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NCCN GUIDELINES FOR PATIENTS®

2018

Myeloproliferative Neoplasms

CLASSIC TYPES

Presented with support from:

NCCN FOUNDATION® Guiding Treatment, Changing Lives.

MPN RESEARCH FOUNDATION CHANGE YOUR PROGNOSIS

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LEARNING that you have cancer can be overwhelming.

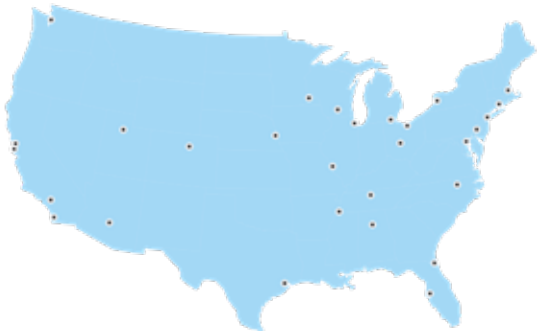
The goal of this book is to help you get the best care. It presents which cancer tests and treatments are recommended by experts in myeloproliferative neoplasms.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat myeloproliferative neoplasms. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of myeloproliferative neoplasms. Key points of the book are summarized in the NCCN Quick Guide™. NCCN also offers patient books on leukemia, lymphoma, myelodysplastic syndromes, and many other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other resources.

About

National Comprehensive Cancer Network®



These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN FOUNDATION®
Guiding Treatment, Changing Lives.

NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.

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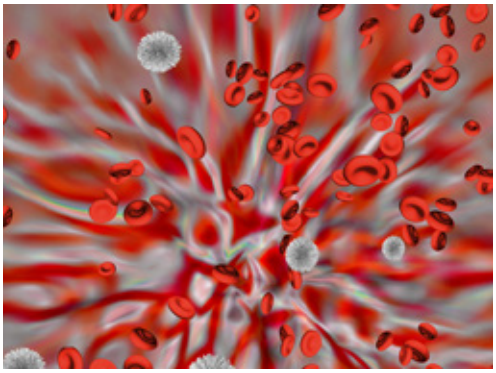
MPN Research Foundation
The NCCN guidelines for myelofibrosis provide clarity for physicians and patients about their options and what to expect upon diagnosis with PV, ET or MF. These are long awaited by the patient community and we are so glad to see it come to fruition. mpnresearchfoundation.org.

Endorsed by

Leukemia & Lymphoma Society
LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients. LLS.org/informationspecialists.

MPN Cancer Connection
MPN Cancer Connection (MPN-CC) recognizes MPN patients are in fact “cancer patients” and should have full access to programs, benefits and resources available in your area. MPN-CC is pleased to support the comprehensive resource provided by the NCCN Patient Guidelines for Myeloproliferative Neoplasms (MPNs). MPNCancerConnection.org.

MPN Education Foundation
Educating physicians and patients about evidence-based diagnostic algorithms and treatment for the myeloproliferative neoplasms will benefit both, and will improve patient access to those treatments. The MPN Education Foundation is pleased to endorse this landmark effort on behalf of those we serve. mpninfo.org.



Contents

How to use this book

Who should read this book?

This book is about treatment for adults with myeloproliferative neoplasms. These cancers are called MPNs, for short. There are several types of MPNs. The focus of this book is on the classic types—essential thrombocythemia, polycythemia vera, and primary myelofibrosis. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It is a good starting point to learn what your options may be.

Are the book chapters in a certain order?

Part 1 explains what MPNs are. It may be a good starting point if you do not know much about MPNs. Tests that doctors use to diagnose and plan treatment for MPNs are described in **Part 2**.

Treatment is discussed in Parts 3 through 5. **Part 3** is a treatment guide for essential thrombocythemia. **Part 4** is a guide to polycythemia vera, and Part 5 is a guide to myelofibrosis. Tips for talking and deciding your options with your doctor are presented in **Part 6**.

Does this book include all options?

This book includes information for many people. Your treatment team can point out what applies to you. They can also give you more information. While reading, make a list of questions to ask your doctors.

The treatment options are based on science and the experience of NCCN experts. However, their recommendations may not be right for you. Your doctors may suggest other options based on your health and other factors. If other options are given, ask your treatment team questions.

Help! What do the words mean?

In this book, many medical words are included. These are words that your treatment team may say to you. Most of these words may be new to you. It may be a lot to learn.

Don't be discouraged as you read. Keep reading and review the information. Ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the *Dictionary*. Acronyms are also defined when first used and in the *Glossary*. Acronyms are short words formed from the first letters of several words. One example is DNA for **d**eoxyribo**n**ucleic **a**cid.

1
MPN basics

You've learned that you have or may have a blood cancer. It's common to feel shocked and confused. Part 1 reviews some basics that may help you learn about myeloproliferative neoplasms.

Blood

To learn about blood cancers, you first must know about blood. Blood is one of the fluids in the body. It consists of blood cells that move within plasma. Plasma is mostly water.

Blood cells

There are three main types of blood cells. One type is red blood cells (also called erythrocytes). Another type is white blood cells (leukocytes). The third type is platelets (thrombocytes).

Blood cells have important jobs. Red blood cells carry oxygen throughout the body. White blood cells help fight germs. Platelets help control bleeding.

Your blood cells don't live forever. Many have a short lifespan. Thus, blood cells are being replaced in your body all the time.

Blood cell formation

Most blood cells are formed in bone marrow. Bone marrow is the sponge-like tissue in the center of most bones. **See Figure 1**.

Within your bone marrow are blood-forming cells. Blood stem cells are the cells from which all blood cells are formed. They are also called hematopoietic stem cells. As shown in **Figure 2**, they start the family tree of blood cells.

Blood stem cells can make exact copies of themselves. They can also make new cells that are a step closer to being a blood cell. These cells are called progenitor cells. Compared to stem cells, progenitor cells are set to become a certain type of blood cell.

There are two types of blood progenitor cells. Lymphoid progenitor cells start one branch of the family tree. Myeloid progenitor cells start another branch.

At the end of the lymphoid branch is a type of white blood cell called lymphocytes. There are three types of lymphocytes. They are NK cells, B-cells, and T-cells. Lymphocytes are released from bone marrow into the bloodstream.

At the end of the myeloid branch are white blood cells, red blood cells, and platelets. These white blood cells are called granulocytes. Granulocytes include neutrophils, eosinophils, and basophils. Red blood cells, platelets, and granulocytes are released from bone marrow into the bloodstream.

A disease of cells

Your body is made of trillions of cells. Cancer is a disease of cells. Each type of cancer is named after the cell from which it is derived.

MPNs (**m**yelo**p**roliferative **n**eoplasms) are a group of rare blood cancers. They are cancers that derive from blood-forming stem cells within the myeloid branch. "Myelo" means marrow. "Proliferative" means growing and refers to making too many cells. A neoplasm is any abnormal growth. MPNs have too many blood-forming cells in the marrow. In turn, there are also too many blood cells.

MDS (**m**yelo**d**ysplastic **s**yndromes) are also cancers of blood-forming cells. However, the blood-forming

Figure 1
Bone marrow

Bone marrow is the sponge-like tissue in the center of most bones. Most blood cells are formed in bone marrow.

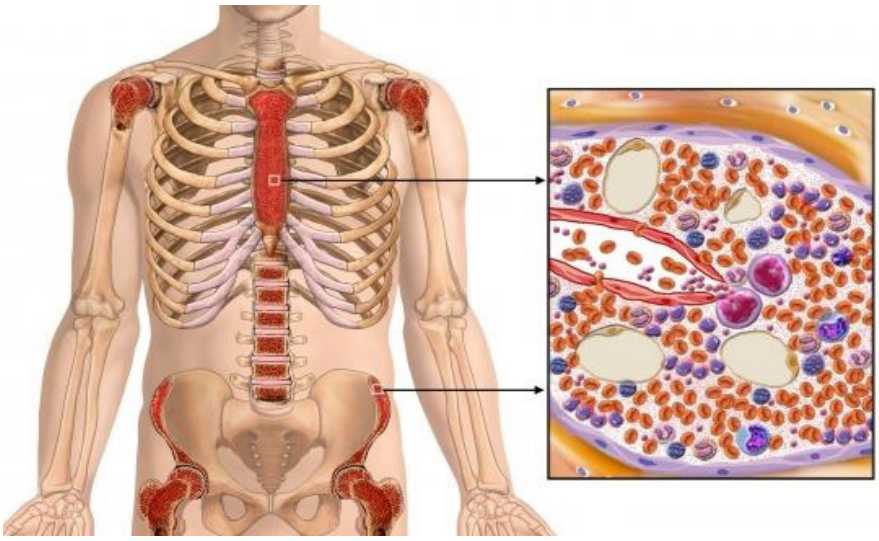
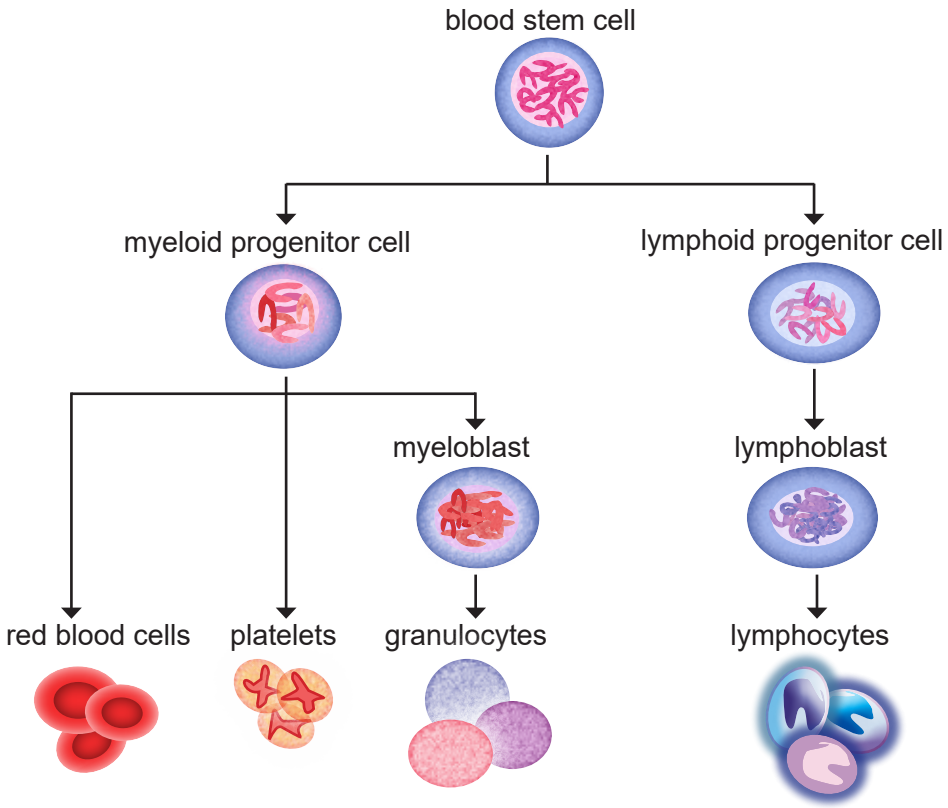


Figure 2
Blood cells

Blood (hematopoietic) stem cells are the cells from which all blood cells are formed. They make two types of progenitor cells. Common lymphoid progenitor cells form into white blood cells called lymphocytes. Common myeloid progenitor cells form into red blood cells, platelets, and white blood cells called granulocytes.



cells in MDS fail to develop into normal blood cells. Thus, there are very few blood cells in MDS.

The cause of MPN

Cells have a control center called the nucleus. The nucleus contains chromosomes, which are long strands of DNA (**d**eoxyribo**n**ucleic **a**cid) tightly wrapped around proteins. **See Figure 3**. Within DNA are coded instructions for building new cells and controlling how cells behave. These instructions are called genes.

There are often abnormal changes in genes within cancer cells. These abnormal changes are called mutations. Mutations cause cancer cells to not behave like normal cells. An example is the making of too many blood cells in MPNs. Also, mutations sometimes cause cancer cells to look very different from normal cells. Read Part 2 to learn more about the known mutations in MPNs.

Classic types

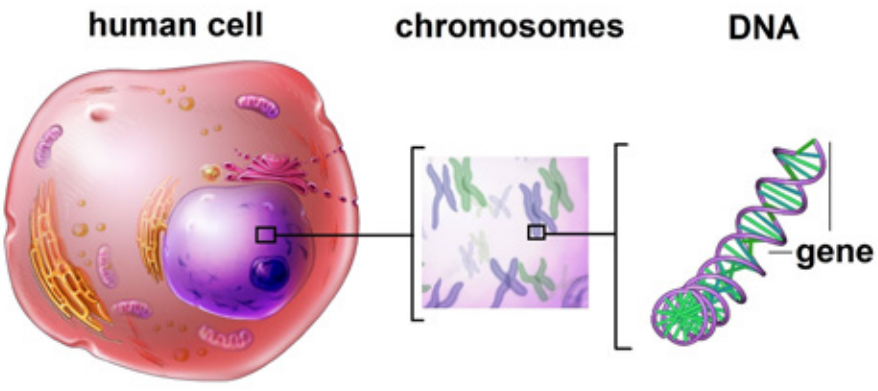
There are three classic types of MPNs. The most common type is ET (**e**ssential **t**hrombocythemia). The other types are PV (**p**olycythemia **v**era) and PMF (**p**rimary **m**yelo**f**ibrosis).

