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Myelofibrosis Facts

No. 14 in a series providing the latest information for patients, caregivers and healthcare professionals

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Highlights

- Myelofibrosis (MF) is a rare bone marrow cancer. It is one of a related group of blood cancers known as "myeloproliferative neoplasms (MPNs)" in which bone marrow cells that produce the blood cells develop and function abnormally. The resulting fibrous scar tissue formation leads to severe anemia, weakness, fatigue and an enlarged spleen and liver.
- MF is a type of chronic leukemia and can occur on its own (primary myelofibrosis) or as a result of another bone marrow disorder. Other MPNs that can progress to myelofibrosis include polycythemia vera and essential thrombocythemia.
- MF develops when a genetic mutation occurs in blood stem cells. The cause of the gene mutation is unknown. Between 50 and 60 percent of people with MF have a mutation of the Janus kinase 2 gene *(JAK2)*. Researchers are investigating other possible gene mutations responsible for MF.
- MF usually develops slowly and some people may live symptom-free for years. Others, however, may get progressively worse, requiring treatment. In both cases, patients do need to be monitored regularly.
- The treatment goal for most patients with MF is to relieve symptoms and reduce the risk of complications. Treatments include blood transfusions, chemotherapy, radiation or removal of the spleen (splenectomy), drugs to treat anemia, and allogeneic stem cell transplantation. Ruxolitinib (Jakafi™) is the first drug approved by the US Food and Drug Administration (FDA) to treat MF because it has been shown to reduce several MF-related symptoms and control spleen enlargement. Other potential therapies for MF treatment are being studied in clinical trials.
- Allogeneic stem cell transplantation (ASCT) is the only potential cure for MF. This treatment has a considerable risk of life-threatening side effects. ASCT is not a good option for most people with MF because of age, the course of their disease or other health problems.

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Introduction

Myelofibrosis (MF) belongs to a group of closely related blood cancers known as "myeloproliferative neoplasms (MPNs)" in which the bone marrow cells that produce the body's blood cells develop and function abnormally. The result is excessive fibrous (scar) tissue formation in the bone marrow, which can lead to severe anemia, weakness, fatigue and an enlarged spleen and liver.

MF can occur on its own, called "primary myelofibrosis," or as a progression of other bone marrow diseases. Other myeloproliferative neoplasms that can progress to myelofibrosis include polycythemia vera (PV) and essential thrombocythemia (ET). Between 10 and 15 percent of MF cases begin as either polycythemia vera or essential thrombocythemia. Myelofibrosis is also known by several other names, including agnogenic myeloid metaplasia, chronic idiopathic myelofibrosis, myelosclerosis with myeloid metaplasia and idiopathic myelofibrosis.

This fact sheet includes information about diagnosis, treatment and expected outcomes of myelofibrosis, information about new treatments being investigated in clinical trials and support resources.

About Myelofibrosis

Myelofibrosis is a rare bone marrow cancer in which the marrow is replaced by fibrous (scar) tissue. Bone marrow is the soft, fatty tissue inside the bones. The cancer develops when a mutation occurs in the DNA of a single hematopoietic (blood-forming) stem cell. Blood stem cells have the ability to reproduce and divide into multiple specialized cells that make up the blood. As the mutated blood cell replicates and divides, it passes along the mutation to new cells. Eventually, this abnormal cell production overtakes the bone marrow's ability to produce enough normal blood cells, including

- Red blood cells, which carry oxygen to the tissues
- White blood cells, which fight infection
- Platelets, which help blood to clot.

When the bone marrow is unable to make enough healthy blood cells, the result can be severe anemia, weakness, bone pain, fatigue and increased risk of infection. The abnormal growth of blood-forming cells can also take place outside of

the bone marrow, called "extramedullary hematopoiesis," in such organs as the liver, spleen, lungs, lymph nodes and spinal cord, causing swelling.

An important constant feature of MF is the production of too many "megakaryocytes," the term for the giant cells in the marrow that break up into fragments and produce hundreds to thousands of platelets. Platelets are small blood cells (comprising about one-tenth the volume of red cells) that stick to the site of a blood vessel injury and form a plug to seal off the injured blood vessel to stop bleeding. Normally, new platelets are made to replace used platelets in the body. With MF, extra megakaryocytes are made, causing too many platelets to be released into the blood and chemicals called "cytokines" to be released into the marrow. The cytokines stimulate the development of fibrous tissue in the marrow. Paradoxically, the number of megakaryocytes can become so abnormal that platelet production decreases in some patients.

