Myeloproliferative Neoplasms

Available online at NCCN.org/patients
It's easy to get lost in the cancer world

Let NCCN Guidelines for Patients® be your guide

- Step-by-step guides to the cancer care options likely to have the best results
- Based on treatment guidelines used by health care providers worldwide
- Designed to help you discuss cancer treatment with your doctors
These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Myeloproliferative Neoplasms, Version 1.2022 — February 28, 2022.

© 2022 National Comprehensive Cancer Network, Inc. All rights reserved. NCCN Guidelines for Patients and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. No one, including doctors or patients, may use the NCCN Guidelines for Patients for any commercial purpose and may not claim, represent, or imply that the NCCN Guidelines for Patients that have been modified in any manner are derived from, based on, related to, or arise out of the NCCN Guidelines for Patients. The NCCN Guidelines are a work in progress that may be redefined as often as new significant data become available. NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for its application or use in any way.

NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation’s promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

National Comprehensive Cancer Network (NCCN) / NCCN Foundation
3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

NCCN Guidelines for Patients®
Myeloproliferative Neoplasms, 2022

2
NCCN Guidelines for Patients are supported by funding from the NCCN Foundation®

To make a gift or learn more, please visit NCCNFoundation.org/donate
or e-mail PatientGuidelines@NCCN.org.

Sponsored by

MPN Research Foundation

The MPN Research Foundation stimulates original research in pursuit of new treatments — and eventually a cure — for the blood cancers polycythemia vera, essential thrombocythemia, and myelofibrosis, known collectively as myeloproliferative neoplasms (MPN). In addition to investing in promising MPN research, we advocate for better treatments and convene patients and their families, doctors, researchers, and drug makers to advance our knowledge of MPNs. Together, we’re committed to changing the prognosis for people living with an MPN. mpnrf.org
Contents

6 MPN basics
13 Know your MPN
23 Symptoms and surveys
28 Clotting complications
43 Myelofibrosis
55 Supportive care for symptoms
60 Making treatment decisions
69 Words to know
74 NCCN Contributors
75 NCCN Cancer Centers
76 Index
1

MPN basics

7 What are MPNs?
8 What are the classic MPNs?
10 How are MPNs found?
11 How serious are MPNs?
12 Key points
Myeloproliferative neoplasms are a type of blood cancer. There are three classic types. These cancers grow slowly and at times may be challenging to diagnose. Many people live long lives but live with distressing symptoms. Research is underway to further improve and extend lives.

What are MPNs?

The human body is made of over 30 trillion cells. Cancer is a disease of abnormal cells that grow out of control. Myeloproliferative neoplasms (MPNs) are a group of rare blood cancers with an unusual name. What exactly does the name mean?

The first part of the first word—myelo—refers to bone marrow. Almost all bones have a soft center, called marrow, where most blood cells are formed.

The second part of the first word—proliferative—refers to the rapid growth of cells.

A neoplasm is an abnormal growth of cells.

Put together, the name myeloproliferative neoplasms means cancers of blood cells in bone marrow. There are many types of blood cells, so there are many types of blood cancers. Let's review on the next page how blood cells are made in order to further understand what MPNs are.

Blood cells

Blood stem cells are the cells from which all blood cells are formed. They go through a series of changes to become mature blood cells. The three main types of blood cells are red blood cells (erythrocytes), white blood cells (granulocytes, monocytes, and lymphocytes), and platelets (thrombocytes).
**How blood cells are made**

Blood cells do not live long, so they need to be replaced often. They arise from changes in a series of cells. The process can be simplified into 3 steps:

- **Step 1** – Hematopoietic stem cells are cells that develop into every type of blood cell. They make exact copies of themselves and make different cells that are a step closer to being blood cells. These different cells are called progenitor cells.

- **Step 2** – Progenitor cells belong to one of two “families” of blood cells—myeloid or lymphoid cell lines. Progenitor cells change into blast cells. Blasts, for short, are young (or immature) blood cells.

- **Step 3** – Each type of blast is set to become a certain type of mature blood cell. Mature blood cells are fully developed cells that perform specific functions. The three main types of blood cells are red blood cells, white blood cells, and platelets.

MPNs affect cells in the first step of blood cell formation. They are cancers of blood stem cells but only affect the myeloid family of cells. Myeloid blasts mature into blood cells, but too many blood cells are made. The type of mature blood cell that is in excess depends on the type of MPN.

**What are the classic MPNs?**

There are several types of MPNs. Each one affects a different type of myeloid cell. This book is about the most common or “classic” types:

- Polycythemia vera (PV)
- Essential thrombocythemia (ET)
- Primary myelofibrosis (PMF)

Chronic myeloid leukemia (CML) is an MPN with too many granulocytes. Some people call it a classic MPN, but it is often discussed by itself. Its treatment is based on a cancer marker that the other classic MPNs do not have. To learn about treatment, see *NCCN Guidelines for Patients: Chronic Myeloid Leukemia* at NCCN.org/patientguidelines.

**Polycythemia vera**

Red blood cells carry oxygen throughout the body. Polycythemia is a term for too many red blood cells. The extra red blood cells cause blood to be thicker than normal. In PV, there may also be too many white blood cells and platelets.
MPN basics

What are the classic MPNs?

**Essential thrombocytopenia**
ET causes too many megakaryocytes and platelets. Megakaryocytes are a type of blood cell within bone marrow. Platelets are tiny pieces of megakaryocytes that control bleeding. Having too many platelets is called thrombocythemia. “Essential” means the thrombocythemia is caused by a problem in the blood cell-making process.

**Primary myelofibrosis**
Myelofibrosis is scarring of the bone marrow. It is caused by an excess of megakaryocytes that overproduce a protein that causes scarring. Over time, scar tissue may replace bone marrow causing the number of blood cells to drop. Blood cells may start forming in unusual parts of the body, such as the liver and spleen, and cause them to enlarge.

Primary myelofibrosis, or PMF, means that you haven’t had another type of MPN before. If you have PV or ET, the MPN can progress into myelofibrosis. This secondary myelofibrosis is called “post-PV myelofibrosis” or “post-ET myelofibrosis.”

**MPNs are not...**

**Myelodysplastic syndromes (MDS)**
Like MPN, MDS are cancers of blood stem cells within the myeloid cell line. MDS cause low numbers of blood cells.

**Myelodysplastic syndromes/myeloproliferative neoplasms (MDS/MPN)**
MDS/MPN is a group of cancers distinct from MPN and MDS. The mature blood cells are abnormal, and there are high numbers of blood cells.

**Systemic mastocytosis**
Systemic mastocytosis is a buildup of a type of white blood cells, called mast cells, in the body, excluding the skin. A subtype called systemic mastocytosis with an associated hematologic neoplasm (SM-AHN) can occur with MPN.

**Acute myeloid leukemia (AML)**
AML is a cancer of myeloid cells in bone marrow. It causes many abnormal myeloid blasts, which cannot become mature blood cells. MPN may transform into AML although it rarely does.

The full library of NCCN Guidelines for Patients is available at NCCN.org/patientguidelines
How are MPNs found?

Many people have symptoms of MPN at diagnosis. Symptoms may start months and sometimes years before diagnosis. Other people have bleeding or blood clots, which are complications of MPNs. The search for the cause of these health problems leads to an MPN diagnosis. It is also common for an MPN to be found because of routine or other blood work and not because of related health problems.

A diagnosis of MPN can be challenging for several reasons. Your symptoms and health conditions may be caused by an MPN, another disease, or both. Symptoms may come and go then come back again. You may get blood work several times before blood counts become abnormal. You may look fine even if the symptoms are hard on you. Health care providers may not suspect cancer if you aren’t at least middle age. Some providers are not very familiar with MPNs. All of these issues may delay diagnosis.

Your primary care provider will refer you to a specialist if you may have an MPN. Reasons for referral include:

- It isn’t clear why your blood counts are staying high or low over time.
- It isn’t clear why you had blood clots.
- Your blood work is abnormal and you have general symptoms, such as unexplained weight loss or fever.

In these cases, you will be referred to a hematologist. Hematologists are doctors who

Why am I so tired?

Symptoms caused by MPNs can also be caused by other conditions. The overlap may make a diagnosis of MPN challenging. Take fatigue, for example. Fatigue is the most common symptom of MPNs. Fatigue is also caused by some medications, many diseases, and poor mental health and physical fitness.
are experts in blood diseases. To diagnose MPNs, a series of tests will be done. These tests are explained in Chapter 2.

How serious are MPNs?

MPNs are chronic cancers. Chronic cancers worsen slowly. Treatment may not be needed right away or ever, but these cancers are not typically cured. Symptoms may not occur right away. Once symptoms start, they may be mild to severe.

People with MPN often live many years with the proper treatment. Many people have near-normal lifespans. But for some, the cancer worsens more quickly. The course of the cancer depends on the MPN type, features of the cancer, and your age and health.

Your cancer team will watch for three major complications of MPNs:

- Abnormal bleeding
- Blood clots
- Disease transformation

Abnormal bleeding (hemorrhage) and blood clots (thrombosis) are most common in PV and ET. Abnormal bleeding is often minor but can be severe. Blood clots can block blood vessels. They can be fatal though this is rare. Treatments that reduce the chance of bleeding and blood clots are discussed in Chapter 4.

MPNs can transform into more severe diseases but most do not. ET and PV can progress into myelofibrosis. Though rare, MPNs can change into acute myeloid leukemia (AML).

The burden of MPN symptoms varies greatly between people. For many people, though, the burden is intense and reduces their quality of life. Symptoms may restrict everyday activities and work hours. In recent years, valid surveys to assess symptoms have been developed. On a regular basis, your cancer care team will assess which symptoms you have.

Treatment of MPNs has improved in recent years. Scientists have found some of the changes in cells that drive cancer growth. New treatments are being developed to address the ways that the cancer cells grow and survive.

This book explains treatment options based on the cancer type and prognosis. A prognosis predicts how your cancer will behave and respond to treatment. Discuss the treatments in this book with your doctor. Together, you can make a treatment plan that’s best for you.

“Don’t panic! It’s very easy to get obsessed or stressed by the idea of having a blood cancer, but many conditions are manageable with a combination of diagnosis, medication, monitoring, and lifestyle adjustments. It is not a death sentence!”

– Martyn
Living with PV
Myeloproliferative neoplasms, also called MPNs, are a type of blood cancer. They are cancers that form from blood-forming stem cells within the myeloid cell line. MPNs cause high numbers of blood cells.

The three classic MPNs are polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). PV causes an excess of red blood cells. ET causes an excess of megakaryocytes and platelets. PMF causes an excess of megakaryocytes that produce a fibrosis-causing protein.

MPNs are often found when their symptoms appear. But, sometimes, they are found because of abnormal blood work. When MPN is suspected, you will be referred to a specialist for more testing.

MPNs are chronic cancers, which means they worsen slowly. With treatment, most people live a long life, though many struggle with intense symptoms. For others, the cancer may worsen quickly or cause a fatal complication.

New treatments are being made to further extend and improve life.

I would tell someone recently diagnosed that they need to seek an MPN specialist if at all possible and that this diagnosis will always be a part of their life, but it doesn’t have to define their life story.”

– Carrie
Living with PV
2

Know your MPN

14 Tests to take
18 Getting a diagnosis
22 Key points
Several tests are needed if your doctor suspects myeloproliferative neoplasm or MPN. These tests are described in this chapter as well as the test results needed to diagnose the classic MPN types. Know which MPN you have, so you can help yourself get the best care.