A key feature of ET is too many megakaryocytes. Megakaryocytes are a type of blood cell within bone marrow. Platelets are tiny pieces of megakaryocytes. Thus, another feature of ET is too many platelets in blood. This is called thrombocythemia. Essential thrombocythemia means the condition is caused by a problem in the blood cell-making process within bone marrow.

A key feature of PV is too many red blood cells. High levels of white blood cells and platelets may also be present. The red blood cells amass in bone marrow and blood. As a result, blood becomes thicker than normal (viscous).

Figure 3
Genetic material in cells

Most human cells contain the "blueprint of life"—the plan by which our bodies are made and work. The plan is found inside of chromosomes, which are long strands of DNA that are tightly wrapped around proteins. Genes are small pieces of DNA that contain instructions for building new cells and controlling how cells behave. Humans have an estimated 20,000 to 25,000 genes.



A key feature of PMF is scarring (or fibrosis) of the bone marrow. However, there may be high blood counts but no scarring in early phases of PMF. The scar tissue may replace bone marrow.

With less bone marrow, the number of blood cells may drop. As a result, the spleen and liver may begin to make blood cells and grow larger in size (enlarge). These organs may also enlarge because they trap abnormal blood cells.

PMF occurs in people without a history of bone marrow problems. However, MF (**m**yelo**f**ibrosis) can also develop in people with either ET or PV. If this occurs, it is called post-ET myelofibrosis or post-PV myelofibrosis based on the cancer.

Health risks

MPNs are chronic blood cancers. They do not go away on their own and, for now, there's no cure. Without treatment, MPNs get worse over time. It can take many years for MPNs to worsen to the point of causing symptoms.

Symptoms

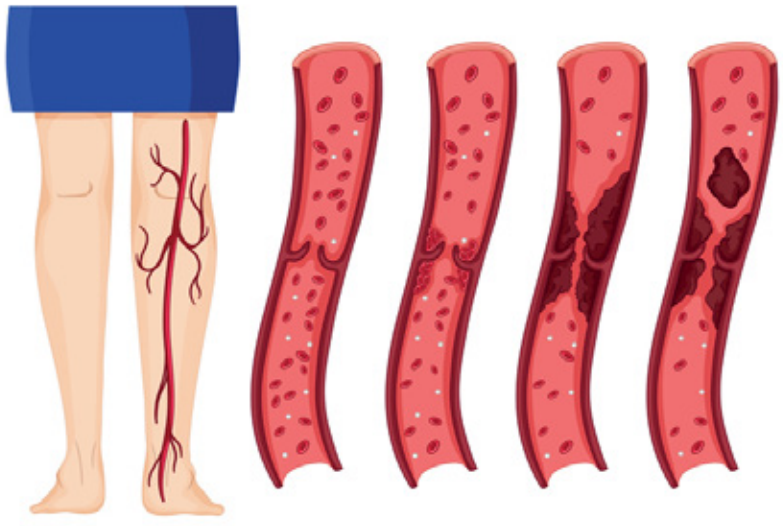
People may have symptoms for a long time before they learn they have a MPN. The most common symptom is feeling tired despite sleep (fatigue). Other symptoms include itchy skin, night sweats, bone pain, fever, and weight loss. These symptoms differ across the MPNs. Read Part 2 for more information about symptoms.

Blood clots and bleeding

MPNs can lead to serious health conditions. MPNs increase the likelihood for blood clots (thrombosis) and bleeding. Bleeding is often minor but can be severe. Blood clots can block blood vessels and can sometimes be deadly. **See Figure 4**. Blockage of

Figure 4
Blood clot

This Figure depicts the formation of a blood clot in a leg vein. On the far right, a piece of the blood clot has detached. It could travel through the heart to the lungs and get stuck. This is called a pulmonary embolism. Pulmonary embolisms can be deadly.



a blood vessel in the lung by a blood clot is called a pulmonary embolism. A blood clot in an artery to the brain can cause a stroke.

Other cancers

MPNs can transform. ET and PV can evolve into MF. Some MPNs change into MDS. Sometimes, MPNs may become a fast-growing cancer called AML (**a**cute **m**yeloid **l**eukemia).

The likelihood to transform into AML differs among the MPN subtypes. MF is the most likely to transform but very rarely happens. ET is the least likely to become AML.

Potentially shorter lifespan

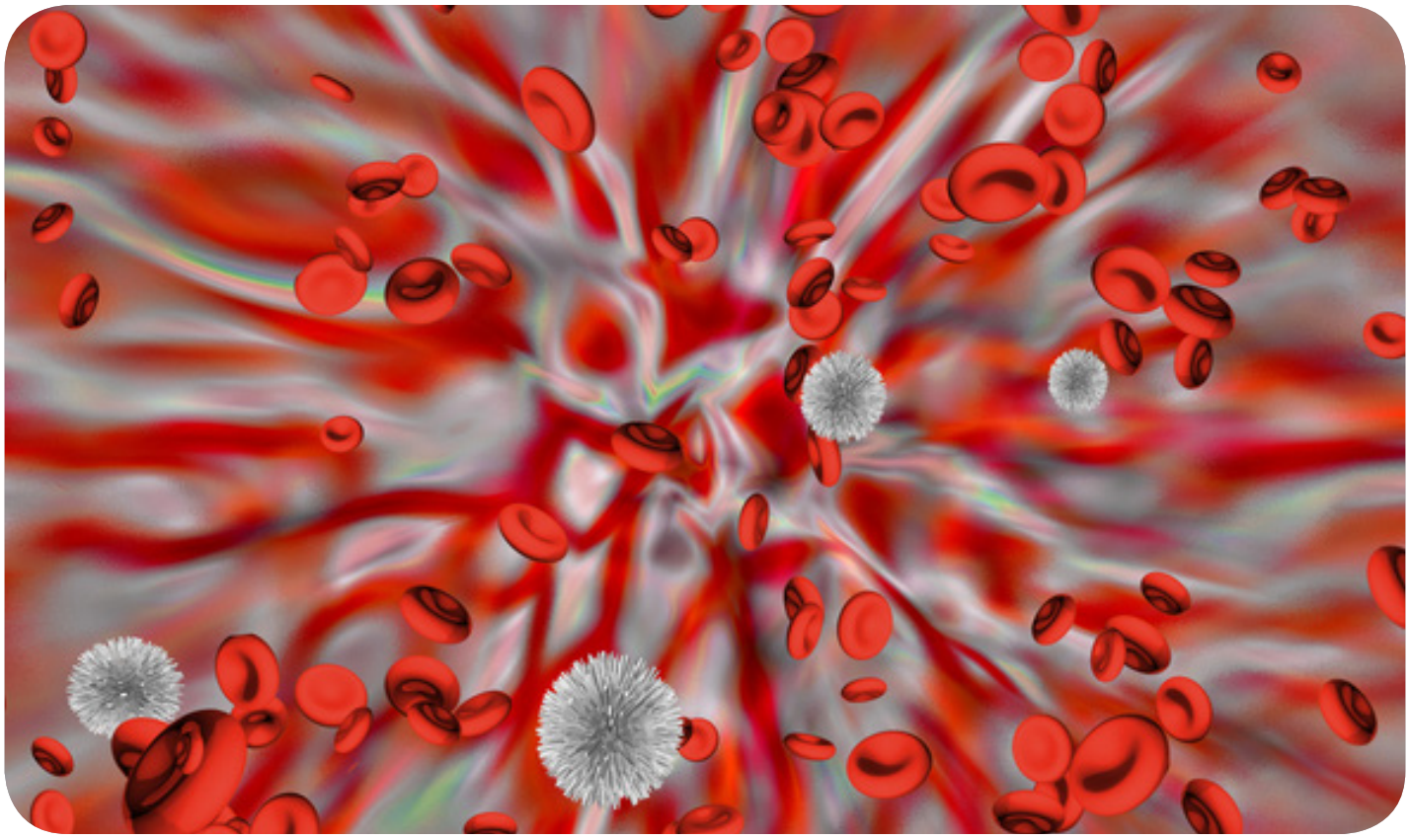
MPNs are slow-growing cancers. Many people can live for years with the proper treatment. However, people with a MPN may have a shorter lifespan compared to their peers. People with MF typically have shorter lifespans than people with ET or PV.

Review

- Most blood cells are formed in bone marrow. Blood (hematopoietic) stem cells are the cells from which all blood cells are formed.
- MPNs are a group of rare blood cancers. They are cancers derived from blood-forming stem cells.
- The three classic MPNs are essential thrombocythemia, polycythemia vera, and primary myelofibrosis.
- People may have symptoms for a long time before they learn they have a MPN.
- MPNs can lead to serious health conditions, such as blood clots and leukemia.

> A rare disease isn't so rare when you have one.
>
> – Jean
> Survivor, Polycythemia vera

2
Testing for MPN



Your doctor may think you have a blood cancer. Part 2 describes the tests used to diagnose MPN. It also describes tests used for treatment planning.

Medical history

Your medical history includes any health events and medicines you've taken in your life. You will be asked about illnesses, injuries, health conditions, and more. It may help to make a list of old and new medications while at home to bring to your doctor's office. Your doctor will also want to know if you've had blood transfusions.

Another important issue is the health of your blood-flowing (cardiovascular) system. Tell your doctor if you have high blood pressure or diabetes. Your doctor will also want to know about your diet, exercise level, and smoking history. Also, tell your doctor if you've had blood clots or abnormal bleeding.

Some cancers and other health conditions can run in families. Thus, your doctor will ask about the medical history of your blood relatives. You doctor may ask about the health of your siblings, your parents and their siblings, and your grandparents and their siblings. Be prepared to tell who in your family has had what diseases and at what ages.

A medical history is needed for diagnosis and treatment planning. See Guide 1 for a complete list of care that is advised prior to treatment. Some tests are for everyone with MPN while others are for a select group.

Symptom survey

Sometimes MPNs cause symptoms. Such symptoms can be assessed with a survey called the MPN-SAF (**M**yelo**p**roliferative **N**eoplasm **S**ymptom **A**ssessment **F**orm). This survey lists 18 symptoms. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms.

This form is used by doctors to assess symptom burden and plan treatment. Your symptoms will also be tracked during treatment. More information on symptom tracking for each classic MPN is in Parts 3 through 5.

Guide 1. Tests for MPN

Test name
• Medical history
• MPN-SAF survey
• Physical exam
• CBC with differential
• Comprehensive metabolic panel
• EPO and iron levels
• Bone marrow aspiration and biopsy
• *BCR-ABL1* testing
• Bone marrow cytogenetics
• Molecular testing for JAK2 mutations and maybe MPL and CALR mutations
• HLA typing for some people
• Coagulation tests for some people

Physical exam

Doctors often perform a physical exam along with taking a medical history. A physical exam is a study of your body for signs of disease. To start, your basic body functions will be measured. These functions include your temperature, blood pressure, and pulse and breathing (respiration) rate. Your weight will also be checked.

During the exam, your doctor will listen to your lungs, heart, and gut. Your doctor will also look at and feel parts of your body. This is done to see if organs are of normal size, are soft or hard, or cause pain when touched. Cancer and other health conditions can cause organs to become enlarged and hard. With MPNs, your spleen and liver may be larger than normal.

Blood tests

Blood tests are useful for diagnosing MPN. They can help to find other diseases, too. They require a sample of your blood. Samples of blood can be removed with a blood draw.

Before a blood draw, you might need to stop drinking and eating for several hours. A needle will be inserted into your vein to remove blood. The needle may bruise your skin. You may feel dizzy from the blood draw.

Your blood sample will be sent to a lab. A pathologist will perform the blood tests. A pathologist is a doctor who's an expert in testing cells to find disease.

CBC with differential

A CBC (**c**omplete **b**lood **c**ount) measures parts of the blood. It is often done with a machine. Test results include counts of white blood cells, red blood cells, and platelets. Another result is the fraction of red blood cells to blood (hematocrit). Hemoglobin levels are also measured. Hemoglobin is a protein within red blood cells. It carries oxygen from your lungs to the rest of your body.

There are several types of white blood cells. A differential counts the number of each type. It also checks if the counts are in balance with each other. Your doctor can determine the cause of an abnormal white blood count from this test.

Cancer and other health problems can cause low or high counts. With MPNs, one or more cell counts are high. Hemoglobin and hematocrit levels are high in PV.

Blood smear

A trained specialist will look at a drop of your blood. The blood drop will first be placed on a glass slide and prepared with a stain. It will then be viewed with a microscope. This is called a blood smear.

A blood smear reveals important information about your blood cells. It can show which types of cells are present. With MPN, sometimes blood-forming cells are present. These cells aren't usually in blood. A blood smear can also reveal if the blood cells look normal or not. Finding cells with an abnormal shape or size can be a clue as to what disease you have.

Comprehensive metabolic panel

Chemicals in your blood come from your liver, bone, and other organs. A comprehensive metabolic panel often includes tests for up to 14 chemicals. The tests show if the level of chemicals is too low or high. Abnormal levels can be caused by cancer or other health problems. Some chemicals in the panel include:

LDH

LDH (**l**actate **d**e**h**ydrogenase) is a protein that is in most cells. Dying cells release LDH into blood. High levels of LDH can be a sign of MF.