MF occurs in about 1.5 out of every 100,000 people in the United States annually. The disease affects both men and women and is usually diagnosed in people over the age of 50, however, MF can occur at any age.

About 50 percent of people with MF have a mutation (a change in their DNA) called "V617F *JAK2*" found in the *JAK2* gene. The gene mutation causes abnormal signaling in the JAK pathway, which regulates blood cell production. This dysregulation of the JAK pathway can lead to an enlarged spleen (splenomegaly) and other serious complications, such as a low platelet count and severe anemia. Between 5 and 10 percent of MF patients will have a myeloproliferative leukemia *(MPL)* gene mutation, which also affects the JAK signaling pathway. In addition, mutations in the *TET2* gene have been found in 5 to 15 percent of patients with myeloproliferative neoplasms. Scientists are investigating the role *TET2* mutations, and other gene mutations in other signaling pathways, may have on MF onset.

The reason these genetic mutations occur in MF is unknown. Exposure to petrochemicals, such as benzene and toluene, and ionizing radiation may raise the risk of developing the cancer. But only a small proportion of people exposed to these chemicals develop MF. A theory about why MF develops in some people is that they have inherited genes that limit their ability to detoxify the causative agents. MF is not an inherited disease. There is no known prevention.

Signs and Symptoms

MF usually develops slowly. In its very early stages, many people—about one-third—do not have symptoms of the disease. However, as disruption of normal blood cell production increases, people may experience the following signs and symptoms:

- Tiredness, weakness, shortness of breath, usually due to low red blood cell count (anemia)
- Pain or a feeling of fullness below the ribs on the left side, as a result of an enlarged spleen (splenomegaly)
- Enlarged liver
- Pale skin
- Easy bleeding or bruising, as a result of a low platelet count (thrombocytopenia)
- Excessive night sweats
- Fever
- Frequent infections, due to a low white blood cell count (neutropenia)
- Bone or joint pain
- Weight loss.

Supportive Care

There are supportive therapies that may be used to help manage a patient's anemia, enlarged spleen or other MF symptoms. These therapies are described below.

Anemia. Replacing nutrients that stimulate red cell production such as iron, folic acid and vitamin B_{12} may help reduce anemia. The following treatments are also used for myelofibrosis-related anemia. Some may have potentially serious side effects, so it is important to talk to your doctor about your options.

- Blood transfusions—Periodic blood transfusions can increase red blood cell count and reduce symptoms of anemia, including fatigue and weakness.
- Androgen therapy—Includes drugs such as the anabolic steroid danazol, given by mouth. Although taking a synthetic version of male hormones (androgens) may help build red cell production, and therefore, improve anemia, the therapy carries some risks, such as liver damage, masculinizing effects in women and growth of prostate cancer cells in men.
- Erythropoietin—This therapy, a hormone that stimulates the production of red blood cells, given intravenously (IV) or by subcutaneous injection, may also be used to treat anemia.
- Glucocorticoids (also called "corticosteroids" or "steroids")—This therapy, given by mouth, may also be used to treat anemia.

- Chemotherapy—Hydroxyurea (Hydrea®) is given by mouth. Cladribine (Leustatin®) is given intravenously (IV).
- Immunomodulators (IMiDs)—Interferon, given by intramuscular or subcutaneous injection; thalidomide (Thalomid®) and lenalidomide (Revlimid®), both given by mouth, are FDA approved in the treatment of the blood cancer myeloma, and are being used to treat anemia in MF patients. Another IMiD, pomalidomide (Actimid®), given by mouth, is also showing positive results in clinical studies in the treatment of myelofibrosis-related anemia. Pomalidomide is also being studied in clinical trials to treat patients with myeloma.