Tests to take

Testing does not differ much between the myeloproliferative neoplasm (MPN) types. Each type—polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF)—will require blood work. Tests of bone marrow are also very common.

Ask for copies of your test results, and take notes as your doctor explains the reports. Don’t let your nerves stop you from asking questions. MPNs can be hard to understand. Bringing someone with you to doctor visits can be helpful. Keep your reports and other paperwork handy and organized in a file for when you need them again.

Health history

Expect your doctor to review your health in detail. This is known as taking a medical history. Your doctor will want to know a lot about your past and current health. You will likely be asked about:

- Illnesses and diseases
- Prescribed and over-the-counter medicines and supplements, surgeries, and blood transfusions
- Lifestyle choices, including your diet, how active you are, and whether you smoke or drink alcohol
- Symptoms and complications of MPNs

MPNs almost never run in families. When they do, most families acquire changes in genes after birth that may lead to MPN. It is very rare to be born with an abnormal gene that causes MPN.

Some other types of cancers and health conditions do run in families. Be prepared to discuss the health problems of your close blood relatives. These include your brothers and sisters, parents, and grandparents.

Physical exam

Your doctor will also perform a thorough physical exam of your body. This exam may include:

- Checking your vital signs—blood pressure, heart rate, breathing rate, and body temperature—and assessing your overall appearance
- Feeling and listening to organs, including your spleen and liver
- Assessing your level of pain, if any, when you are touched

Lab and biomarker tests

Lab and biomarker tests play an important role in diagnosing MPNs. These tests are performed on either blood or bone marrow samples. Some tests are done with a machine while others need a pathologist to complete. A pathologist is a doctor who’s an expert in tissues and cells. See Guide 1 for a full list of lab tests used to diagnose MPNs.
### Guide 1
Lab and biomarker tests to diagnose MPNs

<table>
<thead>
<tr>
<th>Test name</th>
<th>What does the test measure?</th>
<th>What sample is needed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count (CBC)</td>
<td>A CBC measures the number of blood cells and some features of blood cells.</td>
<td>Blood</td>
</tr>
<tr>
<td>Differential</td>
<td>A differential measures the number of each type of white blood cell. It also checks if the cell counts are in balance with each other.</td>
<td>Blood</td>
</tr>
<tr>
<td>Blood smear</td>
<td>A blood smear is a study of a drop of blood using a microscope.</td>
<td>Blood</td>
</tr>
<tr>
<td>Bone marrow histology</td>
<td>Bone marrow histology is the study of marrow using special stains and a microscope.</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>Comprehensive metabolic panel</td>
<td>This panel measures up to 14 types of chemicals that come from your organs.</td>
<td>Blood</td>
</tr>
<tr>
<td>Liver function tests (LFTs)</td>
<td>LFTs measure a yellow-colored fluid called bile and liver proteins and enzymes.</td>
<td>Blood</td>
</tr>
<tr>
<td>Lactate dehydrogenase (LDH)</td>
<td>LDH is a protein in most cells.</td>
<td>Blood</td>
</tr>
<tr>
<td>Uric acid</td>
<td>Uric acid is a chemical in most cells.</td>
<td>Blood</td>
</tr>
<tr>
<td>Erythropoietin (EPO)</td>
<td>EPO is a hormone made by the kidneys.</td>
<td>Blood</td>
</tr>
<tr>
<td>Fluorescence in situ hybridization (FISH) or multiplex RT-PCR for BCR-ABL1</td>
<td>FISH and multiplex RT-PCR detect genetic markers of cancer cells. <em>BCR-ABL1</em> is an abnormal gene inside of chronic myeloid leukemia (CML) cells.</td>
<td>Blood or bone marrow</td>
</tr>
<tr>
<td>Molecular tests or multigene next-generation sequencing (NGS) for JAK2, CALR, and MPL mutations</td>
<td>Molecular tests and NGS detect genetic markers of cancer cells. <em>JAK2</em>, <em>CALR</em>, and <em>MPL</em> mutations are abnormal genes commonly found in myeloproliferative neoplasms (MPNs).</td>
<td>Blood or bone marrow</td>
</tr>
<tr>
<td>Cytogenetics using karyotype with or without FISH</td>
<td>A karyotype is a picture of chromosomes.</td>
<td>Bone marrow or blood</td>
</tr>
</tbody>
</table>
Know your MPN Tests to take

Lab tests
A complete blood count (CBC) with differential is a very common lab test. It is used to identify blood cancers and other diseases. Test results include:

- Counts of white blood cells, red blood cells, and platelets
- The percentage of red blood cells in blood (called hematocrit)
- The amount of a protein called hemoglobin within red blood cells
- Counts of the most common types of white blood cells in blood—basophils, neutrophils, eosinophils, monocytes, and lymphocytes

A pathologist can see the size and shape of blood cells with a blood smear. Abnormal features can be a clue as to what disease you have. A blood smear can also show if there are immature blood cells called blasts in blood. Normally, blasts are only in bone marrow, but sometimes myelofibrosis forces them out.

In addition to a blood smear, a pathologist will inspect your bone marrow. This is known as bone marrow histology. Histology can detect abnormal numbers of bone marrow cells including megakaryocytes. It can also show how much bone marrow is scarred (fibrosis).

A comprehensive metabolic panel is a screening test for many diseases. It can also show if the MPN is affecting your organs, such as your bones and liver. Likewise, liver function tests (LFTs) are used to assess if the MPN is affecting your liver.

High levels of lactate dehydrogenase (LDH) and uric acid may be signs of myelofibrosis. During certain phases, myelofibrosis causes many blood cells to die. Dying blood cells release LDH and uric acid.

Removing bone marrow samples

Samples of your bone marrow may need to be removed and tested for diagnosis or treatment planning. A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a small piece of bone with marrow. These procedures are often done on the back of the hip one after the other.
Erythropoietin (EPO) helps to make red blood cells, and iron is needed to make hemoglobin in red blood cells. Blood tests of EPO and iron help diagnose PV. In PV, high red blood cell counts suppress EPO levels. Also, iron levels may be low despite having high hemoglobin levels.

**Biomarker tests**

Biomarker tests look for biological clues, or markers, of cancer. Molecular tests are a type of biomarker test that look for abnormal genes called mutations. Some people call them genetic tests.

The hallmark of chronic myeloid leukemia (CML) is the **BCR-ABL1** fusion gene. Its absence rules out the cancer. Fluorescence in situ hybridization (FISH) and multiplex RT-PCR are molecular tests that detect **BCR-ABL1**.

If CML is ruled out, molecular testing is used to look for markers of classic MPNs. One of the markers is the **JAK2 V617F** mutation. If this marker is not found, testing of **JAK2** exon 12 mutations may be done next if PV is suspected. If ET or PMF is suspected, testing of **CALR** and **MPL** mutations will be done.

A newer technology called next-generation sequencing (NGS) can test for multiple genetic markers at the same time. It may be used instead of single molecular tests. If tests confirm that you have an MPN, NGS testing is recommended to assess for prognosis if it wasn’t done before. A prognosis predicts how the cancer will behave and respond to treatment.

Cytogenetics are useful for diagnosis and treatment planning. Results can help with identifying MPN subtypes, grading bone marrow fibrosis, and assessing the prognosis of the cancer.
Getting a diagnosis

The World Health Organization (WHO) has created diagnostic standards for MPN. These standards include the core “major” criteria and a related “minor” criterion. The WHO criteria were updated in recent years to help doctors diagnose MPNs. However, making a diagnosis can still be tricky. Some of the challenges to diagnosis are as follows:

- Signs and symptoms of MPNs can have other causes, too. Other causes need to be ruled out.
- The three classic MPNs can have very similar test results. Early PMF may look like ET because there may be little bone marrow scarring (fibrosis).
- Recent bleeding can change test results and hide the correct diagnosis.
- Symptoms and test results differ between the early, middle, and late phases of an MPN. Doctors need to know what each MPN looks like as it progresses.

The goal of testing is to confirm or exclude a diagnosis of MPN. The pathologist will identify the MPN subtype when possible. Although rare, there are times when the MPN subtype is not clear. These cancers are called MPN, not otherwise specified (NOS).

Criteria for PV

The first major WHO criterion for PV is a high hemoglobin, hematocrit, or red cell mass. Your doctor may reorder blood work to check that a high level persists. Check your blood report for hemoglobin that is greater than 16.5 g/dL if your assigned sex at birth was male or 16.0 g/dL for female assigned sex. Hematocrit

Polycythemia vera

The criteria for diagnosis are:

1. High hematocrit, hemoglobin, or red cell mass
2. High number of cells in bone marrow
3. One of the following:
   - JAK2 V617F or JAK2 exon 12 mutation
   - Low EPO

Plasma

Hematocrit

% red blood cells

Red blood-cell mass

Volume of red blood cells

Normal blood

PV

Tubes of blood after being spun in a machine

NCCN Guidelines for Patients®
Myeloproliferative Neoplasms, 2022
is high when greater than 49 percent in males and 48 percent in females.

Red cell mass is the volume of red blood cells in the blood. It is a nuclear medicine test and is not often used to diagnose MPNs. It is high when it is 25 percent greater than the normal value.

After abnormal results from blood work, bone marrow studies may be done. The second criterion for PV is a high number of bone marrow cells compared to fat cells. This is called hypercellularity. The hypercellularity consists of myeloid cells—red blood cells, granulocytes, and megakaryocytes. Megakaryocytes vary in size.

The third criterion for PV is a JAK2 mutation, but it is not required for diagnosis. Almost everyone with PV has a JAK2 V617F mutation. The few people without this mutation most often have a JAK2 exon 12 mutation instead.

If no JAK2 mutation is found, PV is diagnosed if the first two major criteria are met and you have low EPO levels (the minor criterion).

Other lab results that are linked to PV include high levels of red blood cells. High levels of neutrophils, platelets, and LDH are also common. Most people with PV have low iron levels.

**Criteria for ET**
The first major criterion for ET is a high platelet count. Check your blood report for a platelet count that is 450 x 10^9/L or higher.

The second criterion is a high number of abnormal megakaryocytes in bone marrow. Megakaryocytes in ET are larger than normal.

---

**Essential thrombocythemia**

The criteria for diagnosis are:

1. High platelet count
2. High number of abnormal megakaryocytes in bone marrow
3. Other blood cancers have been ruled out
4. One of the following:
   - JAK2, CALR, or MPL mutation
   - Another mutation that causes a clonal cancer or no underlying cause of high platelet counts

---

Normal bone marrow; megakaryocytes (blue)  
Enlarged, hyperlobulated megakaryocyte in ET
Their nucleus—the “brain” of the cell—has more divisions (lobes) than normal.

ET can only be diagnosed after other blood cancers have been excluded. The third criterion requires other types of MPN, myelodysplastic syndromes (MDS), and other myeloid neoplasms to be ruled out.

The fourth criterion is having a $JAK^2$, $CALR$, or $MPL$ mutation, but it is not required for diagnosis. A $JAK^2$ mutation is the most common, and a $CALR$ mutation is the second most common. About 1 out of 10 people with ET don’t have any of these three mutations. In these cases, the MPN is described as “triple negative.”