Uric acid
Certain phases of MPNs produce many bone marrow cells. In turn, uric acid levels increase. High uric acid levels can cause gout and kidney stones. Testing for uric acid is done to assess if you have excess uric acid in your blood (hyperuricemia).

Liver function tests
Your liver is an organ in the upper right side of your abdomen. It does many important jobs, such as remove toxins from your blood. Liver function tests assess for chemicals that are made or processed by the liver. With MPN, there may be abnormal results if the cancer is in the bone or liver.

EPO and iron levels

EPO (**e**rythro**po**ietin) and iron levels can impact red blood cells. EPO is a hormone made by your kidneys. It is needed to make red blood cells. You may have low counts of red blood cells. Testing may reveal that low EPO levels—instead of cancer—are the cause.

EPO testing also helps to diagnose PV. Features of PV include high red blood cell counts and hemoglobin level. These high amounts suppress EPO levels. In PV, blood tests usually show low EPO levels.

Iron is a mineral that is part of hemoglobin. Low levels of iron can cause hemoglobin levels to drop (anemia). In turn, iron-deficiency anemia can cause high counts of platelets. Iron testing may help reveal that iron deficiency—instead of cancer—is causing increased platelets.

Low iron levels also occur in PV. The supply of iron is used to create red blood cells. Thus, in contrast to iron-deficiency anemia, PV causes high red blood cell counts and hemoglobin levels.

> “A diagnosis was made because of migraines due to a high platelet count and following blood work and a bone marrow biopsy confirmed ET.
>
> – Antje
> Survivor, Essential thrombocythemia

Bone marrow exam

A bone marrow exam can be very helpful. It can be used to confirm MPN and get a sense of its outlook (prognosis). It can also show how much scarring (fibrosis) is present.

A bone marrow exam consists of two procedures. A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a sample of bone and soft bone marrow.

Often, these procedures are done at the same time. They are performed on the back of the hip bone. You may receive a light sedative beforehand.

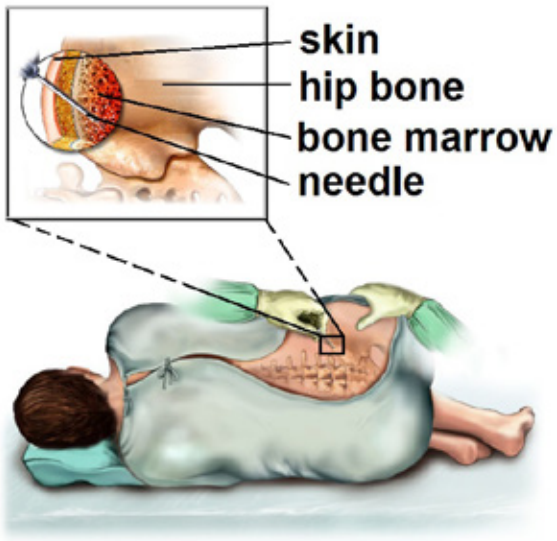
You will likely lie on your side as shown in **Figure 5**. Some people lie on their belly. Your doctor will first clean and numb your skin.

For aspiration, a hollow needle will be inserted into your skin and pushed into the bone. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be inserted into your bone and rotated to remove a core sample. You may feel bone pain during and after the procedures for a few days. Your skin may bruise.

The samples will be sent to a lab for testing. Reticulin and trichrome stains will be applied. These stains show how much scarring is present.

Figure 5
Bone marrow exam

A bone marrow exam removes a sample of bone and marrow for testing. The procedure is often done on the back of the hip.



Genetic tests

Genetic tests assess for abnormal changes in genes and chromosomes. These tests are used for diagnosis and treatment planning. The genetic tests for MPN are described next.

BCR-ABL1

CML (**c**hronic **m**yeloid **l**eukemia) is a type of MPN. It is the only cancer that has the *BCR-ABL1* fusion gene. Normal blood cells do not have this gene. It is formed when parts of chromosomes 9 and 22 break off and switch with each other. Testing for *BCR-ABL1* is advised to rule out CML. One of the following two tests can be used.

QPCR

QPCR (**q**uantitative reverse transcriptase-**p**olymerase **c**hain **r**eaction) measures the number of cells that have the *BCR-ABL1* fusion gene. Either a bone marrow or blood sample can be used. QPCR is very sensitive. It can find one CML cell among more than 100,000 normal cells.

FISH

FISH (**f**luorescence **i**n **s**itu **h**ybridization) uses special color dyes—called probes. The probes attach to the *BCR* gene and the *ABL* gene. The *BCR-ABL1* fusion gene is detected when the colors of the probes overlap. This test can be performed on either a bone marrow or blood sample.

Bone marrow cytogenetics

Cytogenetics is the study of chromosomes. For MPNs, bone marrow cells should be tested. Blood may be used if a marrow sample can't be obtained. However, finding an abnormal change is less likely when using blood.

Doctors use cytogenetics for a few reasons. It may be used to assess clonality but molecular testing is often used instead. MPNs are a clonal disease. This means all the cancer cells came from the same parent cell.

In the late phases of MPNs, it is common for cells to have abnormal chromosomes. There are many types of chromosome defects. A part of or the entire chromosome may be missing. There may be an extra part in a chromosome. Parts of chromosomes may have switched places with each other. The outlook (prognosis) is usually worse if many abnormal changes are present.

Cytogenetics are also used to assess treatment results. Treatment is working well if tests show the defects are no longer present. Defects reappear when treatment stops working. More information on checking treatment results is in Parts 3 through 5.

Karyotype ± FISH

Cytogenetics for MPN is done with a karyotype. FISH may be used, too. A karyotype is a picture of the chromosomes in cells. **See Figure 6**. A chemical will be added to the marrow sample to start cell growth. Then, an expert will study the cells with a microscope. A "complex karyotype" may be present. A complex karyotype is when there are 3 or more unrelated defects in chromosomes that occur in more than one cell.

Molecular testing

Molecular testing includes tests of genes or their products (proteins). There are three common gene mutations among MPNs as well as others. Testing for these mutations is needed for diagnosis. The outlook of the disease also depends on which mutations are present. A blood sample may be used for testing. Molecular testing for MPN includes the following:

JAK2 mutations

The most common mutation among MPNs is the *JAK2 V617F* mutation. It occurs in chromosome 9 in a part of the *JAK2* gene called exon 14. It is present in almost everyone with PV. It is also present in over

half of people with ET or PMF. Testing for *JAK2 V617F* is needed for anyone who may have a MPN.

A small subset of people with PV may have another *JAK2* mutation. This mutation occurs in exon 12. If the *JAK2 V617F* mutation is absent, testing for the *JAK2 exon 12* mutation should be done.

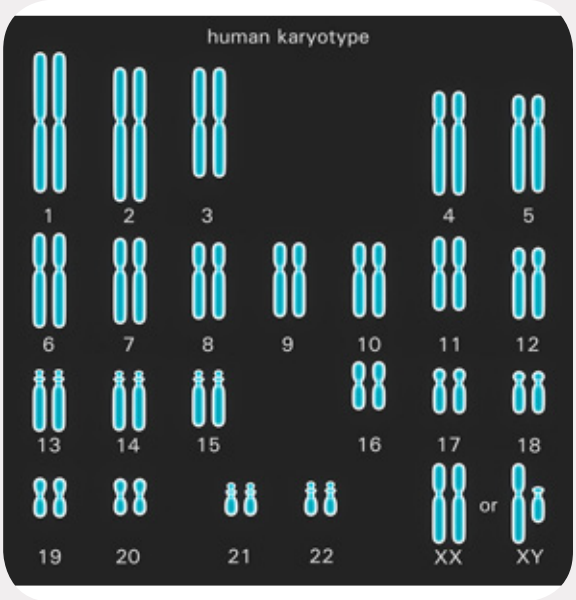
CALR mutations
The *CALR* gene is on chromosome 19. *CALR* mutations occur in 20 to 30 out of every 100 people with ET or MF (20% to 30%). If the *JAK2 V617F* mutation is absent, testing for the *CALR* mutations is needed for ET and MF.

MPL mutations
The *MPL* gene is on chromosome 1. *MPL W515* mutations are less common than *CALR* mutations. They occur in 5 to 10 out of every 100 people with ET or MF (5% to 10%). If the *JAK2 V617F* mutation is absent, testing for the MPL mutations is needed for ET and MF.

Other mutations
About 10 out of every 100 people with MF or ET do not have *JAK2*, *MPL*, and *CALR* mutations. These cancers are called triple-negative MPN. Mutations in *ASXL1*, *EZH2*, *TET2*, *IDH1*, *IDH2*, *SRSF2*, and *SF3B1* genes may help to diagnosis PMF.

Figure 6
Karyotype

A karyotype is a picture of the chromosomes in cells. It is a test that shows abnormal changes in chromosomes.



HLA typing

HLAs (**h**uman **l**eukocyte **a**ntigens) are proteins found on the surface of most cells. They are markers of your body's cells. They allow your body to tell which cells are its own and which are foreign.

HLAs do not differ between cells within a person. In other words, all your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

HLA typing is a test that detects a person's HLA type. You will receive this test if a transplant of healthy stem cells from a donor may be a treatment option. This treatment is described more in Part 5. HLA typing is performed on a blood sample.

HLA typing is needed to find the right donor for you. A donor's HLA type must be a near-perfect match to you for treatment to work. Otherwise, your body will reject the donor's stem cells.

Coagulation tests

Your body stops bleeding by turning blood into a gel-like form. This process is called coagulation. Proteins, called coagulation factors, are needed for this process. Coagulation tests assess how well these proteins work and sometimes protein levels. A sample of your blood is needed for testing.

Coagulation tests are advised for certain people. This test may be done if you have 1) abnormal bleeding; 2) increased platelets, especially over 1 million; 3) an enlarged spleen; or 4) a surgery scheduled that may cause major bleeding. It's important to learn if your blood coagulates normally.

Some health problems limit coagulation. One example is acquired VWD (**v**on **W**illebrand **d**isease). "Acquired" means the disorder was not passed down from your parents. Acquired VWD occurs more often with ET than with other MPNs. It usually occurs when platelet counts are very high. The high platelet counts limit how well the von Willebrand proteins clot.

Review

- A medical history is a report of all health events in your lifetime. It will include questions about your family's health, too.
- Your doctor will examine your body for signs of disease. He or she will touch parts of your body to see if anything feels abnormal.
- Blood tests assess the parts of your blood. Your doctor will use the blood results to help decide if and what type of disease is present.
- A bone marrow exam removes bone and marrow for testing.
- Genetic tests assess for abnormal changes in chromosomes and genes. Results can help your doctor identify a disease and plan treatment.
- HLA typing is needed if you will receive a transplant of stem cells from a donor.
- Coagulation tests on your blood may be needed.

"Family and online education and support sites (MPN-NET) have been vital to my emotional stability and critical to my understanding of PV.

– Susan
Survivor, Polycythemia vera

3
Treatment guide: Essential thrombocythemia

Part 3 is a treatment guide for essential thrombocythemia (ET, for short). It starts with describing how ET is found. Part 3 also explains the treatment process and options. Your doctor may suggest other options based on your health and wishes. Fully discuss your options with your doctor.

ET is diagnosed based on certain standards. Your platelet count must remain very high over time. Your bone marrow must contain many abnormal platelet-forming cells (megakaryocytes). **See Figure 7**. Other types of MPN, MDS, and other myeloid neoplasms must be excluded. There must be no secondary cause for the high platelet counts. Last, usually there is a common mutation like *JAK2*, *CALR*, or *MPL* mutations.

Diagnosis

ET is commonly found after a blood test that was given for another reason. It is also found due to related symptoms or health events. Common symptoms of ET are fatigue, headaches, dizziness, or vision changes. ET can cause serious health problems. Such problems include blood clots (thrombosis), abnormal bleeding (hemorrhage), and miscarriage during pregnancy.

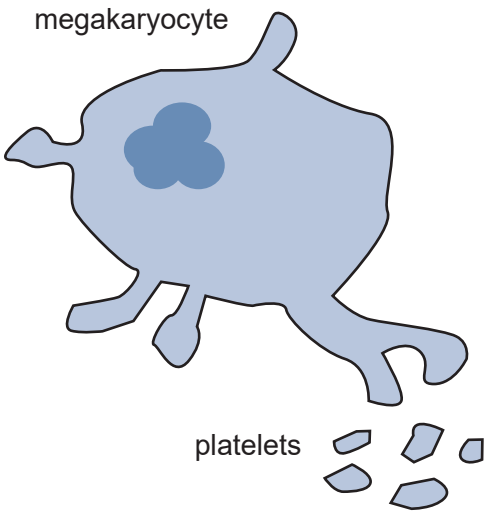
“

Routine blood work showed high platelets and a following bone marrow biopsy confirmed the ET diagnosis.

– Lyn
Survivor, Essential thrombocythemia

Figure 7
Key ET Features

A diagnosis of ET requires high numbers of megakaryocytes and platelets. A megakaryocyte is a rare type of bone marrow cell. When mature, it extends its arms through the wall of a blood vessel and releases platelets into the bloodstream.



Initial treatment

There are two treatment goals for ET. The first is to prevent serious health conditions caused by ET. The second goal is to relieve symptoms. In general, people with ET have a normal or near-normal lifespan.

