Figure 2** on page 11). The karyotype shows if there are any abnormal changes in the size, shape, structure or number of the chromosomes.

In some cases of MDS, the chromosomes of the cancer cells have abnormal changes that can be seen under a microscope. These changes may include one or more of the following: an extra chromosome, fewer chromosomes than normal, or a deletion or an inversion within a chromosome. A deletion occurs when part of a chromosome is missing. An inversion occurs when a part of a chromosome breaks off, turns upside down and reattaches. People with MDS most commonly have abnormalities in chromosomes 5, 7, 8 and 20.

Certain cytogenetic abnormalities are useful in predicting survival or progression to acute myeloid leukemia (AML) and are incorporated into the most common prognostic scoring systems for MDS. See page 16 for more information on

prognostic scoring systems. In some cases, cytogenetic analysis can also help guide treatment decisions. For example, MDS with deletion of the long arm of chromosome 5 as a single abnormality, known as MDS with del(5q), generally has a relatively good prognosis and is highly responsive to treatment with the drug lenalidomide (Revlimid®).

Figure 2. Normal Karyotype



Fluorescence In Situ Hybridization (FISH). This very sensitive test is used to examine genes or chromosomes in cells and tissues. Doctors use FISH testing to detect certain abnormal changes in the chromosomes and genes of cancer cells. This test identifies specific gene or chromosome changes that are common in MDS patients.

Next-Generation Sequencing (NGS). Next-generation sequencing refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. This makes it possible to identify a variety of genetic changes found in a patient's cancer cells.

These changes are important in guiding risk assessment and prognosis and may also inform treatment decisions. The information these tests provide can help doctors determine which patients are at high risk and may need more intensive treatment.

The term "next-generation sequencing (NGS)" is a catch-all term used to describe a number of different modern sequencing technologies. These technologies allow for sequencing of DNA and RNA much more quickly and cheaply than sequencing methods that were used previously.

There are targeted sequencing tests (also called "multigene panels") that look for specific mutations in the cancer cells. These tests focus on specific sets of genes or areas of DNA that are most commonly mutated in MDS. There are also broad DNA sequencing tests that analyze the sequence of large regions of DNA rather than looking for mutations of specific genes. Doctors may also order sequencing of all the DNA in the cancer cells and/or normal cells in the body. This test is known as "whole genome sequencing."

Next-generation sequencing should be done when the cancer is first diagnosed and may also be done after a relapse. This is because it is possible for patients to acquire additional genetic abnormalities after the completion of their initial "first-line" treatment. Next-generation sequencing can also help patients find a clinical trial to join. Some studies enroll people based on the gene mutations in their cancer.

DNA mutations may be found in 80 percent to 90 percent of patients with MDS (see **Table 1** on page 13). Certain mutations are associated with either a better or a worse prognosis (outcome) and may help plan treatment. While some of the mutations in **Table 1** are not currently used in the routine diagnosis and treatment planning, they may represent important targets in the future.

Certain mutations are important in guiding risk assessment and prognosis, and they are also used to guide treatment decisions. For example:

- Some patients may be eligible to receive drugs called "inhibitors" that target specific gene mutations such as those in *FLT3, IDH1* and *IDH2*.
- Although it is rare, some MDS patients have a mutation of the *NPM1* gene. These patients may be potentially cured with cytarabine (Ara-C, Cytosar®) and an allogeneic stem cell transplantation.

Other mutations are associated with a better or worse prognosis or can help predict response to different treatments.

- Patients with only an *SF3B1* mutation tend to have a more favorable prognosis, favorable outcomes, and longer survival.
- Mutations of several other genes, including *TP53, EZH2, RUNX1* and *ASXL1,* are associated with a decrease in overall survival, according to several studies.

See the free LLS booklets *Understanding Genetics, Biomarker Testing for Cancer Treatment* and *Understanding Lab and Imaging Tests* for more information about these tests.

Table 1. Common Gene Abnormalities in MDS

Gene	% of MDS patients
SF3B1	28
TET2	21
ASXL1	14
SRSF2	12
RUNX1	9
TP53	8
U2AF1	7
EZH2	6
NRAS	4
JAK2	3
ETV6	3
CBL	2
IDH2	2
NPM1	2
IDH1	1
KRAS	<1
GNAS	<1
PTPN11	<1
BRAF	<1
PTEN	<1
CDKN2A	<1

Source: Garcia-Manero G. Myelodysplastic syndromes: 2023 update on diagnosis, risk-stratification, and management. *American Journal Hematology*. 2023;98(8):1307-1325.

Diagnosis

The classification of MDS has evolved over the last several decades. In 1982, the French-American-British (FAB) Work Group devised a system for classifying myelodysplastic syndromes. The FAB classification divided MDS into five subtypes based on the percentage of blast cells present in the bone marrow and the peripheral blood (blood that is circulating throughout the body); the number of ring sideroblasts (portion of immature red blood cells containing rings of iron deposits around the center); and the degree of monocytosis (elevated number of monocytes, a type of white blood cell).

The FAB classification is rarely used anymore. However, definitions of the five FAB subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation and chronic myelomonocytic leukemia) are included in the *Health Terms* section starting on page 45.

In 2001, the World Health Organization (WHO) proposed a new classification that was a modified version of the original FAB classification. Since then, the WHO classification has been updated, most recently in 2022, and describes several subtypes of MDS.

An MDS diagnosis and subtype are determined from the results of blood and bone marrow test and are based on:

- Cytopenias (low blood cell counts). People with MDS have one or more low blood cell counts (red blood cells, white blood cells and/or platelets).
- Percentage of myeloblasts in the bone marrow and peripheral blood. In healthy people, there are usually no blast cells in the blood, and blast cells should make up less than 5 percent of all bone marrow cells. In MDS patients, up to 20 percent of cells in the bone marrow may be blast cells. A blast cell count of 20 percent or higher is considered acute myeloid leukemia (AML). Patients with 10 percent to 19 percent bone marrow blasts cells may also be diagnosed with AML, and not MDS, if they have certain genetic mutations more typically found in specific types of AML.
- Dysplasia (cells that have an abnormal size or shape). In people with MDS, dysplasia affects at least 10 percent of red blood cells, white blood cells and/or platelets.
- Specific MDS-associated biomarkers such as isolated del(5q) chromosome abnormality, *SF3B1* gene mutation or *TP53* gene mutation.

The 5th edition of the WHO Classification of MDS, which was updated in 2022, renamed MDS to “myelodysplastic neoplasms” (while retaining the “MDS” abbreviation). It now groups MDS based on genetic abnormalities and morphologically defined features (the appearance and number of the cells under the microscope). See **Table 2** on page 15.

Table 2. The WHO 2022 Classification of MDS

MDS with Defining Genetic Abnormalities
MDS with low blasts and isolated 5q deletion (MDS-5q) ○ Cytogenetics: del(5q) alone or with 1 other abnormality other than a chromosome 7 abnormality ○ Blasts: bone marrow blasts less than 5 percent and peripheral blood blasts less than 2 percent
MDS with low blasts and *SF3B1* mutation (MDS-*SF3B1*) ○ Mutations: *SF3B1* mutation ○ Cytogenetics: absence of 5q deletion, monosomy 7 or complex karyotype (3 or more chromosomal abnormalities) ○ Blasts: bone marrow blasts less than 5 percent and peripheral blood blasts less than 2 percent ○ Most patients in this group have increased ring sideroblasts (immature red blood cells that have rings of iron deposits). Detection of 15 percent or more ring sideroblasts in the absence of an *SF3B1* mutation would place a patient into the separate category of MDS with ring sideroblasts (MDS-LS-RS).
MDS with biallelic *TP53* inactivation (MDS-bi*TP53*) ○ Mutations: 2 or more *TP53* mutations or 1 mutation with evidence of *TP53* copy number loss or cnLOH* ○ Cytogenetics: usually a complex karyotype ○ Blasts: bone marrow and peripheral blood blasts less than 20 percent
Morphologically defined
MDS with low blasts (MDS-LB) ○ Blasts: bone marrow blasts less than 5 percent and peripheral blood blasts less than 2 percent
MDS with low blasts and ring sideroblasts (MDS-LB-RS) ○ Bone marrow blasts are less than 5 percent and peripheral blood blasts are less than 2 percent ○ Ring sideroblasts are greater than 15 percent without an *SF3B1* mutation
MDS, hypoplastic (MDS-h) ○ Blasts: bone marrow blasts less than 5 percent and peripheral blood blasts less than 2 percent ○ Bone marrow cellularity 25 percent or less (adjusted for age). Bone marrow cellularity refers to the amount or percentage of blood stem cells relative to bone marrow fat.