Enlarged spleen. There are several options for dealing with the painful effects of an enlarged spleen (splenomegaly) caused by MF, including

- Surgical removal of the spleen (splenectomy)—Removal of the spleen may be considered if other forms of therapy have not reduced the pain or complications associated with an enlarged spleen. However, the benefits and risks of this procedure need to be weighed before a decision is made. Benefits include a reduction of symptoms, decreased portal hypertension (see *Complications,* below) and less need for red cell transfusions. MF patients who will be undergoing splenectomy need to be evaluated prior to surgery and then monitored afterward for an increased risk of bleeding complications, including blood clot formation leading to a stroke or pulmonary embolism; infection; liver enlargement; and an increase in platelet count.
- Chemotherapy—Hydroxyurea (Hydrea®)
- Immunomodulators (IMiDs)—Interferon, thalidomide (Thalomid®) and lenalidomide (Revlimid®)
- A JAK inhibitor—Ruxolitinib (Jakafi™), given by mouth, is the first drug that has been approved by the FDA to treat MF because it has been shown to reduce several MF-related symptoms and control spleen enlargement. (see *Treatment* on page 4)
- Radiation therapy—Radiation therapy uses high-powered beams, such as x-rays, to kill cancer cells. When other treatment methods have failed and surgical removal of the spleen is not a viable option, radiation therapy can be used to help reduce the size of the spleen.

Complications

As MF progresses, complications may arise.

- Portal hypertension—Increased blood flow from an enlarged spleen can lead to high blood pressure within the portal vein, which carries blood from the spleen to the liver. This can force excess blood into smaller veins in the stomach and esophagus, potentially causing the veins to rupture and bleed.
- Extramedullary hematopoiesis—Formation of blood cells outside the bone marrow, called "extramedullary hematopoiesis," may create clumps (tumors) of developing blood cells in other areas of the body. These tumors may cause such problems as bleeding in the gastrointestinal system, coughing or spitting up blood, compression of the spinal cord or seizures.
- Hardening and inflammation of bone tissue—Myelofibrosis can cause hardening of the bone marrow and inflammation of the connective tissue that surrounds the bones, resulting in severe bone and joint pain and tenderness.
- Gout—Because MF increases the body's production of uric acid, a byproduct of the breakdown of purines—a substance found naturally in the body—needlelike deposits of uric acid can form in the joints, causing joint pain and inflammation (gout).
- Acute myeloid leukemia (AML)—In about 12 percent of patients with myelofibrosis, MF will transform to AML, a type of blood and bone marrow cancer that progresses rapidly.

Diagnosis

A diagnosis of MF is made based on the World Health Organization (WHO) criteria. In people who have no symptoms, MF may be suspected when a routine medical checkup reveals an enlarged spleen and abnormal blood test results. The results of a blood test (a complete blood count, or CBC) that suggest a diagnosis of MF often include

- A decrease below the normal range in the number of red blood cells (anemia)
- An increase in the normal range in the number of white blood cells
- An increase above the normal range in platelet counts (for about one-third of patients)
- A mild to moderate decrease below the normal range in platelet counts (for about one-third of patients).

In addition to blood cell counts, blood tests may also show

- Teardrop-shaped red cells and immature red cells and white cells in the blood (seen by microscopic examination of the blood cells)
- Giant platelets, abnormal platelet formation and circulating dwarf megakaryocytes (bone marrow cells responsible for the production of platelets)
- Elevated serum levels of uric acid, lactic dehydrogenase (LDH), alkaline phosphatase and bilirubin

- Decreased serum levels of albumin, total cholesterol and high-density lipoprotein (HDL).

Because there are several other blood diseases, such as leukemia and lymphoma that can cause marrow fibrosis, to confirm a diagnosis of MF, the following tests may also be performed.

- Imaging tests—Ultrasound tests may be used to determine the size of the spleen. Magnetic resonance imaging (MRI) tests may be used to identify changes in the bone marrow that indicate MF.
- Bone marrow examination—Bone marrow biopsy and aspiration findings can confirm a diagnosis of MF. In these procedures (usually done together), a small amount of bone and marrow is removed and then examined under a microscope by a hematopathologist (a doctor specializing in evaluating cells, tissues and organs to diagnose disease). Studying genetic components of the bone marrow cells can show mutations in the cells that may help eliminate other types of bone marrow disorders. For example, the absence of the Philadelphia chromosome or the *BCR/ABL* translocation can rule out chronic myeloid leukemia (CML). A blood or bone marrow sample may also be used for a test called a "karyotype." In this test, a microscope is used to examine the size, shape and number of chromosomes in a sampling of cells. The results of the karyotype may be helpful in making certain treatment decisions.
- Gene tests—A sample of blood or bone marrow may be analyzed in a laboratory to look for gene mutations, such as the *JAK2* mutation, present in 50 to 60 percent of MF patients.