Younger women with ET may want to have a baby. Before getting pregnant, it may help to meet with a high-risk obstetrician and a blood specialist (hematologist). These doctors can tell you what health care you will need during pregnancy.

Guide 2 lists the treatment options for ET. Options are based on your chance for having a blood clot. Some blood clots can cause a heart attack, stroke, or serious breathing problems. If pregnant, blood clots may harm you and your baby. Your doctor will assess whether you are at very low, low, intermediate, or high risk.

- **Very low risk** describes people who are 60 years of age or younger, don't have a *JAK2* mutation, and never had a blood clot.
- **Low risk** describes people who are 60 years of age or younger, have a *JAK2* mutation, and never had a blood clot.
- **Intermediate risk** describes people who are older than 60 years of age, don't have a *JAK2* mutation, and never had a blood clot.
- **High risk** describes people who 1) have had a blood clot or 2) are older than 60 years and have a *JAK2* mutation.

Guide 2. Initial ET treatment by risk group

What are the options?	Very Low	Low	Intermediate	High
• Assess for secondary health problems	✓	✓	✓	✓
• Reduce cardiovascular risk factors (ie, high blood pressure, diabetes, smoking)	✓	✓	✓	✓
• Aspirin for vascular symptoms	✓	✓	✓	✓
• Observation instead of aspirin	✓	✓	—	—
• Cytoreductive treatment (ie, hydroxyurea, interferons, anagrelide)	—	—	—	✓

Secondary health problems

ET can cause serious health conditions. Your doctor will assess you for these conditions. This is advised for all risk groups. Finding a health condition early may help prevent life-threatening events.

Blood clots

Your doctor will ask you about certain symptoms. Blood clots may cause leg pain, leg or arm swelling, and chest pain. You may have numbness or weakness on one side of your body. Your mental state may have suddenly changed.

Your doctor may suggest getting an imaging test. Imaging tests make pictures of the insides of your body. They allow your doctor to see blood flow, blood clots, or both. Such tests include ultrasound, CT (**c**omputed **t**omography), and MRI (**m**agnetic **r**esonance **i**maging). Venography involves an injection of a dye followed by x-rays.

Your doctor may prescribe an anticoagulant if you have a blood clot. Anticoagulants are also called blood thinners. LMWH (**l**ow-**m**olecular-**w**eight **h**eparin) is a medicine that you inject into your skin at home. Dabigatran, rivaroxaban, apixaban, and edoxaban are newer types of oral anticoagulants. Warfarin is the most commonly used anticoagulant. These medications should be withheld if you will have surgery soon.

If the clot is life threatening, you may receive plateletpheresis. This procedure withdraws your blood and removes platelets. Your platelet-reduced blood will then be returned to your body.

Major bleeding

Bleeding problems aren't very common for ET. They are more likely if platelet counts are very high. Bleeding related to ET includes easy bruising, nosebleeds, or heavy menstrual periods. ET may also cause bleeding in your digestive track or blood in your urine.

Your doctor will ask about symptoms and will perform a physical exam. You may see a liver or bowel expert if sudden bleeding occurs. You may receive plateletpheresis if bleeding is severe.

Acquired VWD

Your doctor will continue to assess for acquired VWD. Testing may be done if your spleen enlarges, platelet counts increase, if bleeding starts, or before having surgery. Coagulation tests are used to diagnose acquired VWD. These tests are described in Part 2.

Cardiovascular risk factors

Cardiovascular is a word that refers to the heart and blood vessels. There are cardiovascular factors that increase your chance for a blood clot. These risk factors include high blood pressure (hypertension), diabetes, and smoking. If you smoke, it's important that you quit.

If needed, your doctor will help you to reduce cardiovascular risk factors. Reducing risk factors is advised for all risk groups. Medications can help treat high blood pressure and diabetes. There are also medications that reduce cravings to smoke.

Healthy living can reduce cardiovascular risk factors. Health experts can help you make and follow plans for healthy living. Such plans can focus on eating healthy foods, exercise, and taking medications as prescribed. You can also get help with a plan to quit smoking.

Aspirin

Most people with ET receive aspirin. It is an option for all risk groups. Your doctor may not prescribe aspirin if you have abnormal bleeding, acquired VWD, or a very high platelet count. It will increase your chance for bleeding.

Aspirin is usually prescribed at a low dose. A low dose consists of 80 to 100 milligrams a day.

Some people receive higher doses based on their symptoms versus risk of bleeding.

Aspirin has many health benefits. These benefits are described next. Smoking blocks the action of aspirin. You'll have to quit smoking for aspirin to work.

Vascular symptoms
Low-dose aspirin is used to relieve vascular symptoms. These symptoms include headaches, dizziness, fainting, and chest pain. There may be abnormal changes in your vision like blind spots. You may also feel "pins and needles" in parts of your body (paresthesia).

Vascular symptoms may include changes in your skin. Your legs or hands may turn red and have a painful, burning sensation. This is called erythromelalgia. A red or purplish net-like pattern may appear on your skin. This is called livedo reticularis. Aspirin may help prevent or relieve these skin problems.

Other benefits
Aspirin is advised to reduce vascular symptoms. However, it may have other benefits. It may prevent blood clots. It may reduce the likelihood of heart attacks and strokes. It may prevent death from cardiovascular causes.

Pregnancy
Taking aspirin during and shortly after pregnancy is advised. For a low-risk pregnancy, LMWH may be received instead of aspirin for 2 weeks before labor. For a high-risk pregnancy, you may take LMWH with aspirin throughout the pregnancy. Aspirin may be stopped 1 to 2 weeks before labor. LMWH should be stopped 12 to 24 hours before labor. After giving birth, restart treatment for 6 weeks.

Surgery
You may need surgery while being treated for ET. If so, stop taking aspirin 1 week before surgery. You may restart treatment 24 hours after surgery unless you have a bleeding risk.

Observation

Observation is a period of testing to watch for changes in status. It is also sometimes called "watch-and wait." Instead of aspirin, observation is an option for very low- and low-risk cancers. Aspirin may be started if symptoms appear or worsen.

Aspirin

Most people with ET receive aspirin. It is used to relieve symptoms like headaches, dizziness, fainting, and chest pain. It may also prevent blood clots.

Cytoreductive treatment

Cytoreductive treatment reduces the number of certain cells. For ET, the goal of treatment is to reduce platelets to normal levels. Normal levels prevent blood clots and other health problems.

Cytoreductive treatment for initial treatment is based on risk group. It is not needed for very low-, low, and intermediate-risk ET. Cytoreductive treatment is advised for high-risk ET.

There are three options for cytoreductive treatment. Hydroxyurea is the gold standard. Most people with ET on cytoreductive treatment take hydroxyurea. It should not be taken during pregnancy or while breastfeeding.

Interferon is another option for some people. You may switch from hydroxyurea to interferon before and during pregnancy. Interferon may be received if you are 60 years of age or younger to avoid developing AML. Some people defer taking hydroxyurea by taking interferon. More information on interferon is on page 37.

Anagrelide has been used as a third option. It works as well as hydroxyurea to control platelet counts. However, its side effects may be worse. There is a greater chance for blood clotting. More information on anagrelide is on page 29.

What is hydroxyurea?

Chemotherapy, or “chemo,” includes drugs that disrupt the life cycle of cancer cells. Hydroxyurea is a type of chemotherapy called an antimetabolite. This type prevents the “building blocks” of DNA from being used. As a result, new cells can’t be made.

Hydroxyurea is made as a pill to be swallowed. Your doctor will tell you what dose you need and how often to take it. Do not take hydroxyurea right before getting pregnant, during pregnancy, or if you’re breastfeeding.

Hydroxyurea lowers blood counts. Thus, you will be at risk for anemia, infection, and bleeding. Other common side effects include minor hair loss, nausea and vomiting, diarrhea, mouth sores, and skin and nail changes.

Not all side effects of hydroxyurea are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Monitoring

After initial treatment, you will need to meet with your doctor often. A visit every 3 to 6 months is advised. You may need more frequent visits if problems arise. Guide 3 list the types of monitoring for each risk group.

Status of ET

Your doctor will assess if the ET is worse. Blood tests may be done. You may complete the MPN-SAF Total Symptom Score. This survey consists of 10 symptoms. Fatigue is also queried. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms.

Need for cytoreductive treatment

Initial treatment for very-low, low-, and intermediate-risk groups doesn't include cytoreductive treatment. During monitoring, your doctor will check if you need to start.

Signs that treatment may be needed include:

- A new blood clot,
- Acquired VWD,
- Major bleeding,
- Increasing spleen size,
- Symptoms caused by enlarged spleen,
- Symptoms caused by too many platelets,
- Rising levels of white blood cells,
- Worsening MPN symptoms, and
- Aspirin isn't relieving symptoms.

Cytoreductive treatment is described on page 26. Before starting, a bone marrow aspirate and biopsy should be done. These tests can show if the cancer has progressed to MF. If it has, the treatment described in Part 5 is needed.

Guide 3. Monitoring ET by risk group

Type of care	Very Low	Low	Intermediate	High
• Assess status of ET	✓	✓	✓	✓
• Assess need for cytoreductive treatment	✓	✓	✓	—
• Assess results of cytoreductive treatment	✓	✓	✓	✓

Results of cytoreductive treatment

Your doctor will assess if treatment is working based on tests. There are four types of treatment response. These responses are described next.

- **Complete remission** is defined by 1) no cancer symptoms and signs for at least 12 weeks; 2) normal or near-normal blood counts for at least 12 weeks; 3) no blood clots or bleeding events and ET isn't changing into another cancer; and 4) normal-looking megakaryocytes and minor, if any, bone marrow fibrosis (Grade 0 or 1).
- **Partial remission** is like a complete remission except abnormal-looking megakaryocytes are present.
- **No response** is anything less than a partial remission.
- **Progressive disease** is a worsening of the cancer.

"

Available treatments have successfully controlled my counts for 25 years. When one treatment loses efficacy, I cycle to another.

– Antje
Survivor, Essential thrombocythemia

Changing treatment

Sometimes treatment works at first then stops. Sometimes it doesn't work enough or at all. When one treatment fails, another treatment may be received.

If ET has transformed into MF or AML, read Part 5 for treatment options. If ET hasn't transformed, changing the type of cytoreductive treatment may be needed. Signs to change your cytoreductive treatment include:

- Severe side effects,
- Treatment stops working,
- A new blood clot,
- Acquired VWD,
- Major bleeding,
- Increasing spleen size,
- Symptoms caused by enlarged spleen,
- Symptoms caused by too many platelets,
- Rising levels of white blood cells,
- Worsening MPN symptoms, and
- Aspirin isn't relieving symptoms.

Guide 4. Second-line treatment

What are the options?
• Hydroxyurea if not received before
• Interferon if not received before
• Anagrelide if no other options
• Clinical trial

Guide 4 list options for second-line treatment. You may receive hydroxyurea or interferon if not received before. Anagrelide may be an option if used short-term and with caution.

There may also be a clinical trial that you can join. Ask your doctor if there's a clinical trial that's right for you. More information on clinical trials is on page 45.

Busulfan is not advised by NCCN experts. It may increase the likelihood of AML and other cancers.

What is anagrelide?

Anagrelide is a medicine that reduces the number of platelets. It works by blocking an enzyme called phospholipase A2. This stops megakaryocytes from maturing and making platelets.

Anagrelide is sold as Agrylin®. It is made as a pill to be swallowed. Your doctor will tell you what dose you need and how often to take it. Do not take anagrelide if you're breastfeeding.

The most common side effect of anagrelide is headaches. Digestive problems are also common. These include diarrhea, nausea, vomiting, abdominal pain, and gas. Other common side effects are weakness, swelling, dizziness, pain, and shortness of breath.

In a large clinical trial, anagrelide caused more strokes and heart attacks than hydroxyurea and aspirin. Contact your doctor if you start having chest pain or abnormal heartbeats. The chance of bleeding is increased if you also take aspirin.

Not all side effects of anagrelide are listed here. Please ask your treatment team for a complete list. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Review

- ET is commonly found after a blood test that was given for another reason. A key feature of ET is a high number of platelets.
- Treatment options are based on risk for blood clots. Aspirin to control symptoms is an option for all risk groups. For high-risk ET, cytoreductive treatment may be an option to reduce blood counts.
- You will need to meet with your doctor often. He or she will assess the status of the cancer and how you feel.
- If the cancer is getting worse, you may receive another type of cytoreductive treatment. Joining a clinical trial is another option.

Family, friends, and medical personnel have provided emotional and spiritual support to me.

– RuthAnne
Survivor, Essential thrombocythemia

4
Treatment guide: Polycythemia vera

Part 4 is a treatment guide for polycythemia vera (PV, for short). It starts with describing how PV is found. Part 4 also explains the treatment process and options. Your doctor may suggest other options based on your health and wishes. Fully discuss your options with your doctor.