MDS with increased blasts
○ MDS-IB1
  ○ Bone marrow blasts between 5 and 9 percent or peripheral blood blasts between 2 and 4 percent
○ MDS-IB2
  ○ Bone marrow blasts between 10 and 19 percent or peripheral blood blasts between 5 and 19 percent or
  ○ Auer rods with any number of blasts up to 9 percent. Auer rods are clumps of abnormal material that form needle-like structures sometimes found in myeloblasts.
○ MDS with fibrosis (MDS-f)
  ○ Blasts: bone marrow blasts between 5 and 19 percent and peripheral blood blasts between 2 and 19 percent
  ○ Fibrosis: build up of scar tissue in the bone marrow

*cnLOH: copy number neutral loss of heterozygosity

Source: Khoury JD, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia* and Mortuza S, et al. Myelodysplastic neoplasms (MDS) with Ring Sideroblasts or SF3B1 mutations. *Current Oncology.* See *References* on page 52.

Treatment Planning

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

If time allows, you may want to seek a second opinion from another doctor, as it may help you feel more confident about the recommended treatment plan. The second opinion should come from another hematologist-oncologist, and preferably one who also treats MDS. These doctors usually have the most knowledge and experience about the latest treatment options for MDS.

If you are unsure about getting a second opinion or feel uncomfortable about how to tell your current doctor that you are seeking one, call our Information Specialists at (800) 955-4572 to discuss a way to do so that makes you feel comfortable. You may also want to check in advance with your insurance company to be sure that your plan covers the cost of getting a second opinion.

See the free LLS booklet *Choosing a Specialist or Treatment Center* for more information about choosing a doctor and treatment center.

Prognostic Scoring Systems. A "prognosis" is a prediction of the likely outcome of a disease. It is your doctor's best estimate of how the cancer will affect you and how it will respond to treatment. In MDS, an important part of prognosis is predicting overall survival and whether the disease will transform to AML.

In MDS, doctors use prognostic scoring systems to estimate prognosis and guide treatment planning. Doctors use certain factors to predict prognosis. These factors are related to the results of blood tests, bone marrow assessment and biomarker testing. These factors are combined to develop scoring systems. Each prognostic factor is assigned a number based on its severity. The scores for all the factors are then added together to put people into MDS risk groups.

Prognostic scoring systems for MDS include these three scoring systems:

- The International Prognostic Scoring System (IPSS)
- The International Prognostic Scoring System-Revised (IPSS-R)
- The International Prognostic Scoring System-Molecular (IPSS-M)

The International Prognostic Scoring System (IPSS). The IPSS was the first widely used prognostic scoring system for MDS when it was developed in 1997. It scores three main factors:

- Percentage of blast cells in the bone marrow
- Cytogenetics (chromosomal changes)
- Cytopenias (low blood cell counts)

Points are assigned to each of the three factors, and then the points are added together to determine one of four overall risk scores: Low, Intermediate-1, Intermediate-2 and High. See **Table 3** below.

The following examples show how IPSS scores are used to determine the IPSS risk category for an MDS patient:

- A patient with less than 5 percent blast cells (0 points); no chromosome changes (0 points); and anemia but normal platelet and neutrophil (white blood cell) counts (0 points), would have a total IPSS risk score of 0. This patient would be categorized in the IPSS "Low" Risk Group.
- A patient with 5 to 10 percent blast cells (0.5 points); an abnormal chromosome 7 (1 point); and normal neutrophil (white blood cell) counts but with low red blood cell and platelet counts that indicate anemia and thrombocytopenia (0.5 points), would have a total IPSS risk score of 2. This patient would be categorized in the IPSS "Intermediate-2" Risk Group.

The IPSS is still in use today but has largely been replaced by newer versions.

Table 3. IPSS Prognostic Scoring System and Risk Groups

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
Percent of blast cells in bone marrow ○ Less than 5 = 0 points ○ 5 to 10 = 0.5 points ○ 11 to 20 = 1.5 points ○ 21 to 30 = 2 points	○ 0 points = Low ○ 0.5 to 1 point = Intermediate-1 ○ 1.5 to 2 points = Intermediate-2 ○ 2.5 or more points = High
Cytogenetics (chromosome changes) ○ None, del(5q), del(20q) = 0 points ○ 3 or more abnormalities, abnormal chromosome 7 = 1 point ○ Other abnormalities = 0.5 points	
Number of cytopenias (low blood cell counts) ○ None or 1 = 0 points ○ 2 or 3 = 0.5 points	

Key. IPSS, International Prognostic Scoring System; del, deletion; q, the long arm of a chromosome (the lower half).

The International Prognostic Scoring System-Revised (IPSS-R). The 2012 revised version of the IPSS aims to improve the ability to further define disease risk by increasing the prognostic significance of cytogenetic (chromosomal) abnormalities. It scores the types and severity of cytopenias (low blood cell counts). It also gives a number value to a wider range of chromosomal changes. It classifies myelodysplastic syndromes into five risk groups: Very Low, Low, Intermediate, High and Very High. See **Table 4** on page 18.

The following example shows how IPSS-R scores are used to determine the IPSS-R risk group for an MDS patient:

- A patient who has a bone marrow blast percentage of 3 percent (1 point); normal cytogenetics (1 point); a hemoglobin concentration of greater than 10 grams per deciliter (0 points); a platelet count of 101 (0 points); and an absolute neutrophil count (ANC) of 0.7 (0.5 points) would have a total IPSS-R risk score of 2.5 points. This patient would be categorized in the IPSS-R "Low" risk group.

Table 4. IPSS-R Prognostic Scoring System and Risk Group

Prognostic Factors Scored	Risk Groups Based on Total Risk Score
Percent of blast cells in bone marrow ○ Less than or equal to 2 = 0 points ○ Greater than 2 to less than 5 = 1 point ○ 5 to 10 = 2 points ○ Greater than 10 = 3 points	○ 1.5 or less points = Very Low ○ 2 to 3 points = Low ○ 3.5 to 4.5 points = Intermediate ○ 5 to 6 points = High ○ 6.5 or more points = Very High
Cytogenetics (chromosome changes) ○ –Y, del(11q) = 0 points ○ Normal, del(5q), del(12p), del(20q), double including del(5q)* = 1 point ○ del(7q), +8, +19, i(17q), any other single or double independent clone** = 2 points ○ –7, inv(3), +(3q), del(3q), double including –7/del(7q),complex: 3 abnormalities = 3 points ○ More than 3 abnormalities = 4 points	
Hemoglobin concentration (g/dL) ○ Equal to or greater than 10 = 0 points ○ 8 to less than 10 = 1 point ○ Less than 8 = 1.5 points	
Platelet count (x 10^9/L of blood) ○ Equal to or greater than 100 = 0 points ○ 50 to less than 100 = 0.5 points ○ Less than 50 = 1 point	
Absolute neutrophil count ([ANC] x 10^9/L of blood) ○ Equal to or greater than 0.8 = 0 points ○ Less than 0.8 = 0.5 points	

*del(5q) plus another cytogenetic abnormality.

**A single clone can have many abnormalities, all of them occurring simultaneously in the same cell.

Key. IPSS-R, International Prognostic Scoring System-Revised; ANC, absolute neutrophil count; del, deletion; g/dL, grams/deciliter; inv, an inversion in a chromosome; p, the short arm of a chromosome (the upper half); q, the long arm of a chromosome (the lower half).

A link on the internet to the Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes Risk Assessment Calculator is available for use by anyone at: https://www.mds-foundation.org/calculator/index.php

The IPSS and the IPSS-R scoring systems alone are not absolute predictors of risk. They do not take into account gene mutations that can influence the prognosis or consider other factors common to older patients, such as comorbidities (other illnesses or diseases), previous cancers or other health issues. Still, scoring system numbers are very important because they are indicators of the patient's prognosis. The IPSS-R has demonstrated that it predicts prognoses better than the IPSS; however, the IPSS continues to be used to determine eligibility for some clinical studies.

The International Prognostic Scoring System-Molecular (IPSS-M). The IPSS-R was updated in 2022 to include the effect of MDS-associated gene mutations. Like the IPSS-R, the IPSS-M considers blood counts, such as anemia and low platelet counts, the percentage of bone marrow blasts and the presence of certain chromosomal abnormalities. Unlike the IPSS-R, the IPSS-M also considers whether certain gene mutations are present and how many genes are mutated. While the IPSS-M requires results from biomarker testing and is more complex to calculate, it has been shown to be more accurate than the IPSS and IPSS-R. The IPSS-M classifies MDS into six risk groups: Very Low, Low, Moderate Low, Moderate High, High and Very High.

A link on the internet to the International Prognostic Scoring System-Molecular (IPSS-M) for Myelodysplastic Syndromes Risk Assessment Calculator is available for use by anyone at https://mds-risk-model.com/

Risk Groups. Each prognostic scoring system has lower-risk and higher-risk MDS groups (see **Table 5** on page 20). The risk groups are based on patient scores. Note that prognostic systems and risk groups do not predict how a patient who has an MDS will respond to treatment. They can, however, indicate how the disease is likely to progress over time without treatment. Doctors use prognostic scoring systems to determine their patient's risk group and plan treatment.