Treatment Planning

Some doctors use a prognostic scoring system to plan a risk-adapted treatment strategy for a patient, which might include observation only; Jakafi; investigational therapies (e.g., other JAK inhibitors, pomalidomide); drug therapy; allogeneic stem cell transplantation or reduced-intensity allogeneic stem cell transplantation; splenectomy; or radiation therapy. One model is The Dynamic International Prognostic Scoring System (DIPSS) Plus, which classifies risk as low (no risk factors), intermediate-1 (one risk factor), intermediate-2 (2 or 3 risk factors) and high (4 or more risk factors). The independent risk factors include thrombocytopenia, anemia, need for red blood cell transfusion, age above 65 years, leukocytosis (high white blood cell count), unfavorable karyotype, circulating blast cells and constitutional symptoms (e.g., weight loss greater than 10 percent in the previous year, unexplained fever or excessive sweating persisting for greater than one month).

Every patient's medical situation is different and should be evaluated individually by an oncologist who specializes in treating blood cancers. It is important for you and members of your medical team to discuss all treatment options, including treatments being studied in clinical trials.

For more information about choosing a doctor or a treatment center, see the free LLS publication *Choosing a Blood Cancer Specialist or Treatment Center*.

Treatment

Currently, there is no drug therapy that can cure MF. An allogeneic stem cell transplant (see *Stem Cell Transplantation* on page 5) is the only potential cure for MF. The procedure is risky in older MF patients, who may also have other health problems, so allogeneic stem cell transplantation is usually appropriate only for a small subset of younger patients, typically less than 5 percent of patients with MF.

Patients who are symptom-free and do not have signs of anemia, an enlarged spleen or other complications are generally not treated. Some people remain stable and symptom-free for many years. However, these patients need to be monitored closely through regular medical checkups and examinations to detect any signs and symptoms of disease progression.

Drug Therapies

- Janus-associated kinase (JAK) inhibitors—This drug class inhibits enzymes called "JAK1" and "JAK2," which are involved in the production of blood cells. Ruxolitinib (Jakafi™), given by mouth, is the first JAK inhibitor and currently the only drug approved by the FDA to treat symptoms and signs of MF, including an enlarged spleen, night sweats, itching and bone or muscle pain. It is indicated for treatment of patients with intermediate- or high-risk myelofibrosis, including primary myelofibrosis, post polycythemia vera myelofibrosis and post essential thrombocythemia myelofibrosis. The most common side effects affecting the blood cells are thrombocytopenia (a decrease below the normal number of platelets) and anemia. Other common side effects include bruising, dizziness and headache.

  Patients should be aware that after discontinuation of Jakafi, myelofibrosis signs and symptoms are expected to return. There have been isolated cases of patients discontinuing Jakafi during acute intervening illnesses after which the patient's clinical course continued to worsen. It has not been established whether discontinuation of therapy contributed to the clinical course of these patients. When discontinuing Jakafi therapy for reasons other than thrombocytopenia, gradual tapering of the dose of Jakafi may be considered.

For more details, please see the full prescribing information for Jakafi available at www.accessdata.fda.gov/drugsatfda_docs/label/2011/202192lbl.pdf or contact an LLS Information Specialist.