Diagnosis

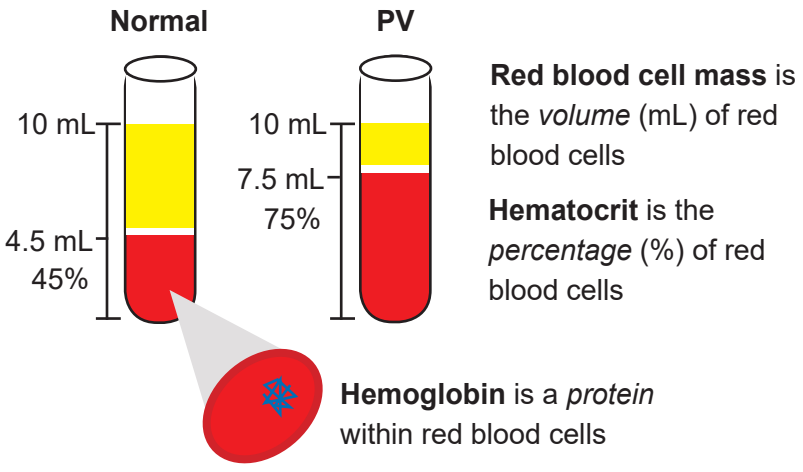
PV is commonly found after a blood test that was given for another reason. The blood test may reveal a high hemoglobin level. **See Figure 8**. Otherwise, a lot of your blood may consist of red blood cells (high hematocrit). More testing may reveal PV.

PV is also found due to related symptoms or health problems. Related health problems include blood clots and bleeding. A common symptom is unpleasant skin sensations. These sensations often occur shortly after a bath or shower. Your skin may itch, tickle, sting, or burn.

> Being diagnosed with PV at age 39 was a shock. I had never heard of MPN.
>
> – Susan
> Survivor, Polycythemia vera

Figure 8
Key PV features

A diagnosis of PV requires a high red cell mass, hematocrit, or hemoglobin level. These values will be obtained from a sample of your blood. Your blood will be spun so fast that the parts of the blood separate. Red cell mass is the volume of red blood cells. Hematocrit compares the volume of red blood cells to the total blood volume. For hemoglobin, your red blood cells will be broken down to free the hemoglobin. Then, the level will be measured.



There are many other common symptoms. You may have headaches, dizziness, vision changes, and fatigue. Your abdomen may hurt. You may quickly feel full when eating.

PV is diagnosed based on certain standards. First, the mass of red blood cells, hematocrit, or hemoglobin must remain high. A high red blood cell mass is called erythrocytosis. Second, there must be too many cells in your bone marrow. Third, the blood cells must have a common *JAK2* mutation or your EPO levels are usually low.

Initial treatment

There are two treatment goals for PV. The first is to reduce your chance for serious related health conditions. This is mostly achieved by reducing red blood cell counts. The second goal is to relieve symptoms. Most people have symptoms when they first learn they have PV.

Younger women with PV may want to have a baby. Before getting pregnant, it may help to meet with a high-risk obstetrician. This doctor can tell you what health care you will need during pregnancy.

Guide 5 lists the treatment options for PV. Options are based on your chance for having a blood clot. Some blood clots can cause a heart attack, stroke, or serious breathing problems. If pregnant, blood clots may harm you and your baby. Your doctor will assess whether you are at low or high risk.

- **Low risk** describes people who are younger than 60 years of age and never had a blood clot.
- **High risk** describes people who are 60 years of age and older or have had a blood clot.

Guide 5. Initial PV treatment by risk group

What are the options?	Low	High
• Assess for secondary health problems	✓	✓
• Reduce cardiovascular risk factors (ie, high blood pressure, diabetes, smoking)	✓	✓
• Aspirin for vascular symptoms	✓	✓
• Phlebotomy to control hematocrit level	✓	✓
• Cytoreductive treatment (ie, hydroxyurea, interferons)	—	✓

Secondary health problems

PV can cause serious health conditions. Your doctor will assess you for these conditions. This is advised for both risk groups. Finding a health condition early may help prevent life-threatening events.

Blood clots

Blood clotting is common in PV. Your doctor will ask you about certain symptoms. Blood clots may cause leg pain, leg or arm swelling, and chest pain. You may have numbness or weakness on one side of your body. Your mental state may have suddenly changed.

Your doctor may suggest getting an imaging test. Imaging tests make pictures of the insides of your body. They allow your doctor to see blood flow, blood clots, or both. Such tests include ultrasound, CT (**c**omputed **t**omography), and MRI (**m**agnetic **r**esonance **i**maging). Venography involves an injection of a dye followed by x-rays.

Your doctor may prescribe an anticoagulant if you have a blood clot. Anticoagulants are also called blood thinners. LMWH (**l**ow-**m**olecular-**w**eight **h**eparin) is a medicine that you inject into your skin at home. Dabigatran, rivaroxaban, apixaban, and edoxaban are newer types of oral anticoagulants. Warfarin is the most commonly used anticoagulant. These medications should be withheld if you will have surgery soon.

If your platelets are very high, you may receive plateletpheresis. This procedure withdraws your blood and removes platelets. Your platelet-reduced blood will then be returned to your body.

Bleeding

Bleeding is common in PV but often isn't severe. Bleeding related to PV includes easy bruising, nosebleeds, or heavy menstrual periods. PV may also cause bleeding in your digestive track or blood in your urine. Your doctor will ask about these symptoms and will perform a physical exam. You may see a liver or bowel expert if sudden bleeding occurs.

Drink plenty of water

It is important that you drink plenty of water. Avoid dehydration because it makes blood more thick (viscous). Remember, the more active you are the more dehydrated you will become.

Cardiovascular risk factors

Cardiovascular is a word that refers to the heart and blood vessels. There are cardiovascular factors that increase your chance for a blood clot. These risk factors include high blood pressure (hypertension), diabetes, and smoking. If you smoke, it's important that you quit.

If needed, your doctor will help you to reduce cardiovascular risk factors. Reducing risk factors is advised for all risk groups. Medications can help treat high blood pressure and diabetes. There are also medications that reduce cravings to smoke.

Healthy living can reduce cardiovascular risk factors. Health experts can help you make and follow plans for healthy living. Such plans can focus on eating healthy foods, exercise, and taking medications as prescribed. You can also get help with a plan to quit smoking.

Aspirin

Most people with PV receive aspirin. It is advised for both risk groups. Your doctor may not prescribe aspirin if you have had major bleeding. Aspirin increases the likelihood of bleeding. Aspirin should be withheld 1 week prior to any surgery.

Aspirin for PV is prescribed at a low dose. A low dose consists of 80 to 100 milligrams a day. Higher doses should be avoided. High doses increase the chance of bleeding in your bowels.

Aspirin has many health benefits. These benefits are described next. Smoking blocks the action of aspirin. You'll have to quit smoking for aspirin to work.

Vascular symptoms

Low-dose aspirin is used to relieve vascular symptoms. These symptoms include headaches, dizziness, fainting, and chest pain. There may be abnormal changes in your vision like blind spots. You may also feel "pins and needles" in parts of your body (paresthesia).

Vascular symptoms may include changes in your skin. Your legs or hands may turn red and have a painful, burning sensation. This is called erythromelalgia. A red or purplish net-like pattern may appear on your skin. This is called livedo reticularis. Aspirin may help prevent or relieve these skin problems.

Other benefits

Aspirin is advised to reduce vascular symptoms. However, it may have other benefits. It may prevent blood clots. It may reduce the likelihood of heart attacks and strokes. It may prevent death from cardiovascular causes.

Pregnancy

Taking aspirin during and shortly after pregnancy is advised. For a low-risk pregnancy, LMWH may be received instead of aspirin for 2 weeks before labor.

For a high-risk pregnancy, you may take LMWH with aspirin throughout the pregnancy. Aspirin may be stopped 1 to 2 weeks before labor. LMWH should be stopped 12 to 24 hours before labor. After giving birth, restart treatment for 6 weeks.

Surgery

You may need surgery while being treated for PV. If so, stop taking aspirin 1 week beforehand. You may restart 24 hours after surgery unless you have a bleeding risk.

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I find it very important to be in the care of a MPN specialist and a local hematologist, who work together on my behalf.

– Eric
Survivor, Polycythemia vera

Phlebotomy

A goal of treatment is to reduce hematocrit. In general, hematocrit should be below 45%. For women, a target of below 42% is often used. Lowering hematocrit will likely reduce blood thickness. As a result, your chance for getting blood clots will decrease. You may also have fewer headaches, less itchiness, and fewer vision problems.

Phlebotomy is key to treating PV. It's a procedure that is likely to reduce hematocrit. It is much like donating blood.

Your blood will be withdrawn with a needle inserted into a vein. **See Figure 9**. Your pulse and blood pressure may be watched as your blood is removed. You may feel dizzy during or right after the procedure. Phlebotomy produces iron deficiency to control PV. Thus, iron supplements should not be taken.

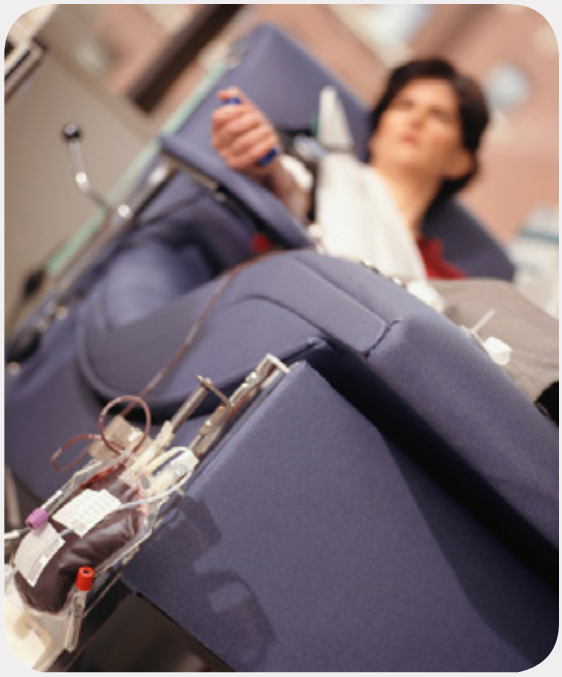
How often phlebotomy is needed differs between people. Some people need it every other week. If your hematocrit is high, you may need it once or twice a week. Often 500 mL of blood is withdrawn. This should reduce hematocrit by 3 points.

Surgery

You may need surgery while being treated for PV. Hematocrit should be below 45% for 3 months prior to surgery. You may need more phlebotomy visits to maintain hematocrit of <45%.

Figure 9
Phlebotomy

Phlebotomy is a procedure that is commonly used to control PV. It involves withdrawing your blood much like when donating blood. The goal is to reduce your hematocrit. This will reduce your chance for getting blood clots. Phlebotomy may also reduce symptoms.



Cytoreductive treatment

Cytoreductive treatment reduces the number of certain cells. For PV, the goal of treatment is to reduce blood cell counts to normal levels. Normal levels prevent blood clots and other health problems.

Cytoreductive treatment for initial treatment is based on risk group. It is not needed for low-risk PV. Cytoreductive treatment is advised for high-risk PV.

There are two options for cytoreductive treatment. Hydroxyurea is the gold standard. Most people with PV on cytoreductive treatment take hydroxyurea. It should not be taken during pregnancy or while breastfeeding. Hydroxyurea is described more on page 26.

Interferon is another option for some people. You may switch from hydroxyurea to interferon before and during pregnancy. Interferon may be received if you are 60 years of age or younger to avoid a slightly increased risk for AML. Some people defer taking hydroxyurea by taking interferon.

What is interferon?

Interferons naturally exist in your body as part of your disease-fighting (immune) system. They can also be made in the lab and be used to treat MPN. When used as treatment, interferon is given in much higher amounts than what the body makes.

How interferon works to treat MPN isn't fully known. It is a type of immunotherapy. Thus, it enhances the activity of immune cells. A high level of interferon also suppresses the making of blood cells. It may take 6 to 12 months before your blood cell counts return to normal.

Interferons for MPN are interferon alfa-2b, peginterferon alfa-2a, and peginterferon alfa-2b. They are received as an injection just under the skin. Most people inject themselves. Your doctor will tell you what dose you need and how often.

Side effects of interferon are related to dose. The higher the dose the worse the side effects. Side effects may lessen over time. Some people have flu-like symptoms after several injections. Other common side effects are headache, nausea, and diarrhea. You may become depressed or have trouble concentrating or remembering. Tell your doctor if you have a history of depression.

Not all side effects of interferon are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Monitoring

After initial treatment, you will need to meet with your doctor often. A visit every 3 to 6 months is advised. You may need more frequent visits if problems arise. Guide 6 list the types of monitoring for each risk group.

Status of PV

Your doctor will assess if the cancer is worse. Blood tests may be done. You may complete the MPN-SAF Total Symptom Score. This survey consists of 10 symptoms. Fatigue is also queried. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms.

Need for cytoreductive treatment

Initial treatment for low-risk PV doesn't include cytoreductive treatment. During monitoring, your doctor will check if you need to start. Signs that treatment may be needed include:

- A new blood clot,
- Acquired VWD,
- Major bleeding,
- Frequent phlebotomy,
- Need for phlebotomies doesn't decrease,
- Increasing spleen size,
- Symptoms caused by enlarged spleen,
- Symptoms caused by too many platelets,
- Rising levels of white blood cells, and
- Worsening MPN symptoms.

Guide 6. Monitoring PV by risk group

Type of care	Low	High
• Assess status of PV	✓	✓
• Assess need for cytoreductive treatment	✓	—
• Assess results of cytoreductive treatment	✓	✓

Cytoreductive treatment is described on page 37. Before starting, a bone marrow aspirate and biopsy should be done. These tests can show if the cancer has progressed to MF. If it has, the treatment described in Part 5 is needed.