Lower-risk MDS tends to grow and progress slowly. Patients may have fewer signs and/or symptoms of disease. Therefore, less intensive treatment is frequently needed. In contrast, higher-risk MDS is likely to progress more quickly. Without treatment, higher-risk MDS may also progress to AML in a shorter time. Higher-risk MDS may also cause more signs and/or symptoms and health complications within a shorter time. Therefore, more intensive treatment is often required.

Table 5. Risk Groups: Lower-Risk Versus Higher-Risk Myelodysplastic Syndromes

Lower-Risk Groups	Higher-Risk Groups
○ **IPSS** Low and Intermediate-1 ○ **IPSS-R** Very Low, Low, Intermediate ○ **IPSS-M** Very Low, Low, and Moderate Low	○ **IPSS** Intermediate-2 and High ○ **IPSS-R** Intermediate, High, Very High ○ **IPSS-M** Moderate High, High, and Very High

This table includes lower-risk and higher-risk MDS categories from each of the three main prognostic scoring systems.

Key. IPSS, International Prognostic Scoring System; IPSS-M, International Prognostic Scoring System-Molecular; IPSS-R, International Prognostic Scoring System-Revised.

Treatment

New treatments may have been approved since this booklet was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4752.

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. Like all treatment options, clinical trials have risks and benefits. By considering all your treatment options, including clinical trials, you will be taking an active role in a very important decision that affects you. For more information on clinical trials, see page 33.

MDS occurs more frequently in older adults; the median age at diagnosis is 77 years. The treatment of MDS in older patients is a challenge. As people age, they can have more difficulty tolerating more intense cancer treatments. Older patients are also more likely to have comorbidities (other medical problems), including diabetes, high blood pressure, high cholesterol levels and heart disease. They may also have a history of stroke or lung disease. These comorbidities can limit treatment options. Many older patients are not offered intensive chemotherapy because they are considered unlikely to survive the rigors of treatment. In some cases, intensive chemotherapy can actually shorten lives.

Not everyone with MDS receives the same type of treatment. Your doctor will tailor your treatment based on your MDS subtype, your prognostic score, and other factors including your age and overall health, caregiver and social support, and goals and preferences.

Some people diagnosed with MDS who do not have very low blood cell counts or other symptoms may not need to start treatment immediately. Instead, the doctor may recommend regular exams and laboratory tests to monitor their condition.

The treatment approach to MDS depends largely on risk stratification of an individual's disease, most commonly using the Revised International Prognostic Scoring System (IPSS-R) or the International Prognostic Scoring

System-Molecular (IPSS-M). MDS can be treated to improve blood cell counts, relieve symptoms and slow disease progression. Certain patients may be cured with allogeneic stem cell transplantation. Many MDS patients, however, are not good candidates for allogeneic stem cell transplantation due to advanced age and other medical conditions.

Supportive Care. Supportive care refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal of supportive care is to improve the patient's quality of life and to relieve discomfort as much as possible. Supportive care is an important part of MDS treatment that helps relieve or prevent the symptoms of MDS, but it does not treat the disease itself.

Supportive care is important regardless of other treatments for MDS. Supportive care may be given alone or along with other treatments for MDS. Supportive care for MDS should be given whenever a person has symptoms that need to be controlled. Supportive care may include blood transfusions, growth factors and antibiotics.

Blood Transfusions. Blood transfusions are part of supportive care for many people with MDS. They help to relieve symptoms of low red blood cell counts and/or low platelet counts. A transfusion can help relieve symptoms for a short time, but more transfusions may be needed over time.

Red Blood Cell Transfusions. A red blood cell transfusion is a procedure in which donated red blood cells are slowly injected into a patient's body through a vein. The doctor will determine whether a transfusion is appropriate based on the patient's hemoglobin concentration, the severity of symptoms, the patient's other treatments and the availability of blood products.

Some patients may require frequent transfusions of donor red blood cells. While transfusions are effective at restoring healthy blood cell levels, many patients become dependent on them, placing them at risk of developing a condition called "iron overload."

Red blood cells contain iron. When a person receives a large number of red blood cell transfusions, too much iron can build up in the liver, heart and other organs, affecting how they work.

Iron overload requires special treatment to remove the extra iron from the body. The treatment is called "iron chelation" therapy. Drugs called "chelating agents" bind with the iron so the body can get rid of it. It can be challenging for patients to tolerate these medications, so it is important for patients to discuss the risks and benefits of this therapy with their doctors.

The most common drugs used in iron chelation therapy include:

- **Deferasirox (Exjade®, Jadenu®).** These iron chelators are taken by mouth. The newer preparation, Jadenu®, can be easier on digestion in some patients, but it is the same medicine as Exjade®.

- **Deferoxamine mesylate (Desferal®).** This drug is usually given subcutaneously (a slow infusion under the skin).

Platelet Transfusion. Platelet transfusions help increase the number of platelets in the blood. They are typically required if a patient's platelet count falls below 10,000/mcL, or if a patient has sudden, severe bleeding. A platelet transfusion is a slow injection of platelets from a donor into a vein.

For patients with severe thrombocytopenia (low platelet count) or who have uncontrolled bleeding that does not respond to platelet transfusions, the antifibrinolytic drugs **aminocaproic acid** and **tranexamic acid** may be recommended. These medications work by stopping blood clots from breaking down too quickly and can reduce blood loss in patients who have recurrent bleeding.

For more information on blood transfusions, see the free LLS booklet *Blood Transfusion*.

Treating and Preventing Infections Due to Low White Blood Cell Counts. MDS and its treatments often cause drops in white blood cell counts. Having a low number of white blood cells can increase the risk of infection. In some cases, infections may be frequent and severe. Members of the treatment team will pay close attention to any infection or unexplained fever. If a bacterial infection is identified or suspected, patients are treated with antibiotics. Antiviral drugs may be used to treat certain viral infections, and antifungal medications may be used to treat certain fungal infections.

White blood cell transfusions are generally not used for patients with MDS. For patients with persistent neutropenia (low white blood cell count) and recurrent or resistant infections, doctors sometimes use growth factors to help increase a patient's white blood cell count. Growth factors stimulate the bone marrow to make new white blood cells. Granulocyte colony-stimulating factors (G-CSF), such as **filgrastim** and **pegfilgrastim**, stimulate the production and release of neutrophils into the bloodstream. Granulocyte-macrophage colony-stimulating factors (GMCSF), such as **sargramostim (Leukine®)**, stimulate the production of three types of white blood cells: neutrophils, macrophages and dendritic cells.

During treatment for MDS, a low white blood cell count can lead to infections from bacteria, viruses and fungi that are normally present in the environment, on the skin, in the nose and mouth, on the gums or in the colon. Because of the increased risk of infection, medical staff and all family and friends need to practice frequent and vigorous handwashing and take other precautions to avoid exposing patients to bacteria, viruses and other infection-causing agents.

Patients at home should seek medical attention immediately if any signs of infection develop. A temperature of 100.4 °F or higher, or the onset of chills, may be the only sign of infection in a patient who has a very low white blood cell

count. Other signs of infection may include persistent coughing, sore throat, pain during urination, or diarrhea.

Patients with MDS are advised to receive certain vaccinations. For adult patients, these include vaccinations for influenza and pneumococcal pneumonia. MDS patients should also receive the inactivated vaccine for the herpes virus, called **Shingrix**. COVID-19 and RSV vaccines are also recommended. Talk to your doctor for more information. If a family member or friend of the patient receives a live vaccine, they should not go near the patient for a certain period of time. (Ask your doctor about the time period needed.)

Treatment of Lower-Risk MDS. Lower-risk MDS is typically slow-growing, and the risk of progression to acute myeloid leukemia (AML) is low. The primary goals for patients with lower-risk MDS is to improve blood cell counts, reduce the need for blood transfusions, lower the risk of infection and improve quality of life. Patients with lower-risk disease are initially treated for specific complications of the disease, such as low blood cell counts.

Lower-risk MDS includes the following prognostic risk groups:

- IPSS: Low and Intermediate-1
- IPSS-R: Very Low, Low, and Intermediate
- IPSS-M: Very Low, Low, and Moderate Low

Lower-risk patients without symptoms may not need immediate treatment. People with lower-risk MDS may have decreased levels of red blood cells, white blood cells or platelets. If these levels are not low enough to cause symptoms, the doctor may recommend the “watch-and-wait” approach. This approach involves careful monitoring that includes regular exams and blood tests. Bone marrow tests may be necessary if the doctor suspects MDS is progressing.