When the fourth criterion is not met, ET can be diagnosed based on the minor criterion. This criterion includes 1) another genetic marker or 2) no underlying cause of the high platelet count. Genetic markers include $ASXL1$, $EZH2$, $TET2$, $IDH1/IDH2$, $SRSF2$, and $SRF3B1$ mutations. An abnormal karyotype is also a marker.

Criteria for PMF

If you haven’t had another type of MPN, myelofibrosis is called primary myelofibrosis or PMF. There are 2 stages of PMF based on the amount of scarring (fibrosis) in bone marrow:

- Prefibrotic PMF (prePMF or early PMF)
- Overt PMF

The first criterion of myelofibrosis is a high number of abnormal megakaryocytes in bone marrow. The bone marrow in prePMF has either minor or no fibrosis, whereas there is major fibrosis in overt PMF. In prePMF, the number of bone marrow cells is higher than normal, although at times the production of red blood cells may be low.

Fibrosis is graded by assessing reticulin in bone marrow. Reticulin is a woven meshwork of thin collagen fibers. There are four grades

In September 2018, I had a routine checkup during which I indicated symptoms of fatigue and weight loss. Blood tests indicated anemia. As my hemoglobin dropped further, I started to have symptoms of itching, night sweats and early satiety. I was scheduled to see a hematologist in November 2018. Bone marrow biopsy indicated PMF. It also showed several of the associated mutations including the $JAK2\ V617F$ mutation.

– Ned

Living with myelofibrosis
of myelofibrosis. PrePMF is grade 0 or 1, and overt PMF is grade 2 or 3.

- **MF-0** – The reticulin branches are spaced apart and do not cross over each other.
- **MF-1** – The reticulin branches have many crossovers, especially near blood vessels.
- **MF-2** – The reticulin is diffuse and dense with many crossovers. There may be a few bundles of thick reticular fibers.
- **MF-3** – The reticulin is diffuse and dense with many crossovers. There are bundles of thick reticular fibers that cause the spongy bone to harden (osteosclerosis).

**Primary myelofibrosis**

The criteria for diagnosis are:

1. Bone marrow with many abnormal megakaryocytes and:
   - Minor or no scarring (fibrosis) in early myelofibrosis
   - Major fibrosis in overt myelofibrosis

2. Other blood cancers have been ruled out

3. **JAK2, CALR, MPL**, or other mutation markers, or there is no underlying cause of the fibrosis

4. One of the following:
   - Anemia that isn’t caused by another health condition
   - High white blood cell count
   - High LDH level
   - Enlarged spleen that can be felt
   - Blasts may be in blood in overt myelofibrosis

In normal bone marrow, the reticulin fibers (red) do not cross over each other.

In myelofibrosis, the reticulin fibers (red) do cross over each other forming fibrosis.
Myelofibrosis can only be diagnosed after other blood cancers have been excluded. The second criterion requires other types of MPN, MDS, and other myeloid neoplasms to be ruled out.

The third criterion is having a JAK2, CALR, or MPL mutation. A JAK2 mutation is the most common, and a CALR mutation is the second most common. About 1 out of 10 people with PMF don’t have any of these three mutations (“triple negative”).

To be PMF, the minor criterion—another sign of myelofibrosis—has to be met. This sign may be low red blood cell counts or hemoglobin (anemia), high levels of white blood cells or LDH, or an enlarged spleen. Another sign of overt PMF is blasts in blood. Blasts are normally only in bone marrow.

Key points

- If MPN is suspected, a group of tests is needed for diagnosis. Testing does not differ much between the MPN types.
- Be ready to tell your doctor about any health problems and treatments you’ve had in your lifetime. Your doctor will examine your body for signs of disease. The exam will include touching parts of your body to see if anything feels abnormal.
- You will also need to provide samples of blood, bone marrow, or both. Your blood and bone marrow will be sent to a lab to be tested for signs of MPNs and other diseases.
- The World Health Organization (WHO) has created criteria to diagnose MPN types. Most MPNs have a genetic marker. These markers include JAK2, CALR, and MPL mutations.
- Fibrosis is scarring of the bone marrow. It is graded on a scale that ranges from 0 to 3. Higher scores represent more fibrosis.

Know your MPN

- What is the subtype?
- What are the mutations, if any?
- What treatment are you on?

It is important to tell any clinician who treats you about the MPN and treatment. Otherwise, you could receive care that is harmful.
3
Symptoms and surveys

24  Types of symptoms
25  The MPN-10
26  Key points
Symptoms and surveys

Symptoms of myeloproliferative neoplasms can have a major impact on life. Your doctor will assess your symptoms on a regular basis. A short symptom survey is often used.

A symptom is a physical or mental change that may be related to a disease. Most people with myeloproliferative neoplasms (MPNs) have symptoms related to the cancer. Symptom burden is often severe even in people with polycythemia vera (PV) or essential thrombocythemia (ET).

Types of symptoms

MPNs cause a wide range of symptoms. Despite the wide range, there are basically 3 types of symptoms. Doctors plan treatment based on these types:

- Microvascular symptoms
- Enlarged spleen symptoms
- Constitutional symptoms

Microvascular symptoms

Microvascular symptoms are caused by slow blood flow in small blood vessels called capillaries. PV reduces blood flow due to high numbers of red blood cells. This can lead to headaches and blurred vision. In ET, high numbers of platelets can cause headaches, dizziness, high-pitched ringing in the ears (tinnitus), and numbness and tingling in the limbs (paresthesia). Other microvascular symptoms include poor concentration, sleep problems, and sexual problems.

Enlarged spleen symptoms

Among people with MPN, bone marrow may become unable to make blood cells. When the bone marrow makes too few blood cells, other parts of the body may start producing the cells instead.

The spleen is a very common backup to bone marrow for blood cell production. It is a small organ to the left of the stomach. When the spleen supplies the body with blood cells, it gets bigger. An enlarged spleen is called splenomegaly. Your doctor will be able to feel an enlarged spleen during an exam.

An enlarged spleen causes symptoms because it presses against other body parts. It may partly fill the space where the stomach is. In turn, you will feel full quicker when eating (early satiety). The spleen may press against the diaphragm, which prevents the lung from fully expanding. In turn, you may have shortness of breath or a cough. An enlarged spleen can also cause discomfort or pain if it presses on a nerve. Many people become less active due to these symptoms.

Constitutional symptoms

Constitutional symptoms are the result of a condition that affects the whole body. They are very general and can be caused by more than one factor. In MPN, doctors believe that constitutional symptoms are related to high levels of small proteins called cytokines. Cytokines trigger inflammation—a defensive reaction—in the body.

One of the most common constitutional symptoms of MPNs is fatigue. Cancer-related fatigue is a distressing, ongoing tiredness that limits one’s ability to do day-to-day tasks. It is a
Symptoms and surveys

The MPN-10

Surveys are commonly used in research to assess symptoms. Surveys used for research may also be used in clinical practice. For MPN, there are several reasons to assess symptoms:

- Symptoms often reduce quality of life
- Symptoms may relate to the outcomes of the MPN
- Tracking symptoms will show if a treatment provides relief

Over a decade ago, the first symptom survey was created for people with myelofibrosis. It is called the Myelofibrosis Symptom Assessment Form (MFSAF). The survey consists of 20 items about symptoms and quality of life.

Symptoms of myelofibrosis are not exclusive to this cancer. People with PV and ET can have these symptoms, too. For this reason and others, a second symptom survey was developed for people with any type of MPN.

"I was first diagnosed with ET, confirmed with the positive JAK2 mutation. For as long as I remember, I had “unexplained” bone pain, migraine headaches with neurological symptoms (including a probable small TIA from sticky platelets), and irritable bowel syndrome, which mysteriously went away once my blood counts were normalized decades later.”

– Ruth

Living with post-ET myelofibrosis
The second survey is called the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF). It consists of 27 items. It added microvascular symptoms common to PV and ET.

A third survey was created to shorten the survey for clinical use. It is called the MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS). It’s also simply called the MPN-10 because the number of items was reduced to 10. See Guide 2 for a list of the top 10 symptoms.

The 10 symptoms in the MPN-10 are the most important and common ones. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms. An online version of the survey can be found at thehematologist.org/mpn-total-symptom-score.

Guide 2
The top 10 symptoms of MPN

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Medical term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing, extreme tiredness</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Feeling full quickly when eating</td>
<td>Early satiety</td>
</tr>
<tr>
<td>Pain in the belly area</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Inactivity</td>
<td>Sedentary</td>
</tr>
<tr>
<td>Unable to focus for an extended time</td>
<td>Poor concentration</td>
</tr>
<tr>
<td>Night sweats</td>
<td>Sleep hyperhidrosis</td>
</tr>
<tr>
<td>Itchy skin</td>
<td>Pruritus</td>
</tr>
<tr>
<td>Bone pain</td>
<td>Osteodynia</td>
</tr>
<tr>
<td>Fevers</td>
<td>Pyrexia</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Cachexia</td>
</tr>
</tbody>
</table>

Key points

- Most people with myeloproliferative neoplasms (MPN) have symptoms related to the cancer.
- There are basically 3 types of MPN symptoms. They are microvascular symptoms, enlarged spleen symptoms, and constitutional symptoms.
Microvascular symptoms are caused by slow blood flow in capillaries. Examples of these symptoms are headaches, dizziness, and tingling in the limbs.

The spleen gets bigger when it starts making blood cells. An enlarged spleen may cause you to feel full quickly when eating. It may also cause belly pain or discomfort, cough, and shortness of breath.

Constitutional symptoms are related to high levels of cytokines. Examples of these symptoms include fatigue, losing weight, and fevers.

The MPN-10 is a short survey of MPN symptoms used in clinical practice.

“At diagnosis I wish my doctor had mentioned that symptoms are very common and drug side effects are almost inevitable. I wish I had been advised to stay vigilant about drug side effects and also to report symptoms. Community hematologists really need to develop more expertise or else refer patients to MPN specialists.”

– Sadhana
Living with PV

We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback
## Clotting complications

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>About blood clots</td>
</tr>
<tr>
<td>30</td>
<td>Preventing blood clots</td>
</tr>
<tr>
<td>35</td>
<td>Treating blood clots</td>
</tr>
<tr>
<td>38</td>
<td>MPN checkups</td>
</tr>
<tr>
<td>39</td>
<td>Changing treatment</td>
</tr>
<tr>
<td>41</td>
<td>Key points</td>
</tr>
</tbody>
</table>
Treatment of polycythemia vera and essential thrombocythemia focuses on preventing blood clots. Blood clots are the leading cause of death. With treatment, many people don’t get blood clots and live for many years.

### About blood clots

A blood clot is a gel-like clump of blood. Blood clots develop to stop bleeding and then dissolve. A blood clot can form inside a blood vessel when there is no bleeding. This type of clot is called a thrombus or thrombi if referring to more than one.

People with polycythemia vera (PV) and essential thrombocythemia (ET) are prone to get thrombi. Thrombi are the most frequent, sometimes life threatening, complication of these two MPNs. Treatment reduces the chance of getting thrombi. With treatment, many people with PV or ET live for many years.

#### Cell congestion and clots

PV and ET may increase the chance of getting a blood clot in a similar way. Both MPNs increase the number of blood cells in the bloodstream. The extra blood cells cause a traffic jam and slow down blood flow in vessels. The extra blood cells also stick together more so than normal blood cells. Slow-moving, sticky blood cells are likely to form blood clots.

#### Fixed and free clots

There are two types of blood clots. Thrombi are attached to a base inside a blood vessel and don’t move. Sometimes, a thrombus breaks free and travels through the bloodstream. These moving blood clots are called emboli and may get stuck in another spot.