- Chemotherapy—Conventional chemotherapies kill cancer cells that divide rapidly. These treatments may also affect rapidly dividing healthy cells, such as cells that form nails and hair follicles, cells that line the gastrointestinal tract and stem cells that produce blood cells. Some systemic chemotherapies for symptoms of MF include
  - Cladribine (Leustatin®)—This chemotherapy, given intravenously (IV), is a purine analogue that interferes with the cell's ability to process DNA. It helps diminish the symptoms of anemia in MF patients.
  - Hydroxyurea (Hydrea®)—This common chemotherapeutic agent, given by mouth, is used to reduce a number of MF symptoms, as well as high platelet and white blood cell counts; an enlarged spleen; night sweats and weight loss.
- Immunomodulators (IMiDs)—The drugs in this class work against cancer cells by affecting the functions of the immune system. Two IMiDs, thalidomide (Thalomid®) and lenalidomide (Revlimid®), both given by mouth, are used to treat MF patients for anemia. Favorable responses to thalidomide have been reported in 20 to 60 percent of MF patients. Another IMiD, pomalidomide (Actimid®), also given by mouth, is showing positive results in clinical studies in the treatment of myelofibrosis-related anemia. Pomalidomide is also being studied in clinical trials to treat patients with myeloma. Interferon alfa (Intron®A, Roferon®-A), given by intramuscular or subcutaneous injection, is a synthetic version of a substance made by cells in the body to fight infection and tumors. It has been used to treat an enlarged spleen, bone pain and high platelet count in selected MF patients.
- Androgen therapy (Oxymetholone [Anadrol-50®], danazol)—These drugs, both given by mouth, are synthetic versions (analogues) of male hormones and can promote red cell production. They are used to relieve the symptoms of severe anemia. About one in three patients has improvement of anemia with androgen treatment. Due to the toxic effects of androgens on the liver, treatment with these drugs includes using blood tests and ultrasound imaging to track liver functions. Androgens may cause facial hair growth or other masculinizing effects in women.
- Recombinant erythropoietin (Epogen®, Procrit®)—This treatment, given intravenously (IV) or by subcutaneous injection, helps regulate red cell production. However, the response in anemia-related symptoms in MF patients has been limited.
- Glucocorticoids (also called "corticosteroids" or "steroids")—Glucocorticoids such as prednisone, given by mouth, are steroid compounds that are used to treat many conditions and may benefit MF patients who have significant anemia. About one in three patients has improvement of anemia with prednisone treatment.
- Bisphosphonates (pamidronate disodium [Aredia®], zoledronic acid [Zometa®])—Bisphosphonates are a class of drugs that prevent bone loss in cancer patients and may relieve bone pain and improve blood counts in MF patients. Both of these drugs are given intravenously (IV).
- Anagrelide hydrocholoride (Agrylin®)—This drug, given by mouth, may be used to treat patients who have a very high platelet count, especially following removal of the spleen ("splenectomy").

For side effects information, please see the free LLS publication *Understanding Drug Therapy and Managing Side Effects* and the FDA drug information webpage www.fda.gov/drugs/resourcesforyou/consumers/default.htm.

Radiation Therapy

Radiation may be useful for a small number of patients to treat an enlarged spleen, bone pain and tumors outside the marrow.

Splenectomy

The spleen can be surgically removed if it is very large and is causing a very low platelet count, severe anemia or portal hypertension. The decision to do a splenectomy is based on weighing the benefits and the risks to an individual patient. MF patients who will be undergoing a splenectomy need to be evaluated before surgery and then monitored afterward for an increased risk of bleeding complications, including blood clot formation leading to a stroke or pulmonary embolism; infection; liver enlargement; and an increase in platelet count.

Stem Cell Transplantation

Allogeneic stem cell transplantation (ASCT) is the only current treatment with the potential to cure myelofibrosis, but it also carries a high risk of life-threatening side effects for most MF patients. In this procedure, the patient receives high doses of chemotherapy or radiation therapy to destroy the diseased bone marrow. Then, healthy hematopoietic (blood-forming) stem cells from a compatible donor (a sibling or unrelated person whose stem cells "match" the patient's) are infused into the MF patient. The transplanted healthy cells travel to the patient's bone marrow, replacing the

defective stem cells. The new cells grow and provide a supply of red cells, white cells (including immune cells) and platelets.

Most patients with MF are older and often have other health conditions that may impair organ function. Older individuals are also more likely to have other medical problems, develop complications from the treatment and have decreased tolerance for the cumulative effects of the intensive chemotherapy and for radiation treatments needed before the transplant. However, these are generalizations. Allogeneic stem cell transplantation can be used in older people when medically appropriate. Whether or not a patient is a candidate for transplantation is determined by medical indications and the availability of a donor. There is no specific age cutoff for stem cell transplantation.

Reduced-intensity or "nonmyeloblative" allogeneic stem cell transplantation is a type of transplant that uses lower doses of chemotherapy or radiation, and it is being used to treat some patients with leukemia, lymphoma or myeloma. Compared to a standard ASCT, a reduced-intensity transplant delivers lower doses of chemotherapy drugs and/or radiation to the patient in preparation for the transplant. The success of reduced-intensity transplantation is a result of the graft-versus-tumor effect of the donor stem cells, rather than of high doses of chemotherapy. This approach may benefit older and sicker patients and other selected patients. Reduced-intensity transplants are now done with results that are increasingly encouraging for MF patients.