If there are signs and symptoms that the MDS is progressing, the doctor will recommend starting treatment. Therapy for lower-risk MDS is selected based on the type of low blood cell count. Management focuses on improving quality of life by treating symptoms and reducing the number of required transfusions.

The current standard of care for patients with lower-risk MDS is typically supportive care and disease-modifying treatment. Disease-modifying treatment for MDS is a treatment that that delays or slows the progression of MDS. This can help MDS patients have fewer blood transfusions.

Red Blood Cell Growth Factors. Many patients face challenges in managing their anemia, causing potentially serious health complications that can affect quality of life. Erythropoietin (EPO) is a hormone needed for normal production of red blood cells. It is made primarily by the kidneys and is released into the blood in response to decreased blood oxygen levels. Drugs with synthetic EPO, called erythropoietin-stimulating agents (ESAs), are available to help stimulate

the bone marrow to make red blood cells. They are used for MDS patients who have anemia associated with low EPO levels. **Epoetin alfa** and **darbepoetin alfa (Aranesp®)** are synthetic forms of EPO. They are given by subcutaneous injection (under the skin). Darbepoetin alfa is a longer-acting form of EPO than epoetin alfa.

Treatment with ESAs may decrease the need for red blood cell transfusions and improve survival outcomes in some patients. Some patients, however, do not respond to the medication or become resistant to therapy. Your doctor may check your body's own EPO level prior to starting a red blood cell growth factor to see how likely you are to respond to this treatment.

ESAs are not FDA-approved to treat MDS, but they can be used as "off-label" treatments. "Off-label" prescribing is when a doctor gives a drug that is FDA approved to treat one condition for another condition.

Erythroid Maturation Agents. These drugs are used to treat anemia in adults who need to have regular blood cell transfusions. It can be used when erythropoietin-stimulating agents (ESAs) are not effective in increasing red blood cell production or as the initial therapy used to treat transfusion-dependent anemia. **Luspatercept-aamt (Reblozyl®)** is an erythroid maturation agent that helps the bone marrow make more healthy, mature red blood cells.

See **Table 6**, *Drug Classes and Drug Mechanisms* and **Table 7**, *FDA-Approved Drugs to Treat MDS* starting on page 30 for more information on luspatercept-aamt.

Immunomodulators. Lenalidomide (Revlimid®) belongs to a class of drugs known as immunomodulators. People with MDS who need frequent red blood cell transfusions and have MDS cells that are missing a part of chromosome 5, referred to as del(5q), may be treated with lenalidomide. Treatment with lenalidomide may reduce the need for red blood cell transfusions in people with MDS with del(5q). It is also being studied in other lower-risk MDS patients who do not have this abnormal chromosome.

See **Table 6**, *Drug Classes and Drug Mechanisms* and **Table 7**, *FDA-Approved Drugs to Treat MDS* starting on page 30 for more information on lenalidomide.

Platelet Growth Factors. MDS patients with a low platelet count can experience easy bruising or uncontrolled bleeding. Low platelet counts are also a common side effect of chemotherapy. Thrombopoietin (TPO) is a hormone made in the body that helps in the production of platelets. **Romiplostim (Nplate®)** and **eltrombopag (Promacta®)** are drugs that act like TPO. These drugs are being investigated for treatment of MDS patients who have low platelet counts. Although romiplostim and eltrombopag are not approved specifically for the treatment of MDS, they can sometimes be helpful for lower-risk MDS patients who have very low platelet counts. It is important for the patient and doctor to discuss the potential risks and benefits of these treatments.

Immunosuppressive Therapy. Drugs that suppress certain parts of the immune system can help some patients with lower-risk MDS. In some types of MDS, lymphocytes, a type of white blood cell, may attack the bone marrow, causing it to stop making enough healthy blood cells. Immunosuppressive therapy lowers the body's immune response to allow bone marrow stem cells to grow and make new blood cells.

Antithymocyte globulin (ATG, Atgam®, Thymoglobulin®), cyclosporine (Neoral®, Sandimmune®) and **tacrolimus (Prograf®)** are the main immunosuppressive therapy drugs used to treat MDS. However, these drugs do not work well for all types of MDS. They are most effective when the disease has features associated with an immune-system attack, such as:

- A low number of cells in the bone marrow (sometime referred to as hypoplastic MDS)
- The presence of a paroxysmal nocturnal hemolysis (PNH) clone in the blood

Antithymocyte globulin is given by IV infusion over a few hours for 4 consecutive days in the hospital. Cyclosporine and tacrolimus are taken orally. It can take several weeks for patients to respond to immunosuppressive therapy. These immunosuppressive therapies are not FDA-approved to treat MDS, but they can be use as off-label treatments for MDS.

Hypomethylating Agents. If other treatments are not effective in helping blood cell counts, hypomethylating agents may be an option. Hypomethylating agents are a type of chemotherapy that work by blocking the DNA that helps cancer cells grow. Doctors may prescribe hypomethylating agents to lower-risk MDS patients who do not respond to other drugs or whose disease worsens.

Hypomethylating agents may help improve blood cell counts, which may lead to fewer blood transfusions and improved quality of life. They may also slow the progression of MDS. These drugs are, in general, less likely to produce severe side effects. **Azacitidine (Vidaza®)**, **decitabine (Dacogen®)** and **decitabine and cedazuridine (Inqovi®)** are hypomethylating agents approved to treat MDS.

See **Table 6**, *Drug Classes and Drug Mechanisms* and **Table 7**, *FDA-Approved Drugs to Treat MDS* starting on page 30 for more information on hypomethylating agents.

Allogenic Stem Cell Transplantation. Certain patients may be cured with an allogeneic stem cell transplantation. Some lower-risk patients, particularly younger patients, may benefit from allogeneic stem cell transplantation. Patients may be considered candidates for this treatment if they have been exposed to multiple therapies and have not responded to treatment. See page 28, *Candidate for Allogeneic Stem Cell Transplantation* for more information on allogeneic stem cell transplantation. These patients may also be candidates for clinical trials.

Higher-Risk MDS. Higher-risk MDS tends to grow quickly and is more likely to progress to acute myeloid leukemia (AML). Patients with higher-risk MDS are also more likely to have multiple types of cytopenias (low blood cell counts) and require blood transfusions and treatment for infections.

Treatment goals for higher-risk MDS patients include:

- Slowing disease progression and improving survival for patients who are not candidates for stem cell transplantation
- Preventing MDS from progressing to acute myeloid leukemia (AML)
- Reducing or eliminating the need for transfusions
- Potentially achieving a cure through stem cell transplantation

Higher-risk MDS includes the following risk groups:

- IPSS: Intermediate-2, High
- IPSS-R: Intermediate, High, and Very High
- IPSS-M: Moderate High, High and Very High

The type of treatment given to higher-risk patients depends on whether they are candidates for an allogeneic stem cell transplantation. Regardless of therapy, supportive care should be given to all patients. See page 21 for more information on supportive care.

Not a Candidate for Stem Cell Transplantation. Most higher-risk MDS patients are not eligible for stem cell transplantation. This may be due to advanced age, other major health problems or unavailability of a stem cell donor. Treatment for those not eligible for stem cell transplantation may include:

Hypomethylating Agents. The major alternative to stem cell transplantation is hypomethylating agents. These drugs are a type of chemotherapy drug that works by blocking the DNA that helps cancer cells grow. Using one of these drugs may help improve blood cell counts which may lead to fewer blood transfusions and improved quality of life. They may also slow the progression of MDS. These include:

- **Azacitidine (Vidaza®)**
- **Decitabine (Dacogen®)**
- **Decitabine and cedazuridine (Inqovi®)**

See **Table 6**, *Drug Classes and Drug Mechanisms* and **Table 7**, *FDA-Approved Drugs to Treat MDS* starting on page 30 for more information on hypomethylating agents.

Targeted Therapy. This type of treatment uses drugs or other substances to identify and attack specific types of cancer cells with less harm to normal cells.

Not all cancers have the same targets. Each type of targeted therapy works a little bit differently, but they all interfere with the growth and survival of cancer cells. To find the most effective treatment, your doctor may run tests to identify genes, proteins and other factors in your cancer cells. This helps the doctor choose the most effective treatment for you based on the specific factors of your disease. Most of these targeted therapies are not FDA-approved to treat MDS but can be used as an off-label treatment for some MDS patients.

Targeted therapy may be used alone or in combination with chemotherapy. Some types of targeted therapy for MDS include:

- **IDH Inhibitors.** In some people with MDS, the cancer cells have a mutation of the *IDH1* or *IDH2* gene. These mutations cause cells to remain immature and divide and multiply too quickly. For these patients, the following targeted therapy, either on- or off-label, may be used:
  - **Ivosidenib (Tibsovo®)** is FDA-approved for adult patients with susceptible *IDH1* mutation with relapsed or refractory MDS.
  - **Enasidenib (Idhifa®)** is an off-label treatment for MDS with an *IDH2* mutation.