### Blood clot in a leg

People with MPN are at risk for blood clots. This image shows a blood clot forming 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.
Blood clots can develop in any type of blood vessel. An arterial thrombus is a blood clot inside of an artery. Arteries transport oxygen-rich blood away from the heart to the whole body. A blood clot in a vein is called a venous thrombus. Veins transport blood that lacks oxygen back to the heart.

The danger of clots
As blood clots worsen, they can block enough blood flow to cause symptoms. Spotting symptoms early and getting timely treatment prevents serious health problems. In contrast, hidden and untreated blood clots may cause long-term problems or be deadly.

Arterial thrombi may restrict blood flow (known as thrombosis) and starve cells of oxygen. Without oxygen, cells die and organs are damaged. Arterial thrombosis may cause strokes, heart attacks, and blindness.

One of the most dangerous venous thrombi develops in major veins deep beneath the skin. Blockage of a major vein is called a deep vein thrombosis (DVT). A pulmonary embolism is a DVT that broke free then traveled to and blocked a lung artery. DVTs and pulmonary embolisms are sometimes referred to as venous thromboembolism (VTE).

Preventing blood clots
The treatment of PV and ET largely focuses on preventing thrombi. Thrombi occur more often than other MPN-related causes of death. However, many people don’t form thrombi. From here on, thrombi will be referred to as blood clots since this term is more familiar.

The plan to prevent clots differs between people. Your plan will be based on what MPN type you have and your risk of clots. Some people have such a low risk of clots that no treatment is needed. For others, one of the first steps to prevent clots is to take aspirin.

People who are highly likely to get clots may take medication that lowers blood counts. These cytoreductive therapies are given to reduce hematocrit in PV and platelets in ET. They are also sometimes given to relieve symptoms when blood clots aren’t likely.

Calculating clot risk
The risk of thrombosis is not the same for everyone. Your doctor will assess your risk and plan treatment based on your risk level. This process is called risk stratification.

People with PV are stratified into one of two groups—low or high risk. People at low risk do not have any key risk factors. People at high risk have both key risk factors:

- Age above 60 years
- A prior blood clot

For ET, a tool called the International Prognostic Score of Thrombosis (IPSET-thrombosis) is used for risk stratification. People are assigned to very-low-, low-, intermediate-, or high-risk levels. These four risk levels are based on:

- Ages 65 years and above
- A prior blood clot
- JAK2 V617F mutation

Treatment options based on risk level are listed in Guide 3 for PV and Guide 4 for ET.
## Guide 3
### Preventing blood clots related to polycythemia vera

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Prevention options</th>
</tr>
</thead>
</table>
| **Low risk of blood clots**     | • Manage cardiovascular risk factors  
• Aspirin  
• Phlebotomy  
• Ropeginterferon alfa-2bnjft (not preferred) |
| **High risk of blood clots**    | • Manage cardiovascular risk factors  
• Aspirin  
• Phlebotomy  
• Cytoreductive therapy to reduce blood counts: Hydroxyurea (preferred), ropeginterferon alfa-2bnjft (preferred), or peginterferon alfa-2a |

## Guide 4
### Preventing blood clots related to essential thrombocythemia

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Prevention options</th>
</tr>
</thead>
</table>
| **Very low risk of blood clots**     | • Manage cardiovascular risk factors  
• Aspirin if you have microvascular symptoms |
| **Low risk of blood clots**          | • Manage cardiovascular risk factors  
• Aspirin                                  |
| **Intermediate risk of blood clots** | • Manage cardiovascular risk factors  
• Aspirin                                  |
| **High risk of blood clots**         | • Manage cardiovascular risk factors  
• Aspirin  
• Cytoreductive therapy to reduce blood counts: Hydroxyurea (preferred), peginterferon alfa-2a, or anagrelide |
Managing cardiovascular risk factors

Your cardiovascular system consists of your heart, blood vessels, and blood. Cardiovascular risk factors are things that will likely damage this system. Having a cardiovascular risk factor may increase your chance of getting a blood clot. Your doctor will assess for and help you manage risks that can be changed:

➤ Smoking
➤ Being overweight
➤ Too little exercise
➤ High blood pressure (hypertension)
➤ High blood sugar (diabetes)

Aspirin

Taking a baby aspirin every day greatly reduces the risk of blood clots. It prevents clots by making platelets less sticky. It may reduce microvascular symptoms in ET. Bleeding is a side effect of aspirin for some people.

Aspirin prevents blood clots among people with either low- or high-risk PV. It also works well among people with ET, but not everyone with ET needs it. Aspirin may cause more harm than good in people with very-low-risk ET, especially those with acquired von Willebrand (VWD) disease. People with VWD are likely to have bleeding because their blood doesn’t clot as it should.

Cardiovascular risk factors

Having a cardiovascular risk factor increases the chance of getting a blood clot. For example, being overweight may lead to the build up of fatty plaque called atherosclerosis in arteries. Plaque may slow down blood flow giving blood cells the chance to stick together. A blood clot could also form if the plaque breaks open. In addition to plaque, blood clots further narrow arteries and block blood flow.
NCCN experts recommend taking 80 to 100 milligrams of aspirin each day. If you still have symptoms, you may take aspirin twice a day. Higher doses should be avoided for most people. High doses increase the chance of bleeding in your bowels. Your blood counts may need to be lowered before starting aspirin. High blood counts increase risk of bleeding.

Smoking blocks the action of aspirin. If you smoke, you’ll have to quit for aspirin to work. Ask your health care providers about counseling and drugs to help you quit.

**Phlebotomy**

Though aspirin works well for PV, the main way to prevent blood clots is to reduce hematocrit. Hematocrit is a measure of red blood cells compared to the total amount of blood. At diagnosis, hematocrit is often above 55 percent (%). Hematocrit should be below 45% for most people. Some people need a target of below 42%.

Phlebotomy is the key strategy to reducing hematocrit. It is a procedure that removes a small amount of blood with a needle like when donating blood. Some people feel dizzy or get a little sweaty afterward. A few faint.

Phlebotomy works by removing the iron-carrying red blood cells from blood. Don’t take iron supplements unless they’re prescribed by your MPN doctor. Low iron can cause fatigue, cognitive problems, headaches, and restless legs.

With less iron in the body, bone marrow makes fewer red blood cells. Blood clots aren’t as likely if the bloodstream is

**Surgery**

You might need surgery. Surgery increases the chance of blood clots and bleeding. Your surgeon may contact your MPN doctor to get your health history. It’s important for your surgeon to know about any blood clots, bleeding, and your medications.

Prior to surgery, your blood counts should be close to normal to prevent blood clots and bleeding.

- You may be put on anticoagulants and cytoreductive therapy before surgery.
- People with PV may need more phlebotomies to stay below 45 percent for 3 months prior to surgery.
- If the surgery has a high risk for venous thromboembolism, you may be given low-molecular-weight heparin (LMWH).

Just prior to surgery, you will need to stop taking some medicines. Aspirin is stopped 1 week before surgery. You may stay on cytoreductive therapy until the surgery unless your surgeon tells you to stop. The time to stop an anticoagulant depends on how long it stays in your body.

After surgery, you will be monitored for blood clots and bleeding. You may restart your medicines if bleeding risk is low. Aspirin is often restarted 24 hours after surgery.
Clotting complications

Preventing blood clots

less congested with red blood cells. After phlebotomy, you may also get quick relief from headaches, itchiness, and blurred vision.

Your doctor will assess how often you need phlebotomy. Some people need it every other week. If your hematocrit is high, you may need it once or twice a week. Once the hematocrit and MPN symptoms are under control, the time between phlebotomies can be lengthened.

Hydroxyurea
Hydroxyurea (Hydrea) has been a standard treatment for a long time. For many people, it lowers blood counts and prevents blood clots for years. Hydroxyurea works by stopping new cells from being made. It is disguised as a natural cell protein but doesn’t work. The result is a breakdown in the process of cells making more cells.

Hydroxyurea is a preferred treatment for reducing blood counts in high-risk PV and ET. It is made as a capsule, so you can take it at home. It is given in low doses, so many people can tolerate its side effects. Hydroxyurea can cause below-normal blood counts, more fatigue, skin changes, diarrhea, constipation, and skin cancer.

Interferon alpha
Interferon alpha naturally exists in your body and helps fight infections. It can also be made in the lab as a treatment. Interferon curbs the making of blood cells in bone marrow. The two interferons used to treat MPN are:

- Pegylated interferon, usually called peginterferon (PEGASYS), is a preferred treatment option for high-risk PV and ET.

- Ropeginterferon alfa-2b-njft (BESREMi) is a treatment option for PV. It is a recommended treatment for high-risk PV. It may be used to treat low-risk PV, but more research is needed.

You can take interferon at home. It is injected under the skin every 2 weeks. Over time, it may be needed less often. Interferon may cause flu-like illness, joint pain, fatigue, itching, throat swelling, musculoskeletal pain, and depression.

Anagrelide
Anagrelide (Agrylin) is a treatment option for high-risk ET. It works by stopping megakaryocytes from maturing and making platelets. Anagrelide is a capsule that is taken twice a day. It may cause headaches, digestive problems, anemia, and heart palpitations.

My first thought was let’s get some sort of medication, kick this thing to the curb, and move on. Then I discovered that ET was something that did not have a cure.”

– Diane
Living with post-ET myelofibrosis
Treating blood clots

You may get a blood clot even though you took steps to prevent it. Many blood clots are safely managed with anticoagulants. Coagulation is another word for blood clotting. Anticoagulants are often called blood thinners though they are not. They slow down the clotting of blood.

Anticoagulants
Research has shown that anticoagulants help treat blood clots in general practice. But, there is little to no research on anticoagulants in people with PV or ET. It is unknown if one anticoagulant works better than another. It is also unknown exactly how long an anticoagulant is needed. Your doctor will decide how long you’ll take an anticoagulant based on the severity of the blood clot.

Three common types of anticoagulants are:

- **Low-molecular-weight heparin (LMWH)** – This medicine enhances the effect of a natural anticoagulant in your body. It is injected into the skin and can be taken at home.

Warning signs of blood clots

- **Clots in the head** may cause headaches, dizziness, slurred speech, and facial weakness.

- **Clots in the abdomen** may cause nausea, vomiting, and loose or bloody stools.

- **Clots in the legs and arms** may cause a limb to feel heavy, cold, numb, or tingling. The limb may swell, cramp, or become weak. Skin may turn a bluish or red color.
Direct oral anticoagulants – These pills disable proteins that help the blood to clot. They include apixaban (Eliquis), betrixaban (BevyxXa), dabigatran (Pradaxa), edoxaban (Savaysa), and rivaroxaban (Xarelto).

Vitamin K blockers – Among these medicines, warfarin (Coumadin, Jantoven) is the most often used. It is a pill taken at home. Warfarin stops the liver from using vitamin K, which is needed to make clotting proteins.

Anticoagulants increase the risk of bleeding. The risk is higher when taking aspirin or treatment that lowers platelet counts. Your doctor may stop these treatments while you’re on an anticoagulant. People with cardiovascular risk factors may stay on aspirin.

Plateletpheresis
If you have a sudden life-threatening clot, you may receive plateletpheresis. This procedure withdraws your blood and removes platelets. Your platelet-reduced blood will then be returned to your body. Plateletpheresis is rarely done as it only slightly decreases platelets and for a short period of time.