Talk to your doctor about whether stem cell transplantation is a treatment option for you. For additional information on stem cell transplantation, please see the free LLS publication *Blood and Marrow Stem Cell Transplantation*.

Side Effects of Treatment for Patients with MF

The side effects of treatment will depend on many factors, including type of treatment and dosage, the age of the patient and coexisting medical conditions. Therapy may induce fatigue, nausea, fever, chills, dizziness, shortness of breath, peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet), temporary loss of hair and other side effects.

Side-effects management is important. If you are having any concerns about your side effects, talk to your doctor to get help. Most side effects are temporary and resolve when treatment is completed. For specific drug information, see the free LLS publication *Understanding Drug Therapy and Managing Side Effects* and the FDA drug information webpage www.fda.gov/drugs/resourcesforyou/consumers/default.htm.

Treatments Under Investigation

The discovery of the *JAK2* gene mutation in 2005 has led to clinical trials of several JAK2 or JAK1/JAK2 inhibitors in the treatment of MF. The *JAK2* mutation is one of several gene mutations believed to be involved in the development of MF. In addition to a number of JAK inhibitors being evaluated in clinical studies, other pathway inhibitors are also being tested in early-phase clinical trials.

Patients may have the opportunity to take part in clinical trials if their doctors feel that these new approaches are warranted. These trials, conducted under rigorous guidelines, help researchers to determine the beneficial effects and possible adverse side effects of new treatments. Studies are also conducted to evaluate new indications for therapies that are already approved for treatment of other cancers or diseases. For more information about clinical trials, see the free LLS publication *Understanding Clinical Trials for Blood Cancers* or visit www.LLS.org/clinicaltrials.

Some of the classes of novel therapies and drugs under investigation include

- JAK inhibitors that target abnormal pathway signaling caused by a specific mutation in the *JAK2* gene. Several JAK inhibitors are now in clinical trials and are showing effectiveness in reducing spleen size and improving anemia and symptoms such as night sweats and fatigue. These potential treatments include CYT387, SAR302503 (TG101348), AZD1480, CEP-701, SB1518 and LY2784544.
- Histone deacetylase (HDAC) inhibitors play an important role in the regulation of gene expression. These HDAC inhibitors are in clinical studies for MF: panobinostat (LBH589), givinostat (ITF2357) and vorinostat (Zolinza®), which is FDA approved for treatment of cutaneous T-cell lymphoma.
- Immunomodulatory drugs (IMiDs) are a class of drugs that work against cancer cells by affecting the functions of the immune system. Three IMiDs are being investigated for the treatment of patients with MF. These are thalidomide (Thalomid®) and lenalidomide (Revlimid®), which are FDA approved to treat myeloma patients and pomalidomide (Actimid®), which is currently being studied in clinical trials for the treatment of myeloma patients. In MF patients, Thalomid has been associated with improvements in anemia, platelet count, enlarged spleen, and symptoms such as night sweats, weakness, fatigue and shortness of breath. Revlimid is active in treating anemia, thrombocythemia, enlarged spleen and marrow fibrosis. Actimid appears effective in treating anemia and improving low platelet counts. Patients taking

Thalomid or Revlimid should be closely monitored for symptoms of peripheral neuropathy (a tingling or burning sensation in the hands and feet) and myelosuppression (decreased production of blood cells). These side effects are less frequent for patients taking Actimid and are linked to higher doses of the drug.

Treatment Outcomes

The prognosis (the likely outcome of a disease) varies widely in patients with MF. Each patient's prognostic risk factors are evaluated individually. While the median survival for people with MF is 3.5 to 5.5 years, people younger than 55 and with good prognostic factors have a median survival of 11 years. However, some people may survive for decades following a diagnosis. It is important to know that outcome data can show how groups of people with MF responded to treatment, but cannot determine how any one person will respond. For these reasons, patients are advised to discuss survival information with their doctors.