For more information on ivosidenib, see **Table 6**, *Drug Classes and Drug Mechanisms* and **Table 7**, *FDA-Approved Drugs to Treat MDS*, starting on page 30.

- **BCL2 Inhibitors.** Overexpression of the BCL2 protein allows cancer cells to evade "programmed cell death," meaning it helps cancer cells live longer than they should. BCL2 inhibitors target the BCL2 protein. This helps restore what is called apoptosis, a process of natural cell death that is disrupted when you have cancer, restoring the body's natural ability to tell cancer cells to die. Once this process is restored, your body can begin to kill cancer cells more effectively. With fewer cancer cells, there is more room for healthy blood cells to grow in the bone marrow.

  Research has shown that **venetoclax (Venclexta®)** in combination with hypomethylating agents may reduce the number of blast cells in the bone marrow for people with high-risk MDS. This drug binds to the leukemia cells and triggers apoptosis, a process that causes the cancer cells to die. Venetoclax is not FDA-approved to treat MDS, but it is sometimes used as an off-label treatment for people with MDS.

- **FLT3 Inhibitors.** Some MDS patients have a mutation in the *FLT3* gene that can increase the growth and division of cancer cells. FLT3 inhibitors are drugs that target these gene mutations. For MDS patients with *CBL* mutations, FLT3 inhibitors may also be helpful in treatment. For these patients, **midostaurin (Rydapt®), gilteritinib (Xospata®), quizartinib (Vanflyta®)** or **sorafenib (Nexavar®)** may be prescribed. These drugs are not FDA-approved to treat MDS, but they are being studied in clinical trials and are also available as off-label treatments.

Intensive Chemotherapy. For patients eligible for intensive therapy but who do not have a stem cell donor, the same intensive chemotherapy regimens used for the treatment of acute myeloid leukemia (AML) may be used. Because these agents tend to cause more severe side effects, they are generally used for higher-risk MDS that is likely to progress to AML. The drugs used may include any of the following:

- **Cytarabine (cytosine arabinoside, Ara-C; Cytosar-U®)**
- **Idarubicin (Idamycin®)**
- **Daunorubicin (Cerubidine®)**
- **Mitoxantrone (Novantrone®)**

Chemotherapy regimens may consist of a single drug or combinations of two or three different drugs (combination chemotherapy). These drugs are not FDA-approved to treat MDS, but they may be prescribed off-label to MDS patients.

Intensive chemotherapy is often recommended for relatively younger patients with favorable risk factors that are candidates for allogeneic stem cell transplantation. It is rarely used in older patients with poor risk factors.

Candidate for Allogeneic Stem Cell Transplantation. Allogeneic stem cell transplantation is a type of treatment that destroys cells in the patient's bone marrow and then replaces them with new, healthy blood-forming stem cells from a matched or partially matched donor.

In most cases, it is important to start a donor search as soon as possible after an MDS diagnosis if allogeneic stem cell transplantation is being considered as a treatment option. This is necessary to identify a suitably matched, related or unrelated donor, and to plan for the best time to perform a transplant safely and successfully.

Allogeneic stem cell transplantation is the only potential cure for MDS, but not everyone can receive one. It is an intense and complex treatment that can cause life-threatening side effects in some patients. It is considered the standard of care for younger people with MDS. Advances in transplant technology now allow for consideration of older, fit patients. It is important to discuss the benefits and risks of this procedure with your doctor.

Before receiving an allogeneic stem cell transplant, patients often receive treatment to reduce the number of blasts in their bone marrow. Patients with less than 5 percent blasts in the bone marrow often show better post-transplant outcomes than patients with higher blast percentages. Treatment to reduce blast count may include one or more of the following:

- Hypomethylating agents
- Hypomethylating agents combined with other drugs
- High-intensity chemotherapy

Once patients are ready for an allogeneic stem cell transplant, they receive a "conditioning therapy." This consists of very high doses of chemotherapy, either with or without radiation, to kill the cancer cells remaining in their bodies. It is also given to suppress their own immune systems, so their bodies do not reject the donor stem cells.

After the conditioning therapy, patients receive a transfusion of donor stem cells. A transfusion is a slow injection of blood products put into a patient's bloodstream through a vein. This procedure can take several hours to complete. Allogeneic transplantation uses healthy blood-forming cells from an appropriately matched donor. They can be from a family member or an unrelated person, or from a donated umbilical cord.

The transplanted blood stem cells travel to the bone marrow where they multiply and grow. The donated stem cells restore the bone marrow's ability to form new blood cells.

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

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality. However, it may be considered for patients with higher-risk MDS, based on their cytogenetic and molecular test results and other prognostic factors. Whether or not to perform an allogeneic transplant also depends on other factors, including the patient's age, physical fitness, comorbidities (other co-existing medical conditions), and social supports (from family members, caregivers, friends). The patient's understanding of the potential benefits and risks plays a role as well.

One possible side effect of allogeneic stem cell transplantation is a serious condition called graft-versus-host disease (GVHD). This occurs when the transplanted immune cells (the graft) from the donor identify the cells in the recipient's body (the host) as "foreign" and attack them. The parts of the body most commonly damaged by GVHD include the skin, liver, stomach, intestines and eyes. GVHD can develop within weeks after transplantation or much later. A doctor can order medications to help prevent or minimize the complications of GVHD. Most patients need to be closely monitored for GVHD for at least the first 100 days after the transplant.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplantation may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used in preparation for a standard allogeneic stem cell transplant. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation. With a reduced-intensity conditioning

regimen, the patient's blood counts may not fall as low as they would with high-dose chemotherapy. Additionally, the less toxic regimens put less strain on the patient's organs, making this regimen safer and more tolerable.

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

Talk to your doctor about:

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

See the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information about allogeneic stem cell transplantation.

Table 6. Drug Classes and Drug Mechanisms

Erythroid Maturation Agent	Treatment that helps red blood cells mature.
Hypomethylating Agent	A type of chemotherapy drug that works by blocking the DNA that helps cancer cells grow. It also activates genes that help cells grow and mature. Using one of these drugs may improve blood cell counts, which, in turn may lead to fewer blood transfusions and improve quality of life.
IDH1 Inhibitor	A targeted therapy for people with MDS whose cancer cells have a mutation in the *IDH1* gene.
Immunomodulator	A drug that changes (modifies) the immune system and may help the body fight cancer.

Table 7. FDA-Approved Drugs to Treat MDS

Drug Name Type of Drug Administration	FDA-Approved Indications
Azacitidine (Vidaza®) Hypomethylating agent Subcutaneous injection Intravenous (IV) injection	Approved for the treatment of adult patients with the following FAB MDS subtypes: ○ Refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions) ○ refractory anemia with excess blasts (RAEB) ○ refractory anemia with excess blasts in transformation (RAEB-T) ○ chronic myelomonocytic leukemia (CMMoL).

Drug Name Type of Drug Administration	FDA-Approved Indications
Decitabine (Dacogen®) Hypomethylating agent Intravenous (IV) injection	Approved for treatment of adult patients with MDS including previously treated and untreated, *de novo* and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.
Decitabine and cedazuridine (Inqovi®) Hypomethylating agent Oral	Approved for the treatment of adult patients with MDS, including previously treated and untreated, *de novo* and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.
Ivosidenib (Tibsovo®) Targeted therapy, IDH1 Inhibitor Oral	Approved for the treatment of adult patients with relapsed or refractory MDS with a susceptible *IDH1* mutation as detected by an FDA-approved test.
Lenalidomide (Revlimid®) Immunomodulator Oral	Approved for the treatment of adult patients with transfusion-dependent anemia due to low- or intermediate-1 risk MDS associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities.
Luspatercept-aamt (Reblozyl®) Erythroid maturation agent Subcutaneous injection	Approved for the treatment of: ○ Anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk MDS who may require regular red blood cell (RBC) transfusions. ○ Anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T). ○ Limitations of Use: REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia.

New treatments may have been approved since this booklet was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4752.

MDS in Children

While MDS typically develops in older adults, it can occur at any age. Pediatric (childhood) MDS is rare, with approximately 1 to 4 cases per million children (people aged 18 years or younger) each year. MDS in children differs biologically from MDS in adults. The World Health Organization (WHO) has a separate category distinct from adults. See **Table 8** below for the different subtypes of MDS in children.

Many cases of pediatric MDS are due to inherited genetic mutations called "germline" mutations. Germline mutations, which are less common in adult patients, can be inherited from parents or can develop before birth, and are found in every cell of the body (not just in the blood cells). Knowing if a genetic mutation is germline can make a difference in your child's prognosis and treatment. It may affect the types of medication your child receives and may also affect which family members are eligible to be stem cell donors.