“In 2007, I was pregnant with my son, and routine blood testing revealed extremely elevated platelet counts. Additional testing revealed that I have the JAK2 V617 mutation. This mutation had only been discovered two years earlier in 2005. Despite my diagnosis, my pregnancy with my son went well, and I was able to carry him to term with only the addition of low-dose aspirin to address my MPN. My son is now 11 years old. He’s healthy and doing great.”

– Karrie
Living with PV
Pregnancy

You may want to have a baby. Think about meeting with an obstetrician who’s an expert in high-risk pregnancies before getting pregnant. This doctor can assess for and manage health risks during pregnancy. Pregnancy is at high risk if you have had a blood clot, bleeding due to an MPN, or related problems during prior pregnancies.

Pregnancy care for everyone with MPN includes:

Hydroxyurea should not be taken while trying to get pregnant, during pregnancy, or while breastfeeding. Hydroxyurea may harm your baby. You may take peginterferon alfa-2a to lower blood counts, but research on this drug during pregnancy is needed.

If you need an anticoagulant while breastfeeding, safe ones to take are unfractionated heparin, low-molecular-weight heparin (LMWH), warfarin, and fondaparinux. Direct oral anticoagulants should be avoided.

If you have PV, the hematocrit target is based on the trimester. Hematocrit should be under 41 percent for the first trimester, under 38 percent for the second trimester, and under 39 percent during the third trimester.

Pregnancy care for those at standard risk includes:

Take a baby aspirin every day until the baby is born. After birth, many people take LMWH for 6 weeks. Aspirin can be restarted once LMWH is finished.

Pregnancy care for those at high risk includes:

After a positive pregnancy test, take baby aspirin every day. Many people also take LMWH throughout pregnancy and for 6 weeks after giving birth. If blood counts are high, they can be lowered with interferon.
MPN checkups

After starting treatment, you will need to meet with your MPN doctor often. NCCN experts advise having a visit every 3 to 6 months. You may need visits more often if problems arise.

Doctor visits

During visits, you will be asked about new or worsening symptoms and new diagnoses. You may be given a symptom survey called the MPN-10 to complete. If you have PV, your doctor will want to know how many phlebotomies you’ve had since the last visit.

Your doctor will perform a physical exam of your body. The size of your spleen and liver will be checked. Your doctor will look for signs of blood clots and bleeding.

Blood work may be ordered. Your doctor will monitor your blood counts and other blood values. Liver and kidney functioning tests may be ordered as well. Now and then, a peripheral blood smear may be done.

Your doctor performs these assessments to answer the following questions:

- Is the MPN causing complications? Have you had any blood clots or bleeding related to the MPN?
- What is the treatment response? Are symptoms improving? Are the blood counts in the normal range? Are organs of normal size?
- Are you tolerating treatment? Do you have side effects from treatment? Are the side effects too severe?
- Is the MPN progressing? Is it transforming into myelofibrosis or leukemia?

Treatment response

In research, there are standards for assessing results of cytoreductive therapy. Know that your treatment may be working but may not match these standards. Your doctor will assess treatment results mostly based on whether symptoms are improving and if blood counts are too abnormal. There are four treatment responses used in research:

Complete remission is defined by:

- A large improvement in MPN symptoms and signs for at least 12 weeks. Your liver and spleen do not feel enlarged on exam. Your symptoms have mostly cleared.
- Bloods counts are normal or near-normal for at least 12 weeks, and in addition for PV, hematocrit is less than 45 percent without phlebotomies.
- You’ve had no blood clots or bleeding events, and the MPN is not changing into another cancer.
- Your bone marrow consists of a normal number of cells, cells that look normal, and minor, if any, bone marrow scarring (fibrosis). Please note that bone marrow biopsies are not routinely done to assess treatment response for PV and ET.

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 MPN.
### Changing treatment

Your treatment will likely not change if symptoms greatly improve. Little to no relief in symptoms or worsening symptoms may trigger a change. Read Guide 5 for a full list of events that signal when a change in treatment may be needed.

**Start cytoreductive therapy**

Cytoreductive therapy may be the next step of care. It may be started if you now have high-risk disease, symptoms, or abnormal bleeding. A bone marrow aspiration and biopsy may be needed before starting a new treatment. Read *Preventing blood clots* to learn more about cytoreductive therapy.

### Guide 5
**Events that signal it may be time to change treatment**

<table>
<thead>
<tr>
<th>Event</th>
<th>Change in treatment of polycythemia vera</th>
<th>Change in treatment of essential thrombocythemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood clot</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Aquired von Willebrand disease</td>
<td></td>
<td>●</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Enlarged spleen</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>High or increasing blood counts</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>New symptoms</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Ongoing microvascular symptoms despite taking aspirin</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>More phlebotomies are needed to keep blood counts low or phlebotomies are causing problems</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Cytoreductive therapy isn’t lowering blood counts or is causing problems</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Bone marrow fibrosis</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Blast cells in bloodstream</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>
Change cytoreductive therapy
Sometimes cytoreductive treatment works at first then stops. Sometimes, it doesn’t work enough or at all. In these cases, changing to a treatment option listed in Guide 6 is needed.

A clinical trial may be an option for you. A clinical trial is a type of medical research study. After being tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA). Read more about clinical trials in Chapter 5.

Ruxolitinib is a preferred option for PV after stopping hydroxyurea. It is sometimes useful among people with ET. Ruxolitinib is a medicine that is called a kinase inhibitor. It blocks a protein called JAK that is inside of blood stem cells and in turn reduces the number of blood cells. Read more about ruxolitinib in Chapter 5.

Guide 6
Treatment options if a change is needed

<table>
<thead>
<tr>
<th>Next step in treatment</th>
<th>Polycythemia vera</th>
<th>Essential thrombocythemia</th>
</tr>
</thead>
</table>
| Medicine that lowers your blood counts (called cytoreductive therapy) may be started if never taken before | The 3 options are:  
  - Hydroxyurea (preferred)  
  - Ropeginterferon alfa-2bnjft (preferred)  
  - Peginterferon alfa-2a | The 3 options are:  
  - Hydroxyurea (preferred)  
  - Peginterferon alfa-2a  
  - Anagrelide |
| If on cytoreductive therapy, it may be stopped and a new treatment may be started | The 2 preferred options are:  
  - Clinical trial  
  - Ruxolitinib | The 2 preferred options are:  
  - Clinical trial  
  - Hydroxyurea if never taken before |
| | Other options are:  
  - Ropeginterferon alfa-2bnjft (preferred)  
  - Peginterferon alfa-2a  
  - Hydroxyurea | Other options are:  
  - Peginterferon alfa-2a if never taken before  
  - Anagrelide if never taken before  
  An option that is sometimes useful is:  
    - Ruxolitinib |
| Current treatment may be switched to treatment of myelofibrosis or leukemia | Read Chapter 5 for options | Read Chapter 5 for options |
Cytoreductive therapies that you have not yet taken may be an option now. If you haven’t taken hydroxyurea, it may be an option. Likewise, interferon may be an option if not yet received. Anagrelide may be an option for ET.

**MPN progression**
PV and ET can transform into myelofibrosis or acute myeloid leukemia (AML). It is unknown why these MPNs progress. Researchers are studying the role of inflammation and abnormal genes.

The risk of progression increases the longer you have PV or ET. It is rare for these MPNs to progress right into leukemia. If PV and ET do progress, they progress into myelofibrosis and then into leukemia.

Once progression starts, it may be slow and take place over many years. An early sign of progression is a steady decline in the need of treatment to reduce blood counts. Your doctor may reduce or stop treatment to see if your blood counts stop falling. If they don’t, you may have myelofibrosis.

**Post-PV and -ET myelofibrosis**
A bone marrow biopsy is needed to confirm myelofibrosis following PV or ET. Both post-PV and post-ET myelofibrosis are defined by a high-grade fibrosis and at least two of the following:

- A drop in red blood cells or hemoglobin to low anemic levels. For PV, instead of anemia, phlebotomy or cytoreductive therapy may not be needed as much.
- The red blood cells in blood are abnormal. Some, called dacryocytes, have a tear-like shape. The blood also contains immature red and white blood cells called blasts.
- Your spleen is steadily getting larger.
- For ET, the LDH level has increased above the normal range.
- You have one or more of these 3 symptoms: You’ve lost more than 10 percent of your body weight in 6 months, you have night sweats, or you have an unexplained fever.

**Acute myeloid leukemia**
AML is a fast-growing cancer. To be diagnosed with AML, at least 20 percent (20%) of bone marrow or the bloodstream must be composed of myeloblasts. This means that at least 1 out of every 5 cells are blasts. AML may be diagnosed with less than 20% blasts if chromosomes have certain abnormal changes.

**Key points**

- A thrombus is a blood clot that formed inside of a blood vessel. A thrombus can be life-threatening if it blocks blood flow to vital organs.
- People with polycythemia vera (PV) and essential thrombocythemia (ET) are prone to getting blood clots. Treatment of these MPNs largely focuses on preventing blood clots. With treatment, most people live for many years.
- Treatment options are based on risk for blood clots. For every risk level, managing cardiovascular risk factors is a goal. Aspirin is also commonly used to prevent clots. For PV, phlebotomy is received to reduce hematocrit. For high-risk MPNs,
Cytoreductive treatment may be an option to reduce blood counts.

- Despite prevention, some people still get blood clots. Medication called anticoagulants is the main treatment for blood clots. Some people get a procedure called plateletpheresis that removes platelets from the blood.
- You will need to meet with your doctor often. During visits, the status of the MPN and the results of treatment will be checked.
- If the MPN is getting worse, your treatment may be changed. The next treatment will depend on the current risk level of the MPN, your prior treatment, and if the MPN progressed.

“ As someone with ET, and who is otherwise perfectly healthy I don’t relate to the condition as a cancer. I find that particularly unhelpful for my state of mind as it stigmatizes the situation. Given that the condition is (presently) incurable, your state of mind can serve as your most powerful tool to assist living as normal a life as possible. I think if you can be successful in quieting the negative or retrograde thought and focus on living a healthy life then the unpleasant things, like being on daily medication and the various side effects, are much easier to cope with. So in summary, be as positive as you can, focus on eating healthy and exercising regularly, and follow the advice of your specialist. Also, surround yourself with positive people.”

– Ross
Living with ET
5
Myelofibrosis

44 Predicting prognosis
46 Initial treatment
50 MPN checkups
52 Advanced myelofibrosis and AML
54 Key points
Myelofibrosis greatly varies between people. It is almost hidden in some people but rapidly progresses in others. New treatments are discussed in this chapter and more are likely to be approved in the near future.

Myelofibrosis is a blood cancer that causes scarring of the bone marrow. It can occur in people with or without a history of an myeloproliferative neoplasm (MPN). If myelofibrosis is the first MPN, it is called primary myelofibrosis (PMF). It can also occur when polycythemia vera (PV) or essential thrombocythemia (ET) progresses. In these cases, it is called secondary myelofibrosis.

Myelofibrosis greatly differs between people. No two people are alike. It differs in terms of its course, speed of progression, and symptoms.

Treatment is partly based on how aggressive the myelofibrosis is predicted to be. Myelofibrosis slowly progresses in many people. It can be stable for many years. For others, the MPN is more active. The first step of treatment planning is to assess the prognosis.