Although there is no staging system for MF, the International Prognostic Scoring System (IPSS), uses the following five risk factors for estimating survival from the time of diagnosis:

- Age—65 years or older
- Anemia—Hemoglobin level lower than 10 grams per deciliter (g/dL)
- Symptoms—Such as fever, night sweats or weight loss
- Leukocytosis—An elevated white cell count of above 30,000/microL
- Circulating blood blast cells—At least 1 percent.

According to the IPSS, patients without any of these adverse features, excluding age, have a median survival of more than ten years. The presence of any two of the above adverse features reduces the median survival to less than three years.

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We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the country and in Canada. To find the chapter nearest you, enter your ZIP code into "Find your Chapter" at www.LLS.org or contact

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Email: infocenter@LLS.org

Callers may speak directly with an Information Specialist Monday through Friday, from 9 a.m. to 6 p.m. ET. You may also contact an Information Specialist between 10 a.m. and 5 p.m. ET by clicking on "Live Chat" at www.LLS.org or by sending an email. Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support and assist with clinical-trial searches for leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms. The LLS website has information about how to find a clinical trial, including a link to TrialCheck®, a clinical-trial search service.

LLS also provides free publications that can be ordered via the 800 number or through the "Free Education Materials" option at www.LLS.org/resourcecenter.

The Leukemia & Lymphoma Society and the MPN Research Foundation are collaborating to advance therapies for patients with myelofibrosis through the MF Challenge, a partnership to fund concept grants to increase scientific understanding that will lead to new treatments for MF patients.

The Leukemia & Lymphoma Society is a part of the MPN Coalition which includes CancerCare, Inc., Cancer Support Community, MPN Education Foundation, MPN Research Foundation and the National Organization for Rare Disorders. The Coalition was formed to provide a forum for discussion of and action on needs and challenges facing those living with an MPN.

Other Resources

Learn about progress in treatments for myelofibrosis patients from the LLS webcast *Advances in Blood Cancers: Update on Treatment for Myelofibrosis.* To access this webcast, please visit www.LLS.org/webcasts.

The MPN Coalition developed a calendar for myelofibrosis patients called *Tracking Your Myelofibrosis Symptoms: Playing an Active Role in Your Health*. You can order a copy by calling our Information Specialists.

Cancer Support Community, in partnership with LLS, the MPN Research Foundation and the MPN Education Foundation, developed an educational booklet for patients and caregivers called *Frankly Speaking about Cancer: Myelofibrosis.* Please visit www.cancersupportcommunity.org/MainMenu/About Cancer/Types-of-Cancer/Myelofibrosis or contact an Information Specialist for more information.

Cancer*Care*
(800) 813-4673
www.cancercare.org

Cancer*Care* provides free, professional support services to anyone affected by cancer. They provide counseling, support groups, education workshops, publications and financial assistance.

Cancer Support Community
(888) 793-9355
www.cancersupportcommunity.org/

Cancer Support Community is an international non profit organization dedicated to providing support, education and hope to people affected by cancer.

MPN Education Foundation
www.mpdinfo.org

The MPN Education Foundation provides information, education and support and looks to advance research and develop drugs to improve the quality of life and care of MPN patients. The Foundation provides patient and doctor conferences and facilitates patient participation and accrual in clinical studies and surveys.

The MPN Research Foundation
www.mpnresearchfoundation.org

The MPN Foundation is a nonprofit organization whose primary mission is to promote, fund and support the most innovative and effective research into the causes, treatments and potentially the cure for essential thrombocythemia, polycythemia vera and MF. The organization also provides information and support to people who have myeloproliferative neoplasms.

The Myeloproliferative Disorders Research Consortium (MPD-RC)
www.mpd-rc.org

The MPD-RC is an international, multi-institutional nonprofit consortium funded by the National Cancer Institute and set up to coordinate, facilitate, and perform basic and clinical research of the Philadelphia Chromosome-negative myeloproliferative neoplasms (Ph-MPNs).

The National Cancer Institute (NCI)
(800) 422-6237
www.cancer.gov

The National Cancer Institute (NCI), part of the National Institutes of Health, is a national resource center for information and education about all forms of cancer, including myeloproliferative neoplasms. The NCI also provides a clinical trial search feature, the PDQ® Cancer Clinical Trial Registry, at www.cancer.gov/clinicaltrials, where MF patients can look for clinical trials.

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