Table 8. Childhood MDS Subtypes

	Blasts
Childhood MDS with low blasts	<5% BM; <2% PB
Hypocellular	
Not otherwise specified	
Childhood MDS with increased blasts	5–19% BM; 2–19% PB

BM bone marrow; PB peripheral blood

Source: Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia.* 2022;36(7):1703-1719.

Treatment for most types of pediatric MDS is allogeneic stem cell transplantation. This is a procedure in which a patient receives healthy bone marrow from a related or unrelated donor. (See page 28 for more information on allogeneic stem cell transplantation). HLA typing should be performed as soon as the diagnosis of MDS is established. Often a sibling or another family member serves as the patient's stem cell donor. If a patient has a hereditary genetic predisposition, all potential family member donors need to be tested for the genetic disorder before donating.

Most children with cancer receive treatment at hospitals that specialize in treating children with cancer. The doctors and other healthcare providers at these centers have special training and expertise in giving comprehensive care to children. These centers are often members of the Children's Oncology Group (COG). This is the world's largest organization devoted to clinical research to improve the care and treatment of children with cancer.

Going to a specialized children's cancer hospital helps ensure that your child will get the best available treatment. You can ask your child's pediatrician or your family doctor for a referral, or you can call an LLS Information Specialist at (800) 955-4572 to find hospitals that specialize in treating children with MDS.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials and they are used to find better ways to care for and treat people with cancer.

In the United States, the FDA (U.S. Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

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

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

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

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **LLS Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (like past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history—because these might impact whether you can take part in certain clinical trials
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel might impact your choice of clinical trials
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical trial process

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

Also, visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers*.

Related Diseases

Myelodysplastic Syndromes/Myeloproliferative Neoplasms (MDS/MPN) Classification. Myelodysplastic syndromes (MDS) are a group of blood cancers where the bone marrow does not make enough healthy blood cells (red blood cells, white blood cells and platelets), and there are abnormal cells in the blood and bone marrow. Myeloproliferative neoplasms (MPN) are a group of blood cancers in which the body makes too many red blood cells, white blood cells and/or platelets.

Myelodysplastic/myeloproliferative neoplasms (MDS/MPN) are blood cancers that have features of both myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs). These disorders have bone marrow cells that are dysplastic (abnormal in shape and size) and proliferative (abnormally multiplying or increasing). See **Table 9** on page 35 for a list of subtypes of MDS/MPNs.

Table 9. 2022 WHO Classification of Myelodysplastic Syndromes/ Myeloproliferative Neoplasms (MDS/MPN)

Chronic myelomonocytic leukemia
Myelodysplastic/myeloproliferative neoplasm with neutrophilia
Myelodysplastic/myeloproliferative neoplasm with *SFB1* mutation and thrombocytosis
Myelodysplastic/myeloproliferative neoplasm, not otherwise specified

Source: Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia*. 2022;36(7):1703-1719.

Treatments vary based on the type of MDS/MPN. Options range from watch-and-wait to chemotherapy to stem cell transplantation. Some cancer centers treat MDS/MPN with regimens for MDS, though patients with specific mutational profiles may benefit from specific therapeutic approaches. Since MDS/MPNs are rare, patients should seek treatment at a cancer center that has experience treating patients with these diseases.

See the free LLS publications *Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML) Facts* and *Myeloproliferative Neoplasms*.

Follow-Up Care

Follow-up care for MDS varies from patient to patient. Patients with MDS require regular follow-up visits with their hematologist-oncologist that will include blood tests to detect worsening cytopenias (low blood cell counts). Bone marrow biopsies are done if there are worsening cytopenias or the appearance of blast cells in the blood. The frequency of these follow-up visits depends on the disease risk and choice of treatment.

If you have been treated for MDS, you are encouraged to:

- Maintain regular follow-up appointments with your hematologist-oncologist. The doctor will monitor you for signs of relapse and detect any side effects from treatment. A follow-up visit may also discover the onset of any other medical problems.
- Keep a record of your cancer diagnosis, treatments and follow-up care needs. This is often called a “survivorship care plan.” Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The plan should include the following information:
  - List of all healthcare providers
  - Diagnosis summary with specifics such as subtype and/or genetic markers

- Treatment summary with specifics such as the names, dates, and dosages of chemotherapy or other drugs, site of radiation treatment, surgery and/or transplantation information, response to treatment and side effects
- Maintenance treatment information, if applicable
- List of possible late effects
- Schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
- Health and wellness recommendations such as nutrition, exercise or other disease screenings

- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as smoking cessation, skin protection against prolonged sun exposure, healthy eating and exercising.

Please visit LLS.org/SurvivorshipWorkbook to view the free LLS survivorship publications *Navigating Life During and After a Blood Cancer Diagnosis* with versions for Adults, Young Adults and Children and Adolescents.

Financial Concerns

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

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

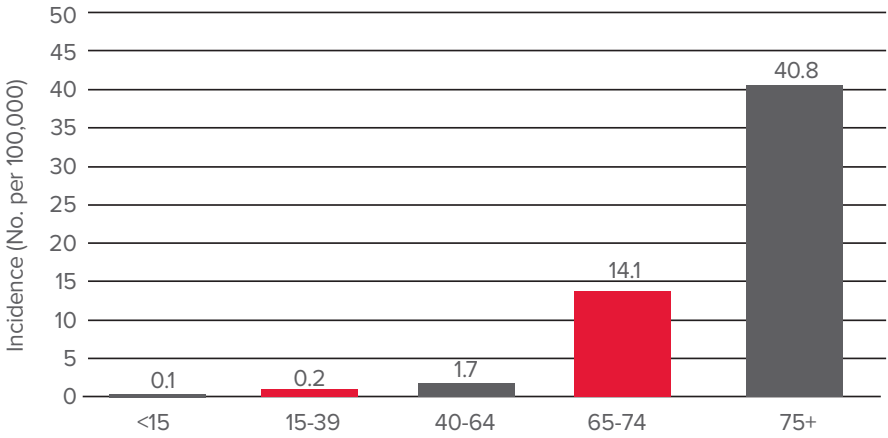
LLS offers financial assistance programs to help with insurance premiums, treatment-related co-payments, travel and other expenses for eligible patients. Other organizations also offer financial assistance programs. You can call an LLS Information Specialist at (800) 955-4572 for more information about our financial assistance programs.

For more information and resources to help cope with the financial costs of cancer care, please see the free LLS booklet *Cancer and Your Finances.*

Incidence, Causes and Risk Factors

Incidence. In the United States, the overall incidence rate of MDS is 4.0 cases per 100,000 population. This rate rises with age. See **Figure 3** below. MDS is rare among children, adolescents and young adults.

Figure 3. Myelodysplastic Syndromes (MDS) Age-Adjusted Incidence Rates, 2015-2019



The horizontal axis represents the age of patients, starting from younger than age 15 years through age 75 and older. The vertical axis shows the incidence of new cases of MDS from 2015 to 2019, per 100,000 people.

Source: SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2023 February 20]. Available from https://seer.cancer.gov/explorer/.

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

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

- Age. The risk of developing MDS increases with age. While MDS can occur at any age, it typically affects older adults. The median age at diagnosis is 77 years old.
- Sex. Males are more likely than females to develop MDS.
- Previous cancer treatment. People who received radiation therapy or chemotherapy have an increased risk of developing MDS.
- Exposure to dangerous chemicals. Long-term exposure to high levels of certain chemicals, such as benzene, is linked to a greater risk of MDS.

- Genetic disorders. Certain genetic conditions present at birth seem to increase the risk of MDS, including:
  - Down syndrome
  - Neurofibromatosis type 1
  - Bloom syndrome
  - Trisomy 8
  - Fanconi anemia
  - Klinefelter syndrome
  - Wiskott-Aldrich syndrome
  - Kostmann syndrome
  - Shwachman-Diamond syndrome
- Familial risk/germline predisposition. Certain gene mutations present at birth may increase the risk of developing MDS.
- Smoking. MDS is linked to smoking and exposure to tobacco smoke, which contains benzene and other cancer-causing substances.
- Workplace exposure. Long-term workplace exposure to benzene can increase the risk of developing MDS. More cases of MDS are reported among agricultural and industrial workers.

Normal Blood and Bone Marrow

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

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

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are proteins that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B12
- Electrolytes, such as calcium, potassium and sodium

Blood Cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as hematopoietic stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis" (see **Figure 4** on page 40). The blood cells are suspended in the plasma.