### Predicting prognosis

Doctors use risk stratification systems to assess the prognosis of myelofibrosis. NCCN experts prefer the MIPPS-70 and MIPSS-70 Plus Version 2.0 for PMF. Other scoring systems are the DIPSS and DIPSS-Plus. The system used for post-PV and post-ET myelofibrosis is the MYSEC-PM. These systems are described in Guide 7.

Clinical information is important for assessing prognosis. In fact, the DIPSS only uses clinical information. It asks about a person’s age, constitutional symptoms, high white blood cell counts, low hemoglobin, and blasts in the bloodstream. Other systems require some of the same information but have other questions as well. They ask about low platelet counts, need for transfusion, or a high fibrosis grade.

Newer risk systems include biomarker test results of genetic abnormalities. The DIPSS-Plus asks about karyotype—a test of chromosomes. The MIPPS-70 and MYSEC-PM ask about molecular test results. Survival is likely longer or shorter depending on the gene mutation. Higher-risk mutations include ASXL1, EZH2, SRSF2, U2AF1 Q157, or IDH1/2. The MIPSS-70 Plus Version 2 requires both karyotype and molecular results.

Points are given for each response that conveys a risk of poor outcomes. Based on the total number of points, people are assigned a risk level. The number of risk levels does not match across systems. Some systems have 3 risk levels while others have 4 or 5 risk levels. NCCN experts divide the total points into two risk groups—lower and higher—to plan treatment.
### Guide 7
Risk systems to assess prognosis of myelofibrosis

<table>
<thead>
<tr>
<th>System</th>
<th>What is this system?</th>
<th>NCCN risk level</th>
</tr>
</thead>
</table>
| **MIPSS-70**         | MIPSS-70 is used to predict survival among people aged 70 years or under. It consists of 10 questions about symptoms, blood work, and molecular testing. The scale identifies people at low, intermediate, or high risk of shorter survival. | • Lower risk is a score of 3 or below  
                          • Higher risk is a score of 4 or above                                                                                                                  |
|                      | Online version: mipss70score.it                                                                                                                                                                                      |------------------------------------------------------------------------------------------------------|
| **MIPSS70-plus version 2.0** | MIPSS70-plus version 2.0 includes 2 questions on cytogenetics in addition to the 10 questions on the MIPSS-70. The scale identifies people at very low, low, intermediate, high, or very high risk based on shorter survival. | • Lower risk is a score of 3 or below  
                          • Higher risk is a score of 4 or above                                                                                                                  |
|                      | Online version: mipss70score.it                                                                                                                                                                                      |------------------------------------------------------------------------------------------------------|
| **DIPSS**            | DIPSS is used to predict survival of people at any age. It consists of 5 questions about age, symptoms, and results of blood work. The scale identifies people at low, intermediate-1 (INT-1), intermediate-2 (INT-2), or high risk of shorter survival. | • Lower risk is a score of 1 or 0  
                          • Higher risk is a score of 2 or above                                                                                                                  |
|                      | Online version: qxmd.com/calculate/calculator_187/dipss-prognosis-in-myelofibrosis                                                                                                                                    |------------------------------------------------------------------------------------------------------|
| **DIPSS-PLUS**       | DIPSS-PLUS further refines the DIPSS. It has 3 additional questions about karyotype, platelet count, and need for transfusion. The scale identifies people at low, intermediate-1 (INT-1), intermediate-2 (INT-2), or high risk of shorter survival. | • Lower risk is a score of 1 or 0  
                          • Higher risk is a score of 2 or above                                                                                                                  |
|                      | Online version: qxmd.com/calculate/calculator_315/dipss-plus-score-for-prognosis-in-myelofibrosis                                                                                                                     |------------------------------------------------------------------------------------------------------|
| **MYSEC-PM**         | MYSEC-PM is used to predict survival of people with post-PV or post-ET myelofibrosis. It consists of 6 questions about age, symptoms, blood work, and molecular testing. The scale identifies people at low, intermediate-1 (INT-1), intermediate-2 (INT-2), or high risk of shorter survival. | • Lower risk is a score of 13 or below  
                          • Higher risk is a score of 14 or above                                                                                                                  |
|                      | Online version: mysec-pm.eu                                                                                                                                                                                         |------------------------------------------------------------------------------------------------------|
Initial treatment

Treatment planning is based on prognosis but also on other information. Your symptoms will be tracked. Your doctor will assess the size of your spleen during exams. Blood cell and blast counts will be monitored. Based on this information, the goals of your treatment may include:

- Relieve symptoms
- Improve blood counts
- Prevent or delay progression to advanced myelofibrosis or leukemia

Lower-risk myelofibrosis is likely to be stable or slowly progress. If needed, symptoms are treated. Today, there is no approved treatment of lower-risk myelofibrosis. Enrolling in a clinical trial of treatment is recommended.

Allogeneic transplant is rarely done to treat low-risk myelofibrosis. It may be an option if platelets are low or the cancer cells have complex cytogenetics. A complex karyotype is when there are 3 or more unrelated defects in chromosomes that occur in 2 or more cells.

High-risk myelofibrosis progresses at a faster rate. Since it's a more aggressive cancer, more aggressive treatments are used. An evaluation for allogeneic transplant is recommended for everyone since it is the only chance for a cure. Other options are JAK inhibitors and clinical trials.

See Guide 8 for treatment options for lower- and higher-risk myelofibrosis.

---

Guide 8
Treatment options for myelofibrosis

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Clinical status</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| Lower risk | You do not have symptoms | • Watch and wait  
| | | • Clinical trial |
| | You do have symptoms | • Clinical trial  
| | | • Sometimes useful: Ruxolitinib, peginterferon alfa-2a, or hydroxyurea |
| Higher risk | Your number of platelets falls within the low to high range (50,000 or higher) | • Allogeneic transplant  
| | | • Ruxolitinib, fedratinib, or a clinical trial  
| | | • Anemia management |
| | You have a very low number of platelets (below 50,000) | • Allogeneic transplant  
| | | • Clinical trial  
| | | • Pacritinib  
| | | • Treatment based on symptoms |
Watch and wait
People with lower-risk myelofibrosis that isn't causing symptoms may start “watch and wait.” Also called observation or watchful waiting, it is a period of testing to assess for changes in MPN status. Treatment may be started if symptoms appear.

Cytoreductive therapy
Cytoreductive therapy is an option for low-risk myelofibrosis that is causing symptoms. The therapies used for myelofibrosis are peginterferon alfa-2a or hydroxyurea. More information on these therapies is in Chapter 4.

Allogeneic transplant
A hematopoietic stem cell is a cell that develops into every type of blood cell. In myelofibrosis, hematopoietic stem cells (also called blood stem cells) and bone marrow are diseased. An allogeneic hematopoietic stem cell transplant forms new, healthy bone marrow that makes healthy blood cells. It extends life and may cure myelofibrosis.

An allogeneic transplant is not safe for everyone. It is an intense treatment, so many people aren’t able to get it. The benefits of a transplant may be worth the risks for high-risk PMF that has high-risk mutations, such as ASXL1, EZH2, and RAS.

Once you are diagnosed with high-risk myelofibrosis, you will be referred to a transplant specialist. This specialist will assess if you are able to have a transplant. An allogeneic transplant uses healthy stem cells from a donor. The specialist will also assess donor options.

There are several steps to receiving an allogeneic transplant. You may stay on cytoreductive treatment to reduce spleen size and improve symptoms until you get a transplant.

Step 1 – Your blood will be tested for cell proteins called human leukocyte antigens (HLAs). HLAs mark your cells so your body knows which cells are yours. A donor’s HLAs must be a near-perfect match to yours for a transplant to work. Otherwise, your body will reject the donor stem cells or the donor cells will attack your body. Even with a near-perfect match, donor cells may attack your body. This is called graft-versus-host disease (GVHD).

Step 2 – You’ll receive treatment called conditioning to kill your bone marrow cells. Conditioning creates room for the healthy stem cells. It also weakens the immune system so your body does not kill the donor cells. Conditioning usually involves chemotherapy. Radiation therapy is sometimes used by itself or with chemotherapy.

Step 3 – Next, you’ll receive the donor cells through a transfusion. A transfusion is a slow injection of blood products into a vein. The donor cells will travel to your bone marrow and grow. They will also attack cancer cells that weren’t killed by prior treatment. New, healthy blood cells will form over the next 2 to 4 weeks. This is called engraftment.

Step 4 – You’ll have to be extra careful to avoid germs for the first few weeks after the transplant. That’s because your infection-fighting immune system will be almost gone. You may stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. You may receive medicine
called immunosuppressants to prevent GVHD. While waiting for the cells to engraft, you will likely feel tired and weak.

To learn more about GVHD, read the NCCN Guidelines for Patients: Graft-Versus-Host Disease at NCCN.org/patientguidelines.

JAK inhibitors
JAK is a cell protein that helps cells grow. It is key to blood stem cells developing into mature blood cells. JAK is overactive in people with myelofibrosis whether there is a JAK mutation or not.

JAK inhibitors stop JAK and reduce the number of new blood cells being made. They also shrink enlarged spleens and reduce core symptoms. The 3 JAK inhibitors for myelofibrosis are:

- Ruxolitinib (Jakafi)
- Fedratinib (INREBIC)
- Pacritinib (Vonjo)

Ruxolitinib is sometimes used to relieve symptoms of low-risk myelofibrosis. For high-risk myelofibrosis, JAK inhibitors may be used when an allogeneic transplant can’t be done. Ruxolitinib and fedratinib are options when your platelet count is greater than 50,000. Pacritinib is an option when your platelet count is less than 50,000.

JAK inhibitors are a pill that is taken at home. Your doctor will determine which dose is right for you and adjust as needed. Don’t stop taking the JAK inhibitor unless your doctor directs you to do so.

JAK inhibitors can cause large decreases in platelet and red blood cell counts. Counts can be increased by adjusting the dose or with transfusions. Fedratinib and pacritinib may cause diarrhea and nausea, which can be controlled with medicines. When on ruxolitinib, you are more likely to get infections, so it’s important to get prescribed vaccines. People taking fedratinib may get encephalopathy if their thiamine (vitamin B1) level is low.

Anemia treatment
Anemia is a term for low levels of hemoglobin. It may cause you to feel tired and cold or look pale. These symptoms are caused by cells not getting enough oxygen.

For high-risk myelofibrosis, treatment for anemia may be the main type of care you will receive. It is an option if you can’t have an allogeneic transplant.

Your doctor will first assess for causes of anemia other than myelofibrosis. All causes of anemia should be treated. You may need to take supplements to replace low iron, folate, or vitamin B12 levels.
Standard treatment of anemia that causes symptoms is a red blood cell transfusion. Most white blood cells should be removed from donated blood for a transfusion. This will help prevent the donated blood from attacking your body. It will also prevent you from getting a cytomegalovirus (CMV) infection.

Additional treatment options are based on erythropoietin (EPO) levels. EPO is a hormone made by the kidneys. It triggers the making of red blood cells in bone marrow.

- If EPO is lower than 500 mU/mL, treatment options include erythropoiesis-stimulating agents (darbepoetin alfa and epoetin alfa) and a clinical trial.
- If EPO is 500 mU/mL or higher, the preferred treatment option is a clinical trial. Luspatercept is currently being tested in clinical trials. Options that are sometimes useful include danazol, lenalidomide with or without short-term prednisone, and thalidomide with or without short-term prednisone.