Results of cytoreductive treatment

Your doctor will assess if treatment is working based on tests. There are four types of treatment response.

- **Complete remission** is defined by 1) no cancer symptoms and signs for at least 12 weeks; 2) hematocrit <45% without phlebotomies and normal or near-normal blood counts for at least 12 weeks; 3) no blood clots or bleeding events and PV isn't changing into another cancer; and 4) bone marrow consists of a normal number of cells, cells that look normal, and minor, if any, bone marrow fibrosis (Grade 0 or 1).
- **Partial remission** is like a complete remission except bone marrow cells are still abnormal.
- **No response** is less than a partial remission.
- **Progressive disease** is a worsening of the cancer.

Changing treatment

Sometimes treatment works at first then stops. Sometimes it doesn't work enough or at all. When one treatment fails, another treatment may be received. If PV has transformed into MF or AML, read Part 5 for treatment options.

If PV hasn't transformed, changing the type of cytoreductive treatment may be needed. Signs to change your cytoreductive treatment include:

- Severe side effects,
- Treatment stops working,
- A new blood clot,
- Acquired VWD,
- Major bleeding,
- Increasing spleen size,
- Symptoms caused by enlarged spleen,
- Symptoms caused by too many platelets,
- Rising levels of white blood cells,
- Worsening MPN symptoms, and
- Aspirin isn't relieving symptoms.

Guide 7. Second-line treatment

What are the options?
• Ruxolitinib if hydroxyurea no longer an option
• Hydroxyurea if not received before
• Interferon if not received before
• Clinical trial

Guide 7 list options for second-line treatment. Hydroxyurea may not be an option for you. It may have stopped working or caused severe side effects. In this case, ruxolitinib may be received. More information on ruxolitinib is on page 47.

Other options are hydroxyurea or interferon if not received before. There may also be a clinical trial that you can join. Ask your doctor if there's a clinical trial that's right for you. More information on clinical trials is on page 45.

Busulfan is not advised by NCCN experts. It may increase the likelihood of AML and other cancers.

"

It is so good to talk to someone that understands what we are going through.

– Jean
Survivor, Polycythemia vera

Review

- PV is commonly found after a blood test that was given for another reason. A key feature of PV is a high number of red blood cells.
- Treatment options are based on risk for blood clots. Aspirin to control symptoms is an option for all risk groups. Phlebotomy may be received to reduce hematocrit. For high-risk PV, cytoreductive treatment may be an option to reduce blood counts.
- You will need to meet with your doctor often. He or she will assess the status of the cancer and how you feel.
- If the cancer is getting worse, you may receive another type of cytoreductive treatment. Ruxolitinib and joining a clinical trial are other options.

"I was diagnosed with PV when I was 57 years old. Now I am 68. Most of the time my disease has been under control.

–Gail
Survivor, Polycythemia vera

5
Treatment guide: Myelofibrosis

Part 5 is a treatment guide for myelofibrosis (MF, for short). It starts with describing how MF is found. Part 5 also explains the treatment process and options. Your doctor may suggest other options based on your health and wishes. Fully discuss your options with your doctor.

Diagnosis

MF (**m**yelo**f**ibrosis) can occur in people without a history of bone marrow problems. This is called PMF (**p**rimary **m**yelo**f**ibrosis). However, MF can also develop in people who have either ET or PV. This disease is respectively called post-ET myelofibrosis and post-PV myelofibrosis.

Primary myelofibrosis

PMF is often found because of symptoms. The most common symptom is severe fatigue. Another common symptom is quickly feeling full when eating. You may have discomfort under your ribs on the left side. Other symptoms include losing weight without trying, low fever, bone pain, and night sweats.

PMF is also found because of tests given for other reasons. Your doctor may detect that your liver or spleen is big. **See Figure 10**. Your blood results may be abnormal. More testing reveals PMF.

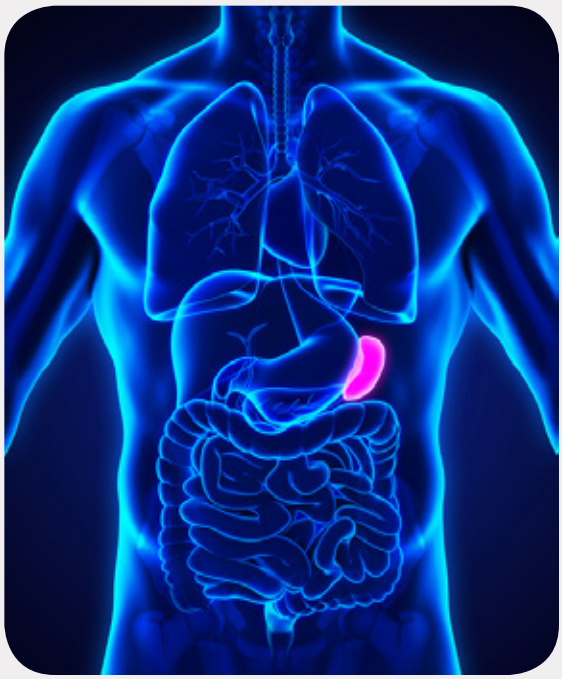
There are two stages of PMF. One stage is called prePMF (**pre**fibrotic **PMF**) or early PMF. The other stage is called overt PMF. These stages were created to help tell prePMF apart from ET. Each stage is diagnosed based on certain standards.

Prefibrotic PMF

Your bone marrow must contain many abnormal platelet-forming cells (megakaryocytes). Other types

Figure 10
Spleen

The spleen is a small organ to the left of your stomach. It is part of your immune system. As scar tissue replaces bone marrow, the number of your blood cells will drop. As a result, your spleen may begin to make blood cells and enlarge. An enlarged spleen is a common symptom of MF. Your liver may enlarge, too.



of marrow and blood cells may be normal or slightly low. There must be none or only minor bone marrow fibrosis (Grade 0 or 1).

Related cancers are excluded. You must not have another type of MPN. You also must not have MDS or another myeloid neoplasm.

A common mutation may be present. *JAK2*, *CALR*, and *MPL* mutations are common. If no common mutation is present, there may be another known marker. Otherwise, there is no other molecular cause for myelofibrosis.

Last, one or more of the following 4 conditions may be present. You may have anemia that isn't caused by another health condition. Your white blood cell count may be high. Your LDH level may be high. Your spleen may be enlarged.

Overt PMF

Your bone marrow must have typical features of PMF. It must contain many abnormal megakaryocytes. There must also be higher-grade bone marrow fibrosis.

Related cancers are excluded. You must not have another type of MPN. You also must not have MDS or another myeloid neoplasm.

There is usually a mutation in *JAK2*, *CALR*, or *MPL* genes. If no common mutation is present, there may be another known marker. Otherwise, there is no other molecular cause for myelofibrosis.

Last, one or more of the following 5 conditions must be present: 1) anemia that isn't caused by another condition; 2) a high white blood cell count; 3) a high LDH level; 4) an enlarged spleen; and 4) immature blood cells in blood that should only be in bone marrow.

Post-ET myelofibrosis

This diagnosis requires that you have had ET with higher-grade bone marrow fibrosis. Two of the following 5 conditions must be present: 1) anemia that isn't caused by another condition; 2) immature blood cells in blood that should only be in bone marrow; 3) a high LDH level; 4) an enlarged spleen; and 5) weight loss or night sweats caused by MF.

Post-PV myelofibrosis

This diagnosis requires that you have had PV with higher-grade bone marrow fibrosis. Two of the following 4 conditions must be present: 1) anemia that isn't caused by another condition; 2) immature blood cells in blood that should only be in bone marrow; 3) an enlarged spleen; and 4) weight loss or night sweats caused by MF.

Initial treatment

There are three treatment goals for MF. The first is to reduce symptoms. Most people have symptoms. Symptoms are often related to an enlarged spleen and anemia. The second treatment goal is to improve blood counts. The third goal is to reduce the chance of MPN progressing to AML.

Guide 8 lists the treatment options for MF. Options are based on risk and the presence of symptoms. The methods of assessing risk and symptoms are described next.

Risk group

There are a few scoring systems for risk. The DIPSS-PLUS (**D**ynamic **I**nternational **P**rognostic **S**coring **S**ystem-**PLUS**) is the preferred system during the course of treatment.

Your doctor will complete the DIPSS-PLUS. Scores are based on several factors. Blood results are used including white blood cell and platelet counts. Your age is another factor. Scores increase if you need a red blood cell transfusion, have abnormal chromosomes, or have MF-related constitutional symptoms. These symptoms include fevers, night sweats, or weight loss.

DIPSS-PLUS total scores range from 0 to 6. Low risk is a score of zero. INT-1 (**int**ermediate-**1**) is a score of 1. INT-2 (**int**ermediate-**2**) is a score of 2 or 3. High risk is a score between 4 and 6.

Symptom survey

Your treatment will also be planned based on which, if any, symptoms are present. The MPN-SAF Total Symptom Score is advised for assessing symptoms. This survey consists of 10 symptoms. Fatigue is also queried. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms.

Observation

Observation is an option for low- and INT-1-risk MF without symptoms. It is a period of testing to watch for changes in cancer status. It is also sometimes called “watch-and wait.” Treatment may be started if symptoms appear. Starting treatment before symptoms appear doesn’t help improve outcomes.

Clinical trial

Joining a clinical trial is an option for all risk groups. The focus of the trial should be one of the following: treatment to reduce bone marrow fibrosis; treatment to improve cell counts and reduce symptoms; treatment to restore transfusion-independence; or treatment to prevent or delay leukemia.

Guide 8. Initial treatment options by risk group

Low risk - no symptoms	Low risk - symptoms	INT-1	INT-2 and high risk
• Observation	• Ruxolitinib	• Observation	• Allogeneic HCT
• Clinical trial	• Interferon	• Ruxolitinib	• Clinical trial
	• Hydroxyurea	• Clinical trial	• Ruxolitinib
	• Clinical trial	• Allogeneic HCT	• Anemia treatment

INT = Intermediate

What are clinical trials?

One of your treatment choices may be to join a clinical trial. Joining a clinical trial is strongly supported. NCCN believes that you will receive the best management in a clinical trial.

New tests and treatments aren't offered to the public as soon as they're made. They first need to be studied. A clinical trial is a type of research that studies a test or treatment in people.

Clinical trials study how safe and helpful tests and treatments are for people. When found to be safe and helpful, they may become tomorrow's standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with MPN. Future tests and treatments that may have better results than today's treatments will depend on clinical trials.

New tests and treatments go through a series of clinical trials. These trials aim to ensure they're safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Some examples of the four phases for treatment are:

- **Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects. These trials often involve about 20 people.
- **Phase II trials** assess if a drug works for a specific type of cancer. These trials often involve 20 to 100 people.
- **Phase III trials** compare a new drug to a standard treatment. These trials often involve hundreds or thousands of people.
- **Phase IV trials** test drugs approved by the U.S. FDA (**F**ood and **D**rug **A**dministration) to learn more about side effects with long-term use.

Joining a clinical trial has benefits. First, you'll have access to the most current cancer care. However, please note that it is unknown how well new treatments work if at all. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may or may not improve your health. In fact, your health may worsen during a trial. Other downsides may include more hospital trips, paperwork, and extra costs for you.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. Thus, if patients improve, it's because of the treatment and not because of differences between them.

To join, you'll need to review and sign an informed consent form. This form describes the study in detail. The study's risks and benefits should be described and may include others than those described above.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 6.

Ruxolitinib

Ruxolitinib is an FDA-approved treatment for INT- and high-risk MF. Among these groups, it has reduced spleen size, improved symptoms, and may extend life in some people. It does not reduce the risk of progression to AML.

NCCN experts recommend ruxolitinib as an option for low- and INT-1-risk MF when symptoms are present. A study on preexisting data found that spleens shrunk and symptoms improved during treatment in these groups. Well-designed studies are needed to learn how well ruxolitinib works in early MF.

Hydroxyurea and interferon

Interferon and hydroxyurea are options for low-risk MF with symptoms. Both control MF by reducing the number of blood cells. Cell counts may return to normal levels.

There is limited research on interferon. Results suggest that interferon prevents cancer progression in a subset of people with early MF. It may reverse bone marrow changes and shrink enlarged spleens. More research is needed. Interferon doesn't work if there is advanced myelofibrosis.

Hydroxyurea may help some people. It helps to lower high blood counts, especially white blood cells and platelets. It may decrease spleen size. However, the decrease is usually modest. Hydroxyurea may reduce certain symptoms. In particular, symptoms caused by high blood counts may decrease. If hydroxyurea doesn't work, interferon or ruxolitinib may be an option.

My PMF has been indolent and progressing very slowly. Exercise and a good diet have helped my quality of life.

– Vivian
Survivor, Primary myelofibrosis

What is ruxolitinib?

Kinases are molecules that move chemicals, called phosphates, from one molecule to another. Kinase inhibitors stop the phosphates from being moved. Kinase inhibitors often block growth signals within cancer cells. This reduces the number of new cancer cells being made.

Ruxolitinib is a kinase inhibitor. It stops a kinase called JAK (**J**anus-**a**ssociated **k**inase). This kinase is part of a receptor on the inside of blood cells. **See Figure 11**. Some receptors are the starting point in cells for growth signals.