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

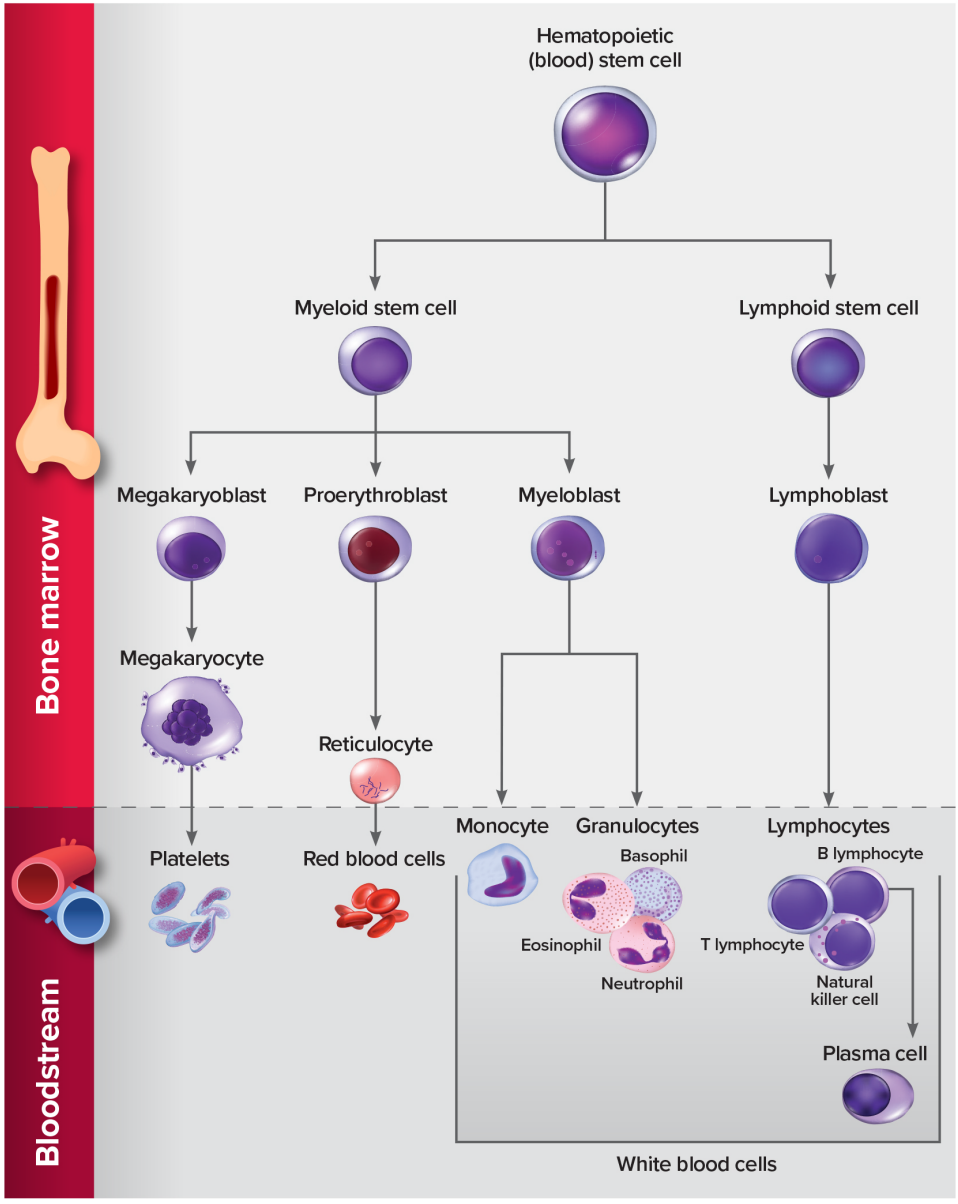
These are:

1. Red blood cells are the cells that carry oxygen; they
    - Make up a little less than half of the body's total blood volume
    - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.
2. Platelets are cells that help blood clot; they
    - Are small cells (one-tenth the size of red blood cells)
    - Help stop bleeding from an injury or cut
    - Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:
    - Neutrophils and monocytes. These are "phagocytes" (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
    - Eosinophils and basophils. These WBCs respond to allergens or parasites.
    - Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
        - T lymphocytes (T cells)
        - B lymphocytes (B cells)
        - Natural killer cells (NK cells)

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

Figure 4. Blood Cell and Lymphocyte Development

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



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

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

Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section lists various resources you may find helpful.

For Help and Information

Consult with an Information Specialist. Information Specialists can assist you through cancer treatment, financial and social challenges and give accurate, up-to-date disease, treatment and support information. Our Information Specialists are highly trained oncology social workers and nurses. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Pediatric and adult patients and caregivers can work with our Clinical Trial Nurse Navigators who will help find clinical trials and provide personalized support throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Nutrition Consultations. Schedule a free one-on-one nutrition consultation with one of our registered dietitians who have expertise in oncology nutrition. Consultations are available to patients and caregivers of all cancer types. Dietitians can assist with information about healthy eating strategies, side effect management and more. Please visit www.LLS.org/nutrition for more information.

Free Information Booklets. LLS offers free education and support booklets for patients, caregivers and healthcare professionals that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial support to eligible individuals with blood cancer for insurance premiums, co-pays, and non-medical expenses like travel, food, utilities, housing, etc.

For more information, please:

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

Resources for Families. Blood cancer occurs in a small number of children. Families face new challenges, and the child, parents and siblings may all need support. LLS has many materials for families including a caregiver workbook, children's book series, emotion flipbook, dry erase calendar, coloring books and coloring app, school re-entry program and other resources.

For more information, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/FamilyWorkbook

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe to access exclusive content, submit ideas and topics, and connect with other listeners.

3D Models. LLS offers interactive 3D images to help visualize and better understand blood cell development, intrathecal therapy, leukemia, lymphoma, myeloma, MDS, MPNs, and lab and imaging tests. Visit www.LLS.org/3D for more.

Free Mobile Apps.

- LLS Coloring For Kids™–Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit www.LLS.org/ ColoringApp to download for free.
- LLS Health Manager™–Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit www.LLS.org/HealthManager to download for free.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Connecting with Patients, Caregivers and Community Resources

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients and caregivers reach out and share information. Please visit www.LLS.org/chat for more information.

Local Programs. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection® Program* (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact your region, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/LocalPrograms

Advocacy and Public Policy. Working closely with dedicated volunteer advocates, LLS's Office of Public Policy elevates the voices of patients to state and federal elected officials, the White House, governors and even courts. Together, we advocate for safe and effective treatments. We pursue policies that would make care more accessible to all patients. And, most of all, we advocate for the hope for a cure. Want to join our work? Visit www.LLS.org/advocacy for more information.

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

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

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

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information, please

- Call: the VA (800) 749-8387
- Visit: www.publichealth.va.gov/exposures/AgentOrange

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

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

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

For more information, please

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

People With Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a two-week period. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Health Terms

Absolute Neutrophil Count (ANC). The measure of the number of neutrophils in the blood. A neutrophil is a type of white blood cells that help the body fight infection.

Acute Myeloid Leukemia (AML). An aggressive, fast-growing type of blood cancer in which there are too many immature white blood cells in the blood and bone marrow. **See the free LLS booklets, *Acute Myeloid Leukemia in Adults* and *Acute Myeloid Leukemia in Children and Teens.***

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to restore a patient's bone marrow that is damaged or diseased after receiving high doses of chemotherapy and/or radiation therapy. **See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation.***

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

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

Basophil. A type of white blood cell that is involved in certain allergic reactions.

Blast Cell. An immature blood cell. In healthy people, blast cells make up no more than 5 percent of the cells in the bone marrow and are not typically found in the blood.

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

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

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

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

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

CBC. See Complete Blood Cell Count.

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

Chromosome. Threadlike structures within cells that carry genes in a linear order. Human cells have 23 pairs of chromosomes. **See the free LLS booklet *Understanding Genetics.***

Chronic Myelomonocytic Leukemia. A type of myelodysplastic/myeloproliferative blood cancer in which there are too many monocytes (a type of white blood cell) in the bone marrow. **See the free LLS booklet *Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML) Facts.***

Colony-Stimulating Factor. See Growth Factor.

Comorbidity. Having two or more diseases at the same time.

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

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

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

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

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

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

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

Erythropoietin (EPO). A hormone needed for normal production of red blood cells. It is made mainly by the kidneys and is released into the blood in response to decreased blood oxygen levels. Drugs with synthetic EPO, called erythropoietin-stimulating agents (ESAs), are available to help the body produce red blood cells.

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

First-Line Treatment. The first treatment given for a disease.

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

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

Graft-Versus-Host Disease (GVHD). A condition that occurs when stem cells transplanted from a donor (the graft) attack the healthy tissues of the transplant recipient (the host). Most often, GVHD affects a patient's skin, liver, stomach and gastrointestinal tract. **See the free LLS booklet *Graft-Versus-Host Disease*.**

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

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

Growth Factor. A substance that causes new blood cells to grow in the bone marrow.

Hematologist-Oncologist. A doctor who has special training in diagnosing and treating blood disorders and blood cancers.