Clinical trial
A clinical trial is an option for all risk groups. A clinical trial is a type of medical research study. It tests potential new ways of fighting cancer in people. Clinical trials can help answer these questions:

- Do treatments of high-risk myelofibrosis improve outcomes in lower-risk myelofibrosis?
- What are all the outcomes of an approved treatment? Does it extend survival? Does it reduce bone marrow fibrosis?

> Does a potential new treatment extend survival more than current treatments?
> Does a potential new treatment prevent or delay leukemia?

Don’t wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Finding a clinical trial

In the United States
NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide
The U.S. National Library of Medicine (NLM)
clinicaltrials.gov/

Need help finding a clinical trial?
NCI’s Cancer Information Service (CIS) 1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact
MPN checkups

After starting MPN treatment, you will need to meet with your MPN doctor often. NCCN experts advise having a visit every 3 to 6 months. You may need visits more often if problems arise.

Doctor visits

During visits, you will be asked about new or worsening symptoms and new diagnoses. You may be given a symptom survey called the MPN-10 to complete. Your doctor will perform a physical exam of your body. The size of your spleen and liver will be checked.

Blood work will be ordered. Your doctor will monitor your blood counts and other blood values. You may undergo a bone marrow biopsy and aspiration if symptoms worsen or there are signs of progression.

Treatment response

In research, there are standards for assessing results of medications. Know that your treatment may be working but may not match these standards. Your doctor will assess treatment results mostly based on whether or not symptoms are improving. The types of treatment responses used in research are listed in Guide 9.

Changing treatment

Your treatment will likely not change if symptoms improve and your blood counts are acceptable. Reasons to change treatment include little to no symptom relief or worsening symptoms. Also, worsening blood counts or signs of progression may trigger a change in treatment.

Treatment decisions may be guided by molecular testing. Testing may find new mutations since diagnosis. Next-generation sequencing (NGS) can detect higher-risk mutations, such as ASXL1, EZH2, and RAS. These mutations suggest that the myelofibrosis is likely to progress and a transplant may be needed.

If myelofibrosis worsens but doesn’t progress, the next treatment is based on current risk level and prior treatment. Ruxolitinib, peginterferon alfa-2a, or hydroxyurea may be given to improve symptoms of low-risk myelofibrosis. New anemia may be treated with medications that improve blood counts. If you have been on a JAK inhibitor, a different one may be started.

“I was diagnosed in 2009 with PV and then it migrated into myelofibrosis. It has greatly affected the way we live. I make frequent trips to my doctors and I’ve been in the emergency room in the middle of the night four times. So it’s changed my life greatly and my husband’s.”

– Jeri

Living with post-PV myelofibrosis
## Guide 9
### Treatment response in myelofibrosis

<table>
<thead>
<tr>
<th>Treatment response</th>
<th>What does this response mean?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>Complete remission is the best outcome. There are no signs of the MPN. Your bone marrow and blood results are normal or near normal. Your symptoms have cleared. Your liver and spleen are of normal size.</td>
</tr>
<tr>
<td>Partial remission</td>
<td>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 of normal size.</td>
</tr>
<tr>
<td>No response</td>
<td>No response is less than a partial remission.</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>Progressive disease is a worsening of the MPN.</td>
</tr>
<tr>
<td>Anemia response</td>
<td>Anemia response is an improvement in hemoglobin level or not needing transfusions anymore.</td>
</tr>
<tr>
<td>Spleen response</td>
<td>Spleen response is a major decrease in spleen size.</td>
</tr>
<tr>
<td>Symptom response</td>
<td>Symptom response is a major decrease in symptoms.</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>Clinical improvement is one or more responses described above and no signs of the MPN worsening.</td>
</tr>
<tr>
<td>Cytogenetic remission</td>
<td>Cytogenetic remission is defined by fewer or the absence of abnormal chromosomes.</td>
</tr>
<tr>
<td>Molecular remission</td>
<td>Molecular remission is defined by fewer or the absence of gene mutations. The quantity of mutation is called the allele burden.</td>
</tr>
</tbody>
</table>
Advanced myelofibrosis and AML

Myelofibrosis can progress to an accelerated phase or to AML. The marker of progression is a high percentage of immature blood cells, called myeloblasts, in bone marrow or the bloodstream. Myeloblasts (simply called blasts) are usually only in bone marrow.

Normally, the blast count in bone marrow is less than 5 percent. In the accelerated phase of myelofibrosis, the blast count is between 10 and 19 percent. The blast phase of myelofibrosis (also called post-MPN AML) has at least a 20 percent blast count. AML may be diagnosed with less than 20 percent blasts if chromosomes have certain abnormal changes.

Lab tests
To confirm progression, lab tests on bone marrow are needed. If bone marrow can’t be removed, blood samples may be used. You may know some of the lab tests used for progression as they are used for MPN diagnosis (see Chapter 2):

- Cytogenetics using karyotype with or without fluorescence in situ hybridization (FISH)
- Flow cytometry
- Molecular testing of mutations related to AML

Treatment planning
Right after progression is confirmed, you and your doctor will discuss treatment. Treatment may include chemotherapy or chemotherapy followed by an allogeneic stem cell transplant. If a transplant is an option, you will be referred to a transplant specialist.

The transplant specialist will assess if you are able to have an allogeneic transplant. This transplant is not safe for everyone. It is an intense treatment, so many people aren’t able to get it. An allogeneic transplant uses healthy stem cells from a donor. The specialist will also assess donor options.

Clinical trial
Whether or not you will get a transplant, NCCN experts recommend clinical trials. A clinical trial is a type of medical research study. It tests potential new ways of fighting cancer in people. Ask your treatment team if there is an open clinical trial that is a good fit for you.

Low-dose chemotherapy
When a transplant isn’t an option, you may be treated with low-dose chemotherapy. One type of low-dose chemotherapy is hypomethylating agents, such as azacitidine and decitabine. A JAK inhibitor may also be part of your treatment. Learn about other low-intensity chemotherapy options in NCCN Guidelines for Patients: Acute Myeloid Leukemia, available at NCCN.org/patientguidelines.
Common questions about clinical trials

What are 4 phases of clinical trials? Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.

- **Phase II trials** study how well the drug or approach works against a specific type of cancer.

- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the U.S. Food and Drug Administration (FDA).

- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll? Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

What is informed consent? Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Will I get a placebo? Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free? There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs of this care that are not covered by your insurance.
**Induction therapy**
Some people who are well enough are treated with induction therapy. The goal of induction therapy is to rid the marrow of blasts. Chemotherapy used to treat AML is often used for induction.

**Allogeneic transplant**
If you’re already taking a JAK inhibitor, it may be continued to reduce spleen size and improve symptoms until you get a transplant.

For advanced cancers, the first step of care is to receive induction therapy before a transplant. Transplants are more successful when induction therapy has good results.

Instead of induction, some people take a hypomethylating agent with or without a JAK inhibitor. There is little data on use of fedratinib or pacritinib in combination with a hypomethylating agent.

There are several steps to receiving an allogeneic transplant. These steps are described in this chapter in the section called *Initial treatment*.

**Key points**

» Myelofibrosis is a blood cancer that results in scarring of the bone marrow. It greatly differs between people. No two people are alike.

» The first step of treatment planning is to assess the prognosis. Doctors use risk stratification systems to assess the prognosis of myelofibrosis. NCCN recommendations for treatment are based on two risk levels—low and high.

» Watch and wait is an option for low-risk myelofibrosis that isn’t causing symptoms. If you have symptoms, they may be treated with ruxolitinib, peginterferon alfa-2a, or hydroxyurea. Another option for low-risk myelofibrosis may be a clinical trial.

» Treatment for high-risk myelofibrosis is based on whether you can undergo an allogeneic stem cell transplant. A transplant has high risks, so many people cannot receive it. If a transplant isn’t an option, you may start taking a JAK inhibitor or receive treatment for anemia. Enrolling in a clinical trial may be another option for high-risk myelofibrosis.

» You will need to meet with your doctor often. During visits, the status of the cancer will be checked as well as how you feel.

» For accelerated-stage myelofibrosis or AML, a clinical trial is an option. Other options include chemotherapy, which can vary in intensity. Chemotherapy may be followed by an allogeneic transplant for some people.
6 Supportive care for symptoms

56 Bleeding
57 Blood clots
57 Bone pain
57 Headaches and tinnitus
58 Infections
58 Itching
58 Iron overload
59 Tumor lysis syndrome
59 Key points
Supportive care aims to improve your quality of life. It is sometimes called palliative care. It is a key part of treatment for everyone, not just people at the end of life. This chapter discusses some of the supportive needs of people with myeloproliferative neoplasms.

Supportive care is very important for myeloproliferative neoplasms (MPNs). It can address many needs. It includes care for health issues caused by MPN or its treatment. You can get help with making treatment decisions. You can get help with coordination of care between health providers. Talk with your treatment team to get the best supportive care for you.

Bleeding

People with MPNs are at increased risk for bleeding. Also called hemorrhaging, bleeding is often mild and occurs when platelet counts are high or low. Bleeding occurs most often in myelofibrosis compared to polycythemia vera (PV) and essential thrombocythemia (ET). It can be severe, especially in people who have anemia or low platelets.

Causes of bleeding

Normally, bleeding is stopped when cells called platelets plug the hole in blood vessels with help from clotting factors. A lot of bleeding may occur when the blood doesn’t clot properly.

There are several causes of bleeding in PV and ET:

- Platelets may not work correctly.
- The number of platelets may be very high. High levels of platelets may lower a clotting factor called von Willebrand.
- Prevention of blood clots with aspirin may thin the blood too much.
- Prevention of blood clots with antiplatelet or cytoreductive therapy may reduce blood counts to very low levels.
- Treating blood clots with anticoagulants may slow down clotting time too much.

The cause of bleeding is simpler in myelofibrosis. Bleeding is caused by a low number of platelets.

Bleeding events differ between people. Some people bruise easily while others get nose bleeds. Menstrual periods may be heavier than normal. Bleeding may occur in your digestive tract. You may see blood in your urine.

von Willebrand disease

Low levels of von Willebrand factor due to high platelet counts is called acquired von Willebrand disease (aVWD). Your doctor may test for aVWD or other diseases if you have:

- Unexplained bleeding
- Increased platelets, especially over 1 million
- An enlarged spleen
- A surgery scheduled that may cause major bleeding
To assess for aVWD or other clotting problems, your doctor will order clotting (coagulation) tests. There are 3 common tests:

- **Prothrombin time** is how long it takes for your blood to clot. It measures how well all clotting factors work together.
- **Partial thromboplastin time** is how long it takes for your blood to clot. It measures clotting factors from two of three pathways.
- **Fibrinogen activity** is a measure of how well a blood protein called fibrinogen is working.

**Treatment in myelofibrosis**

You may receive a platelet transfusion to prevent bleeding if your platelet count is lower than 10,000 m$^3$. Platelet transfusions are also used for treatment of bleeding. 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 infected with cytomegalovirus (CMV).

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

**Treatment in PV and ET**

Your MPN doctor will identify and treat all causes of bleeding. Aspirin will be stopped until the platelet count is normal. Treatment to reduce platelet counts may be given. If you have ET, you may receive plateletpheresis if bleeding is severe but this is rare.

**Blood clots**

The frequency of blood clots in people with myelofibrosis may be similar to those with ET. Treatment of blood clots in myelofibrosis follows what is done for other MPNs. It may consist of anticoagulants and antiplatelet medicines. Read *Treating blood clots* in Chapter 4 to learn more about these treatments. Also, like the other MPNs, decreasing cardiovascular risk factors and taking aspirin may help prevent blood clots in people with myelofibrosis.