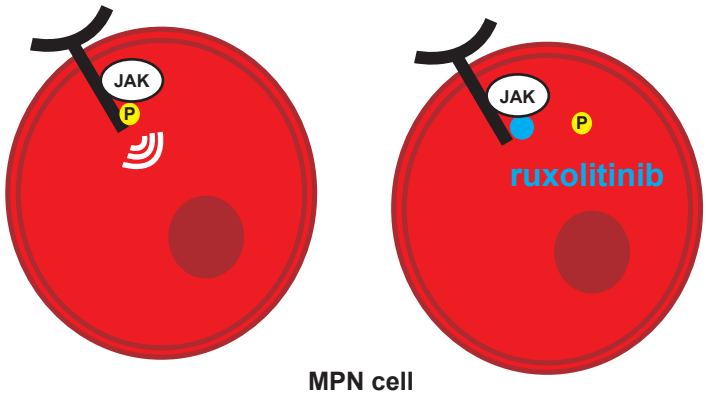
Ruxolitinib is sold as Jakafi®. It is made in pill form and taken twice a day. It should be taken around the same times each day. Your doctor will tell you what dose you need. Do not stop or skip taking ruxolitinib without your doctor's approval. Symptoms can return very quickly.

Common side effects of ruxolitinib include low blood cell counts, bruising, dizziness, and headache. It can also increase your chances for infections, other cancers, and high cholesterol. Women who are pregnant, trying to get pregnant, or are breastfeeding should not take ruxolitinib.

Not all side effects of ruxolitinib are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Figure 11
Ruxolitinib

JAKs are protein kinases within growth signal pathways. Kinases move chemicals, called phosphates, from one molecule to another. The phosphate "turns on" the next molecule in the signal pathway. Ruxolitinib blocks the transfer of phosphate by JAKs and in turn stops cell growth signals.



Allogeneic HCT

Allogeneic HCT (**h**ematopoietic **c**ell **t**ransplant) is an option for INT-2- and high-risk MF. It may also be an option for INT-1 if platelets are low and complex cytogenetics are present. It provides the only chance for a cure. However, it is not safe for everyone. Most people will not be able to undergo allogeneic HCT.

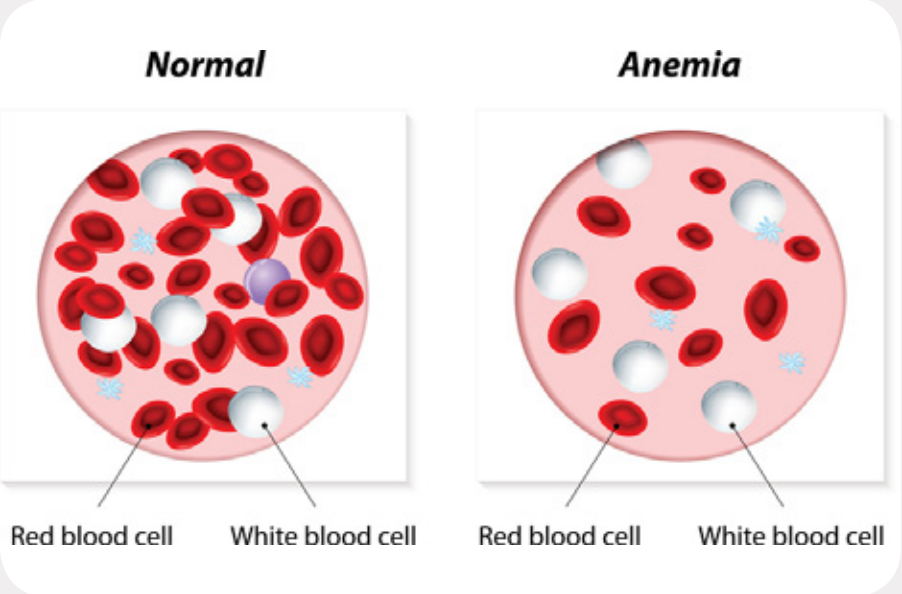
Your doctor will assess if a transplant is right for you. He or she will consider your age, health, preference, and other factors. For PMF, higher-risk gene mutations may be considered. Such mutations, including *ASXL1*, increase the chance for acute leukemia. If present, your doctor may advise undergoing an allogeneic transplant.

Anemia treatment

Many people with MF have anemia. Anemia is a condition of low red blood cells or hemoglobin. **See Figure 12**. Treatment for anemia is described in the next section. For INT-2 and high-risk MF, treatment for anemia may be the main type of care you will receive. It is an option if you can't have an allogeneic HCT and you don't have other symptoms.

Figure 12
Anemia

Many people with MF have anemia. Anemia is a health condition of low red blood cells or hemoglobin.



What is allogeneic HCT?

A stem cell transplant replaces damaged or destroyed stem cells with healthy stem cells. An allogeneic stem cell transplant uses healthy stem cells from a donor. The donor may be related to you or not. This transplant is also called an allogeneic HCT (**h**ematopoietic **c**ell **t**ransplant).

The healthy stem cells will form into new marrow and blood cells. This creates a new immune system. Another benefit of this transplant is the GVL (**g**raft-**v**ersus-**l**eukemia) effect. The GVL effect is an attack on cancer cells by the transplanted stem cells. The steps of an allogeneic HCT are briefly described next.

HLA typing

Special testing must be done to find the right donor for you. The donor and your tissue type must be a near-perfect match for this treatment to work. The test used to check tissue type is called HLA (**h**uman **l**eukocyte **a**ntigen) typing. A blood sample is needed to perform the test.

Conditioning

Before the transplant, you will receive treatment that destroys bone marrow cells. The death of the cells creates room for the healthy stem cells. It also weakens your immune system so your body won't kill the transplanted cells.

There are two main types of conditioning treatment. High-dose conditioning consists of high doses of strong chemotherapy. Reduced-intensity conditioning consists of low doses of strong chemotherapy. It may also consist of low-intensity drugs. Radiation therapy may also be given as part of conditioning treatment.

High-dose conditioning can cause very bad side effects. It can be deadly. Also, not everybody can tolerate it. Your doctor will decide if you are healthy enough for this treatment. Reduced-intensity conditioning may be used for people who are older or less healthy overall. However, the chance for a cancer relapse is greater.

Transplanting stem cells

After chemotherapy, you will receive the healthy stem cells through a transfusion. A transfusion is a slow injection of blood products through a central line into a large vein. A central line (or central venous catheter) is a thin tube. The tube will be inserted into your skin through one cut and into your vein through a second cut. Local anesthesia is used. This process can take several hours to complete.

The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks.

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

Supportive care

Guide 9 lists some of the supportive care needs of people with MF. Supportive care doesn't aim to treat cancer but aims to improve quality of life. It is sometimes called palliative care.

Anemia

Your doctor will first assess for causes of anemia other than MF. Common causes include bleeding, breakdown of red blood cells, and low iron, B12, or folate levels. If present, these causes should be treated.

Standard treatment of anemia with symptoms is a red blood cell transfusion. The donated blood should be processed to remove most white blood cells. This will help prevent the donated blood from attacking your body. It also prevents you from getting CMV (**c**yto**m**egalo**v**irus).

Additional treatment options are based on EPO levels. There are two options if EPO <500 mU/mL. One is ESAs (**e**rythropoiesis-**s**timulating **a**gents) and the other is a clinical trial. ESAs include darbepoetin and epoetin. These medicines do not work if transfusions are often needed for anemia.

Guide 9. Supportive care

Health conditions	What are the options?
Anemia	**Everyone** ◦ Red blood cell transfusions **If EPO <500 mU/mL** ◦ ESAs ◦ Clinical trials **If EPO ≥500 mU/mL** ◦ Danazol ◦ Other androgen ◦ Lenalidomide, thalidomide, or pomalidomide ± prednisone ◦ Clinical trial
Iron overload	• Iron chelation
Bleeding or low platelet counts	• Platelet transfusions • Antifibrinolytic agents if transfusions fail
Infections	• Vaccinations • Antibiotics for recurrent infections • G-CSF or GM-CSF for recurrent infections when neutrophils are low
Tumor lysis syndrome	• Drink lots of water (hydration) • Allopurinol or rasburicase to reduce uric acid
Heart (cardiovascular) disease	• Counseling and treatment
High blood counts in PMF	• Cytoreductive therapy

There are three options if EPO ≥500 mU/mL. Danazol or another androgen are two options. Immunomodulatory agents with or without prednisone are another option. These drugs include lenalidomide, thalidomide, and pomalidomide. Another option is a clinical trial.

Iron overload

Iron overload is too much iron in your body. It can occur if you've had many red blood cell transfusions. Iron chelation is a type of drug that removes extra iron from your body. It is an option at times for low- and INT-1-risk MF. Your doctor may prescribe iron chelation if you've had more than 20 transfusions, blood ferritin is >2500 ng/mL, or both.

Bleeding

Platelet transfusion is used to treat bleeding caused by low platelets. You may also receive a transfusion if your platelet count is <10,000 m^3. Most white blood cells should be removed from the donated blood. This will help prevent the blood from attacking your body. It also prevents you from getting CMV.

Transfusions may not stop blooding. In this case, antifibrinolytic agents may be received. These drugs help your blood to clot.

Infections

You may be prone to infections because of the cancer, treatment, or both. Ask your doctor which vaccinations are safe for you. If you get infections often, your doctor may prescribe antibiotics.

Instead of antibiotics, you may receive G-CSF or GM-CSF if you have low neutrophil counts. These medicines can cause your spleen to rupture. Thus, they should be used with caution if you have an enlarged spleen.

Tumor lysis syndrome

TLS (**t**umor **l**ysis **s**yndrome) occurs when the waste released by dead cells is not quickly cleared out of your body. This results in kidney damage and severe blood electrolyte disturbances. It can be life threatening.

Induction chemotherapy may cause TLS. Induction chemotherapy is a treatment for advanced-stage MF or AML. This treatment kills many cancer cells and results in too much waste too quickly.

TLS may be prevented by drinking lots of water during chemotherapy. Decreasing uric acid levels with allopurinol or rasburicase is another option. Rasburicase may be given as the first treatment if your blast cells are quickly increasing. It may also be first received if your uric acid level is high or your kidney(s) are damaged.

Heart (cardiovascular) disease

Cardiovascular is a word that refers to the heart and blood vessels. Cardiovascular risk factors increase your chance for heart disease. They include high blood pressure (hypertension), diabetes, and smoking.

If needed, your doctor will help you to reduce cardiovascular risk factors. Medications can help treat high blood pressure and diabetes. There are also medications that reduce cravings to smoke.

Healthy living can reduce cardiovascular risk factors. Health experts can help you make and follow plans for healthy living. Such plans can focus on eating healthy foods, exercise, and taking medications as prescribed. You can also get help with a plan to quit smoking.

High blood counts

You may have high blood counts if you have PMF. In this case, you may receive cytoreductive treatment such as hydroxyurea. Cytoreductive treatment is sometimes received in addition to other treatments to relieve certain symptoms.

Monitoring

After initial treatment, you will need to meet with your doctor often. A visit every 3 to 6 months is advised. You may need more frequent visits if problems arise. The types of monitoring are described next.

Status of MF

Your doctor will assess if the cancer is worse. Blood tests may be done. Your symptoms should also be assessed. MPN-SAF Total Symptom Score may be used. If the cancer appears worse, a bone marrow aspirate and biopsy are advised.

Treatment results

Your doctor will assess if treatment is working based on tests. There are many types of treatment responses. These main responses are described next.

- **Complete remission** is the best outcome. There are no signs of the cancer. Your bone marrow and blood results are normal or near normal. Your symptoms have cleared. Your liver and spleen are normal size.
- **Partial remission** is a good response. Your blood work may be normal. Otherwise, your bone marrow results are normal and your blood results are returning to normal. Your symptoms have cleared. Your liver and spleen are normal size.
- **Progressive disease** is a worsening of the cancer.
- **Stable disease** is defined by results that don't match the 3 types of responses above.

You may hear of other types of responses. Anemia response is an improvement in hemoglobin level or not needing transfusions anymore. Spleen response is a major decrease in spleen size. Symptom response is a major decrease in symptoms. Clinical improvement is one or more of these responses without signs of the cancer worsening.

MF may also be assessed for changes in cell structures. Cytogenetic remission is defined by fewer or the absence of abnormal chromosomes. Molecular remission is defined by fewer or the absence of molecular markers of MF.

Sometimes treatment works at first then stops. This is called treatment relapse. Sometimes it doesn't work enough or at all. When one treatment fails, another treatment may be received. Treatment options for advanced-stage MF or AML are discussed in the next section. Otherwise, read the *Initial treatment* section to learn treatment options based on risk groups.

> "Our MPNs are so individual and respond differently to different treatments.
>
> – Lyn
> Survivor, Post-ET myelofibrosis

Advanced-stage MF or AML

Treatment options for advanced-stage MF or AML are listed in Guide 10. Options are based on whether allogeneic HCT is an option. Allogeneic HCT is not safe for everyone. Most people will not be able to receive it. Your doctor will assess if a transplant is right for you. He or she will consider your age, health, wishes, and other factors.

Before a transplant, treatment to cause cancer remission will be given. You may receive hypomethylating agents or intensive induction chemotherapy. Hypomethylating agents include azacitidine and decitabine.

If you can't receive a transplant, you may have two options. One option is to join a clinical trial. The second option is to receive hypomethylating agents or low-intensity induction chemotherapy. These treatments may reduce symptoms. If treatment works well, allogeneic HCT may become an option.