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

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

Hemoglobin. A protein inside red blood cells that carries oxygen from the lungs to tissues and organs in the body and carries carbon dioxide back to the lungs.

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

Intravenous Injection. An injection into a vein.

Inversion. A genetic abnormality that occurs when a section of a chromosome breaks off, turns upside down and then reattaches. As a result, the genetic material is inverted and is now in a different order. **See the free LLS booklet *Understanding Genetics.***

Iron Chelation Therapy. Treatment to remove excess iron from the body.

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

Leukocyte. See White Blood Cell.

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

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

Monosomy. A type of numerical chromosome abnormality. Normally people are born with 23 chromosome pairs, or 46 chromosomes. The term "monosomy" describes the absence of one pair of chromosomes. Therefore, there are 45 chromosomes in the cells instead of the usual 46.

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

Myeloblast. A type of immature white blood cell that forms in the bone marrow. Myeloblasts become mature white blood cells called granulocytes (neutrophils, basophils and eosinophils).

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

Neutrophil. A type of white blood cell, and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main kind of cell that combats infection.

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

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

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

Peripheral Blood. The blood that circulates throughout the body.

Peripheral Blood Smear. A procedure in which a sample of blood cells is stained (dyed) and examined under a microscope to check for unusual changes in the size, shape and appearance of various types of blood cells and for the presence of blast cells in the blood.

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

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

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

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

Prognostic Scoring System. A method doctors use to rate the severity of MDS and to classify it into groups based on the likely outcome (prognosis).

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

Reduced-Intensity Allogeneic Stem Cell Transplantation. A type of allogeneic stem cell transplantation in which patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. The chemotherapy and radiation do not completely kill all the cancer cells, but the new immune cells that the patient receives in the transplant may attack the patient's cancer cells. This protocol may be safer than a traditional high-dose conditioning allogeneic stem cell transplant, especially for older patients. **See the free LLS booklet, *Blood and Marrow Stem Cell Transplantation.***

Refractory Anemia (RA). In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) with these characteristics: anemia (low red blood cell count); a high number of abnormal, immature red blood cells in the bone marrow; less than 5 percent of blasts in the bone marrow; and less than 1 percent blasts in the blood.

Refractory Anemia With Excess Blasts (RAEB). In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) with these characteristics: one or more low blood cell counts and excess blasts in the bone marrow and blood.

Refractory Anemia With Excess Blasts in Transformation (RAEB-T). In the French-American-British (FAB) classification, RAEB-T is a myelodysplastic syndrome (MDS) in which the bone marrow blast ranges from 20 to 30 percent.

Refractory Anemia With Ring Sideroblasts (RARS). In the French-American-British (FAB) classification, a myelodysplastic syndrome (MDS) in which the bone marrow produces ringed sideroblasts rather than healthy red blood cells. When abnormal sideroblasts are present, large amounts of iron are trapped in the developing red blood cells in abnormal sites.

Remission. When signs of a disease disappear, usually following treatment.

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

RNA. Abbreviation for ribonucleic acid, one of two types of nucleic acid made by cells. RNA contains information that has been copied from DNA (the other type of nucleic acid). Cells make several different forms of RNA, and each form has a specific job in the cell. Many forms of RNA have functions related to making proteins.

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

Stem Cell Transplantation. See Allogeneic Stem Cell Transplantation; Reduced-Intensity (Nonmyeloablative) Allogeneic Stem Cell Transplantation.

Subcutaneous Injection. An injection given in the fatty tissue between the skin and muscle.

Supportive Care. Care given to improve the quality of life of patients who have a serious disease. The goal of supportive care is to prevent or treat the symptoms of disease and side effects caused by treatment.

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

Transfusion. A procedure in which whole blood or parts of blood are slowly injected into a patient's bloodstream through a vein.

Watch-and-Wait. Closely watching a patient's condition but not giving any treatment unless signs or symptoms appear or change. During watch-and-wait, certain exams and tests may be done periodically to monitor the condition.

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

World Health Organization (WHO). An agency of the United Nations that deals with major health issues around the world. The WHO sets standards for healthcare and medicines and publishes scientific papers and reports.

References

Aster JC, Stone RM. Clinical manifestations, diagnosis, and classification of myelodysplastic syndromes (MDS). In: UpToDate, Larson RA (Section Ed). Wolters Kluwer; [Publication Date Not Provided]. Available from: https://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-classification-of-myelodysplastic-syndromes-mds. Accessed December 21, 2023.

Carraway HE, Saygin C. Therapy for lower-risk MDS. Hematology American Society of Hematology Education Program. 2020;(1):426-433.

Cazzola M. Myelodysplastic syndromes. *New England Journal of Medicine.* 2020;383(14):1358-1374.

Chandhok NS, Boddu PC, Gore SD, et al. What are the most promising new agents in myelodysplastic syndromes? *Current Opinion in Hematology.* 2019;26(2):77-87.

Fenaux P, Hasse D, Santini V, et al. Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology.* 2021;32(2):142-156.

Garcia-Manero G. Myelodysplastic syndromes: 2023 update on diagnosis, risk-stratification, and management. *American Journal Hematology.* 2023;98(8):1307-1325.

Hasserjian RP, Buckstein R, Patnaik MM. Navigating myelodysplastic and myelodysplastic/myeloproliferative overlap syndromes. *American Society Clinical Oncology Education Book.* 2021;41:328-350.

Hasserjian RP, Germing U, Malcovati L. Diagnosis and classification of myelodysplastic syndromes. *Blood.* 2023;142(26):2247-2257.

Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia.* 2022;36(7):1703-1719.

Koenig KL, Borate U. New investigational combinations for higher-risk MDS. *Hematology American Society of Hematology Education Program.* 2022;1:368-374.

Locatelli F, Strahm B. How I treat myelodysplastic syndromes of childhood. *Blood.* 2018;131(13):1406-1414.

Montalban-Bravo G, Garcia-Manero G. Myelodysplastic syndromes: 2018 update on diagnosis, risk stratification and management. *American Journal of Hematology.* 2018;93(1):129-147.

Montoro J, Yerlikaya A, Ali A, et al. Improving treatment for myelodysplastic syndromes patients. *Current Treatment Options Oncology.* 2018;19(12):66.

Mortuza S, Chin-Yee, B, James TE, et al. Myelodysplastic neoplasms (MDS) with Ring Sideroblasts or *SF3B1* mutations: the improved clinical utility of World Health Organization and International Consensus Classification 2022 definitions, a single-centre retrospective chart review. *Current Oncology.* 2024;29;31(4):1762-1773.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Version 3.2023. Myelodysplastic Syndromes. Available from: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed November 6, 2023.

National Comprehensive Cancer Network. NCCN Guidelines for Patients. Myelodysplastic Syndromes 2021. Available from: https://www.nccn.org/patients/guidelines/content/PDF/mds-patient.pdf. Accessed November 6, 2023.

Platzbecker U, Kubasch AS, Homer-Bouthiette C, Prebet T. Current challenges and unmet medical needs in myelodysplastic syndromes. *Leukemia.* 2021;35(8):2182-2198.

Sasaki K, Jabbour E, Montalban-Bravo G, et al. Low-dose decitabine versus low-dose azacitidine in lower-risk MDS. *New England Journal of Medicine Evidence.* 2022;1(10). Published August 9, 2022.

Scott BL. Existing agents, novel agents, or transplantation for high-risk MDS. *Hematology American Society Hematology Education Program.* 2020;(1):411-417.

Sekeres MA, Kim N, DeZern AE, et al. Considerations for drug development in myelodysplastic syndromes. *Clinical Cancer Research.* 2023;29(14):2573-2579.

Sekeres MA, Taylor J. Diagnosis and treatment of myelodysplastic syndromes: a review. *JAMA*. 2022;328(9):872-880.

Weinberg OK, Hasserjian RP. The current approach to the diagnosis of myelodysplastic syndromes. *Seminars in Hematology.* 2019;56:15-21.

Zeidan AM, Shallis RM, Wang R, Davidoff A, Ma X. Epidemiology of myelodysplastic syndromes: Why characterizing the beast is a prerequisite to taming it. *Blood Review.* 2019;34:1-15.

NOTES

LEUKEMIA & LYMPHOMA SOCIETY®

The Leukemia & Lymphoma Society© team consists of highly trained oncology social workers and nurses who are available by phone, email and live chat Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individualized clinical-trial searches
- Get connected to resources

Contact us at
800.955.4572
or **www.LLS.org/InformationSpecialists**

(Language interpreters can be requested.)

LEUKEMIA & LYMPHOMA SOCIETY®

For more information, please contact our Information Specialists **800.955.4572** (Language interpreters available upon request).

National Office 3 International Drive, Suite 200 Rye Brook, NY 10573

The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at www.LLS.org.

PS22 15M 5/24