Review

- PMF occurs in the absence of prior bone marrow problems. ET and PV can progress to MF. This disease is respectively called post-ET myelofibrosis and post-PV myelofibrosis.
- A key feature of MF is scarring of the bone marrow. Scar tissue may cause blood cell counts to drop. Scarring may not be present in early MF.
- Treatment options are based on risk group. Observation is an option for low- and intermediate-1-risk cancers without symptoms. If symptoms are present, ruxolitinib or cytoreductive treatment may be an option. Allogeneic HCT is an option for high-risk MF.
- Besides cancer treatment, you may receive supportive care to prevent or reduce symptoms related to the cancer.
- You will need to meet with your doctor often. He or she will assess the status of the cancer and how you feel.
- If the cancer is getting worse, you may receive allogeneic HCT. Other options are joining a clinical trial and hypomethylating agents or chemotherapy to reduce symptoms.

Guide 10. Treatment for advanced MF or AML

Transplant status	What are the options?
Allogeneic HCT is an option	• Hypomethylating agents or intensive induction chemotherapy followed by allogeneic HCT
Allogeneic HCT is not an option	• Clinical trial
	• Hypomethylating agents or low-intensity induction chemotherapy

6
Making treatment decisions

Having cancer is very stressful. While absorbing the fact that you have cancer, you have to learn about tests and treatments. In addition, the time you have to accept a treatment plan feels short. Parts 1 through 5 described the cancer and treatment options. Part 6 aims to help you make decisions that are in line with your beliefs, wishes, and values.

It's your choice

The role each person wants in choosing his or her treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which option to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Questions to ask your doctors

You may meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also take notes and get copies of your medical records.

It may be helpful to have your spouse, partner, family member, or a friend with you at these visits. A patient advocate or navigator might also be able to come. They can help to ask questions and remember what was said. Suggested questions to ask are listed on the following pages.

I discuss my treatment plan and changes with my local hematologist and then involve my specialist in the final decision. This way we are all on the same page and find the best treatment for me.

– Antje
Survivor, Essential thrombocythemia

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctor can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1. Where did the cancer start? In what type of cell? Is this cancer common?
2. What is the cancer risk group? Does this group mean the cancer is advanced?
3. Is this a fast- or slow-growing MPN?
4. What are my chances that MPN will become AML?
5. What tests do you recommend for me?
6. Where will the tests take place? How long will the tests take and will any test hurt?
7. What if I am pregnant?
8. How do I prepare for testing?
9. Should I bring a list of my medications?
10. Should I bring someone with me?
11. How often are these tests wrong?
12. Would you give me a copy of the pathology report and other test results?
13. Who will talk with me about the next steps? When?

What are my options?

There is no single treatment practice that is best for all people. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Are you suggesting options other than what NCCN recommends? If yes, why?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options? What if I am pregnant?
7. Which option is proven to work best?
8. Which options lack scientific proof?
9. What are the benefits of each option? Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
10. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
11. How do you know if treatment is working?
12. What are my options if my treatment stops working?
13. What can be done to prevent or relieve the side effects of treatment?

What does each option require of me?

Many patients consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you:

1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2. What do I need to think about if I will travel for treatment?
3. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
4. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
5. Should I bring someone with me when I get treated?
6. Will the treatment hurt?
7. How much will the treatment cost me? What does my insurance cover?
8. Will I miss work or school? Will I be able to drive?
9. Is home care after treatment needed? If yes, what type?
10. How soon will I be able to manage my own health?
11. When will I be able to return to my normal activities?

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

1. Are you board certified? If yes, in what area?
2. How many patients like me have you treated?
3. How many procedures like the one you're suggesting have you done?
4. Is this treatment a major part of your practice?
5. How many of your patients have had complications?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another. Some ways to decide on treatment are discussed next.

2nd opinion

The time around deciding a treatment is very stressful. People with cancer often want to get treated as soon as possible. They want to make their cancer go away before it spreads farther. While cancer can't be ignored, usually there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion about which option is best can help.

Copies of the pathology report, a DVD of the imaging tests, and other test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn't cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about the treatment you accept to have. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between your options. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups

Besides talking to health experts, it may help to talk to other people who have walked in your shoes. At support groups, you can ask questions and hear about the experiences of other people with MPN. Find a support group at the websites listed on page 61.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.

> "It is important to seek a second opinion from a specialist to confirm the diagnosis and lay out future plans."
>
> – Kye
> Survivor, Polycythemia vera

Websites

Leukemia & Lymphoma Society
LLS.org/informationspecialists

MPN Cancer Connection
MPNCancerConnection.org

MPN Education Foundation
mpninfo.org

MPN Research Foundation
mpnresearchfoundation.org

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

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox

NCCN for Patients®
nccn.org/patients

Voices of MPN (Supported by Incyte)
voicesofmpn.com

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and downsides may help you decide which treatment is best for you.

myMPN

myMPN is the first-ever natural history databank for classic MPNs. Your information will be used to find better treatments. You will also be informed about new clinical trials. All information is protected. You decide how your information is used. Visit mpnresearchfoundation.org/myMPN for more information and to register.

Glossary

Dictionary

acute myeloid leukemia (AML)
A fast-growing cancer that starts in the bone marrow and causes too many immature white blood cells to be made.

allogeneic hematopoietic cell transplant (HCT)
A cancer treatment that replaces blood stem cells with donor stem cells which in turn make a new immune system and attack the cancer cells.

anemia
A condition in which the number of red blood cells is low.

anticoagulant
A medicine that reduces blood clotting. Also called blood thinner.

***BCR-ABL1* gene**
An abnormal gene that is formed when parts of chromosomes 9 and 22 break off and switch with each other. This gene is found on the Philadelphia chromosome and is the key feature of chronic myeloid leukemia.

biopsy
Removal of small amounts of tissue from the body to be tested for disease.

blood clot
A thickened mass of blood. Also called a thrombosis.

blood smear
A test that involves viewing a drop of blood with a microscope to assess features of blood cells.

blood stem cell
A blood-forming cell from which all other types of blood cells are formed. Also called hematopoietic stem cell.

bone marrow
The soft, sponge-like tissue in the center of most bones where blood cells are made.

bone marrow aspiration
The removal of a small amount of liquid bone marrow to test for disease.

bone marrow biopsy
The removal of a small amount of solid bone and bone marrow to test for disease.

chemotherapy
Drugs that stop the life cycle of cells so they don't increase in number.

chromosome
Long strands that contain bundles of coded instructions in cells for making and controlling cells.

chronic myeloid leukemia (CML)
A cancer of blood-forming cells that causes too many white blood cells called granulocytes to form.

clinical trial
Research on a test or treatment to assess its safety or how well it works.

coagulation test
A test of the proteins that cause blood to clot.

complete blood count (CBC)
A test of the number of blood cells in a sample.

complete remission
No signs of cancer are present after treatment.

complex karyotype
The presence of 3 or more unrelated defects in chromosomes that occur in more than one cell.

comprehensive metabolic panel
Tests of up to 14 chemicals in your blood.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the inside of the body.

conditioning treatment
Treatment that is used to destroy cells in the bone marrow to prepare your body for a stem cell transplant.

cytogenetic testing
A test that uses a microscope to examine a cell's chromosomes.

cytoreductive treatment
Treatment that reduces the number of cells.

deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions for making and controlling cells.

diagnosis
To identify a disease.

differential
Measurement of the different types of white blood cells present in a blood sample.

erythromelalgia
A health condition that turns skin red and may cause painful, burning sensations.

erythropoiesis-stimulating agent (ESA)
A drug that helps bone marrow to make more red blood cells.

erythropoietin (EPO)
A substance that helps bone marrow to make more red blood cells.

essential thrombocythemia (ET)
A cancer of blood-forming cells that causes a high number of platelets.

fatigue
Severe tiredness despite getting enough sleep that limits one's ability to function.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal changes in a cell's genes and chromosomes.

gene
A set of coded instructions in cells for making and controlling cells.

graft-versus-host disease (GVHD)
An attack on normal cells by transplanted blood stem cells from a donor.

graft-versus-leukemia (GVL) effect
An attack on cancer cells by transplanted blood stem cells from a donor.

granulocyte colony-stimulating factor (G-CSF)
A substance that helps (stimulates) the bone marrow to make more white blood cells called neutrophils. It is made naturally in the body but can also be made in a lab.

hematocrit
The percentage of red blood cells to total blood.

hematopoietic stem cell or hematopoietic cell
A blood-forming cell from which all other types of blood cells are made. Also called blood stem cell.

hemoglobin
A protein in red blood cells that carries oxygen.

high-intensity chemotherapy
Treatment with high doses of strong cancer drugs that are more likely to cause severe side effects.

human leukocyte antigen (HLA)
Special proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

human leukocyte antigen (HLA) type
The unique set of proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

human leukocyte antigen (HLA) typing
A blood test that finds a person's HLA type—the unique set of proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

imaging test
A test that makes pictures of the insides of your body.

immune system
Your body's natural defense against infection and disease.

immunomodulator
A medicine that changes some parts of your body's disease-fighting system.

immunotherapy
A medicine that increases the activity of your body's disease-fighting system.

iron
A mineral needed to make new red blood cells.

iron chelation therapy
Treatment that is used to remove excess iron from your body.

iron overload
The buildup of excess iron in your body.

karyotype
A test that uses a microscope to examine a cell's chromosomes.

lactate dehydrogenase (LDH)
A protein that helps to make energy in cells.

liver function tests
Tests that measure chemicals made or processed by the liver.

medical history
All health events and medications taken to date.

megakaryocyte
A bone marrow cell that makes platelets.

magnetic resonance imaging (MRI)
A test that uses a magnetic field and radio waves to make pictures of the insides of the body.

mutation
An abnormal change in the instructions within cells for making and controlling cells.

myelodysplastic neoplasm (MDS)
A cancer of blood-forming cells that causes too few blood cells to form.

myeloproliferative neoplasm (MPN)
A cancer of blood-forming cells that causes too many blood cells to form.

no response
Test results show no meaningful change in cancer status after treatment.

observation
A period of testing for changes in cancer status.

partial response
Test results still show signs of cancer but also improvement after treatment.

pathologist
A doctor who's an expert in testing cells and tissue to find disease.

phlebotomy
Withdrawal of blood.

physical exam
A review of the body by a health expert for signs of disease.

platelet
A type of blood cell that helps control bleeding. Also called thrombocyte.

plateletpheresis
A procedure that withdraws blood, removes platelets, and then returns your altered blood to your body.

platelet transfusion
A slow injection of platelets into a vein.

polycythemia vera
Cancer of blood-forming cells that causes too many red blood cells.

prognosis
The pattern and outcome of a disease.

post-ET myelofibrosis
Advanced essential thrombocythemia with scarring in the bone marrow.

post-PV myelofibrosis
Advanced polycythemia vera with scarring in the bone marrow.

primary myelofibrosis (PMF)
Scarring of the bone marrow not due to other bone marrow problems.

progression
The course of a disease as it grows, gets worse, or spreads in the body.

red blood cell
A type of blood cell that carries oxygen from the lungs to the rest of the body.

red blood cell transfusion
A slow injection of red blood cells into a vein.

relapse
The return or worsening of cancer after a period of improvement.

side effect
An unhealthy or unpleasant physical or emotional condition caused by treatment.

spleen
A small organ to the left of your stomach that is part of the immune system.

supportive care
Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

white blood cell
A type of blood cell that helps fight infections in the body.

Acronyms

AML
acute myeloid leukemia

CBC
complete blood count

CML
chronic myeloid leukemia

CMV
cytomegalovirus

CT
computed tomography

DIPSS-PLUS
Dynamic International Prognostic Scoring System-PLUS

DNA
deoxyribonucleic acid

EPO
erythropoietin

ESA
erythropoiesis-stimulating agent

ET
essential thrombocythemia

FDA
Food and Drug Administration

FISH
fluorescence in situ hybridization

GVL
graft-versus-leukemia

HCT
hematopoietic cell transplant

HLAs
human leukocyte antigens

INT-1
intermediate-1

INT-2
intermediate-2

JAK
Janus-associated kinase

LDH
lactate dehydrogenase

LMWH
low-molecular-weight heparin

MDS
myelodysplastic syndrome

MF
myelofibrosis

MPN
myeloproliferative neoplasm

MPN-SAF
Myeloproliferative Neoplasm Symptom Assessment Form

MRI
magnetic resonance imaging

NCCN
National Comprehensive Cancer Network

PMF
primary myelofibrosis

prePMF
prefibrotic PMF

PV
polycythemia vera

QPCR
quantitative reverse transcriptase-polymerase chain reaction

TLS
tumor lysis syndrome

VWD
von Willebrand disease

Notes

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Mayo Clinic Cancer Center
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904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/departments-centers/mayo-clinic-cancer-center

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225
mskcc.org

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066
cancer.osu.edu

Roswell Park Cancer Institute
Buffalo, New York
877.275.7724
roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
St. Louis, Missouri
800.600.3606
siteman.wustl.edu

St. Jude Children's Research Hospital
The University of Tennessee Health Science Center
Memphis, Tennessee
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

Stanford Cancer Institute
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mcancer.org

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mdanderson.org

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Vanderbilt-Ingram Cancer Center
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vicc.org

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