**Bone pain**

Your MPN doctor will perform an evaluation to assess if your pain is caused by the MPN. This is needed because treatment of MPN-related bone pain differs from treatment of joint pain.

In one MPN study, ruxolitinib stabilized bone and muscle pain. For some people, loratadine and non-steroidal anti-inflammatory drugs (NSAIDs) may provide relief. A low dose of radiation may provide short-term relief of bone pain.

**Headaches and tinnitus**

You may have a blood clot if you start to have headaches. Also, sounds made the body and not heard by others (tinnitus), such as high-pitch ringing, may be a symptom of a blood clot. Tell your MPN doctor if you have these symptoms.

Headaches as well as other vascular symptoms may be relieved with low-dose aspirin. If symptoms persist, taking aspirin...
twice a day or taking an antiplatelet agent (clopidogrel) may have better results. Aspirin may be taken with an antiplatelet agent. Taking an NSAID with aspirin should be done with caution.

There are several options in addition to aspirin. Headaches in people with PV may be relieved with phlebotomy or ruxolitinib. For all MPNs, cytoreduction therapy reduces headaches and other vascular symptoms. Migraine headaches may be prevented as well as treated with triptans or topiramate.

Infections

You may be prone to infections because of myelofibrosis or its treatment. Ask your doctor which vaccinations are safe for you. Your doctor may prescribe the recombinant (killed) zoster vaccine if taking ruxolitinib or fedratinib. COVID vaccinations are also recommended for all people with an MPN.

Learn more at NCCN.org/covid-19.

If you get infections often, your doctor may prescribe antibiotics for prevention. Instead of antibiotics, you may receive granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) if you have low neutrophil counts. These medicines should be used with caution because, though rare, enlarged spleens may rupture.

Itching

Itching (pruritus) is a common problem among people with MPNs. The first approach to relieve itching is to practice sensitive skin care. This care includes taking short showers, using mild soap, and moisturizing your skin. Antihistamines (cetirizine, diphenhydramine) and topical steroids may also be helpful.

If needed, the next step to relieve itching will be based on the benefits and downsides of treatments. Ruxolitinib relieves itching. Early research on selective serotonin reuptake inhibitors (SSRIs) shows promise. Other options include peginterferon alfa-2a, gabapentin, aprepitant, and immunosuppressant agents, such as cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or dupilumab.

Iron overload

Iron overload is a term for 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 lower-risk myelofibrosis. Your doctor may prescribe iron chelation if you’ve had more than
Tumor lysis syndrome

Tumor lysis syndrome (TLS) occurs when the waste released by dead cells is not quickly cleared out of the body. The waste can cause kidney damage and severe blood electrolyte disturbances. TLS can be life-threatening.

Induction chemotherapy may cause TLS. Induction chemotherapy is a treatment for advanced myelofibrosis or acute myeloid leukemia (AML). This treatment kills many cancer cells and results in too much waste too quickly.

TLS may be prevented by high amounts of fluids during chemotherapy. Fluids may help clear out the cell waste. Decreasing uric acid levels with allopurinol or rasburicase is another option. Rasburicase may be given as the first treatment if you have high uric acid or if it’s affecting your kidneys.

Key points

- Supportive care is an important part of your MPN care.
- Bleeding may occur in people with an MPN due to the MPN or treatment. Your blood may be tested if your doctor suspects clotting problems. Treatment options vary between MPN types to target the cause of bleeding.
- Blood clots are a focus of treatment for PV and ET, but also occur in people with myelofibrosis. They are treated with anticoagulants and antiplatelet medicines and can be prevented by taking care of your cardiovascular health.
- Treatment of bone pain includes ruxolitinib, loratadine, NSAIDs, and low-dose radiation.
- Aspirin relieves headaches as well as other vascular symptoms of MPN. Other options include other antiplatelet agents, phlebotomy and ruxolitinib (for PV), and cyto reduction therapy. Triptans or topiramate help prevent and treat migraines.
- Vaccinations may be your best defense against infections. If you're at risk for infections, your doctor may prescribe antibiotics or growth factors to prevent illness.
- Itching is a common problem. Take care of your skin by taking short showers, using mild soap, and moisturizing your skin. Antihistamines and topical steroids may also be helpful. Talk to your doctor about other options if itching persists despite these methods.
- Iron chelation is a treatment for high levels of iron in the body.
- Induction chemotherapy may cause TLS because it kills many cells. Fluids to clear out cell waste may prevent TLS. Allopurinol and rasburicase are other treatment options.
7 Making treatment decisions

61 It’s your choice
63 Questions to ask your doctors
67 Resources
It is important to be comfortable with the MPN treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It’s your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like transplants or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported.

"I was diagnosed with ET 11 years ago when I was only 29. My hematologist had limited experience with patients at my young age, so I was referred to the Mayo Clinic. I’m so grateful he did this. I received excellent care and was sent home with a new treatment plan. The piece of advice I got from that doctor was ‘Don’t alter the plan of your life around this. People get hit by cars every day.’ I was newly married and hoping to have kids, so this advice was exactly what I needed to hear during this scary time. I continue to be in good health, take the low-dose aspirin every day, and visit my hematologist every 3 to 6 months. I went on to have 3 beautiful children.”

– Trisha

Living with ET
when considering options and making treatment decisions.

Second opinion
It is normal to want to start treatment as soon as possible. While the MPN should not be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it’s a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Get group support

Many people with an MPN find a lot of value in a support group. In support groups, you can ask questions and hear about the experiences of other people with MPN. Some people may be newly diagnosed, while others may be on a second treatment.

A support group can help with emotional and psychological needs. A support group can also be a good source of practical advice and helpful tips. People with common ground can share information on their experiences, financial and emotional burdens, coping strategies, and knowledge about research and treatments.

Ask your doctors or supportive care team about finding an MPN support community. Support groups can be found online and in-person groups are often available in larger communities.
Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment. Keep a notebook handy to record answers to your questions.

Questions to ask about testing

1. What tests will I have? Do I need a biopsy?
2. How do I prepare for testing?
3. What if I am pregnant or planning to get pregnant?
4. Where do I go to get tested? How long will the tests take and will any test hurt?
5. Should I bring someone with me? Should I bring a list of my medications?
6. How soon will I know the results and who will explain them to me?
7. Would you give me a copy of the pathology report and other test results?
8. What type of MPN do I have? Is this a fast- or slow-growing MPN? What are the possible complications? What are my chances that the MPN will become leukemia?
9. What are the symptoms and signs that the MPN may be changing?
10. Who will talk with me about the next steps? When?
Questions to ask about treatment options

1. What are the goals of treatment?

2. What are my treatment options? Does any option offer a cure? Are my chances any better for one option than another?

3. Are you suggesting options other than what NCCN recommends? If yes, why?

4. Do your suggested options include clinical trials? Please explain why.

5. What will happen if I do nothing?

6. What if I am pregnant or planning to get pregnant?

7. How might the recommended treatment interact with other medications that I am already taking? What are the short- and long-term side effects of treatment?

8. Who should I call if I have concerns or questions about my MPN treatment after I start taking it?

9. What supportive care services are available to me during and after treatment? What can be done to prevent or relieve the side effects of treatment?

10. What are my options if the MPN progresses?
Questions to ask about clinical trials

1. Is a clinical trial right for me?

2. What is the purpose of the study?

3. How many people will be in the clinical trial?

4. What are the tests and interventions for this study? How often will they take place?

5. Has the drug been used before? Has it been used for other types of cancers?

6. Will every participant in this trial receive the study drug?

7. What side effects can I expect? Can the side effects be controlled?

8. How long will I be in the clinical trial?

9. Will you know if the drug is working?

10. Will I be able to get other treatment if this treatment doesn’t work?

11. Who will help me understand the costs of the clinical trial?
Questions to ask about getting treated

1. Do I have a choice of when to begin treatment?

2. Does the treatment require traveling to a health center? How often will I have to go? How long is each visit?

3. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?

4. Should I bring someone with me when I get treated?

5. Will the treatment hurt?

6. What should I do if a side effect gets bad when my care center is closed?

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?
Resources

Visit these websites to learn more about MPNs, find support groups, and when you’re ready, help others living with an MPN.

**Leukemia & Lymphoma Society**
[LLS.org/PatientSupport](LLS.org/PatientSupport)

**MPN Cancer Connection**
[MPNCancerConnection.org](MPNCancerConnection.org)

**MPN Education Foundation**
[mpninfo.org](mpninfo.org)

**MPN Research Foundation**
[mpnresearchfoundation.org](mpnresearchfoundation.org)

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

**NCCN Patient Resources**
[NCCN.org/patientresources](NCCN.org/patientresources)

**PV Reporter**
[pvreporter.com](pvreporter.com)

**U.S. National Library of Medicine Clinical Trials Database**
[clinicaltrials.gov](clinicaltrials.gov)

---

“I wish my doctor had told me two things: first, that there were hematologists in my area that actually specialized in PV, and secondly, what resources there were out there to learn more about PV and then told me of resources to connect with others dealing with the same thing.”

– Carrie
Living with PV

---

**Take our survey**
And help make the NCCN Guidelines for Patients better for everyone!

[NCCN.org/patients/comments](NCCN.org/patients/comments)
Words to know

acral paresthesia
A burning feeling in the hands and feet.

acute myeloid leukemia (AML)
A blood cancer of young white blood cells called myeloblasts.

allogeneic hematopoietic stem cell transplant
A cancer treatment that replaces blood stem cells with donor stem cells, which in turn make a new, healthy bone marrow.

anemia
Low levels of healthy red blood cells that cannot provide enough oxygen to tissue.

anticoagulant
A treatment that slows down the clotting of blood.

artery
A blood vessel that moves blood away from the heart to the rest of the body.

BCR-ABL1
An abnormal gene that is the hallmark of chronic myeloid leukemia.

biomarker test
A lab test of a molecule in your body to assess your health.

blast
An early form of a blood cell that is unable to function like a mature blood cell.

blood clot
A gel-like clump of blood. Also called thrombus.

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

bone marrow
A soft, spongy material inside of bones where most 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.

chromosome
A long but tightly coiled structure within cells that contains coded instructions for cell behavior.

chronic myeloid leukemia (CML)
A blood cancer 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.

CMV
cytomegalovirus

coaigulation 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.

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

constitutional symptom
A physical condition that is a general effect of a disease.
Words to know

cytogenetics
The study of chromosomes using a microscope.

cytokine
A protein that boosts or activates the immune system.

cytoreductive therapy
A treatment that reduces the number of blood cells.
dacryocyte
A red blood cell that is shaped like a teardrop.
deevee thrombosis (DVT)
A blockage of blood flow within a vein deep under the skin.
dehoxyribonucleic acid (DNA)
A ladder-shaped chain of chemicals in cells that contains contain coded instructions for cell behavior. Also called the “blueprint of life.”
diabetes
A disease that causes high levels of blood sugar.
diagnosis
The identification of an illness based on tests.
differential
Measurement of the different types of white blood cells in a blood sample.
DIPSS
Dynamic International Prognostic Scoring System
dysuria
The feeling of pain during urination.
embolus
A blood clot that is not attached to a base and moves through the bloodstream.
erthrocyte
A type of blood cell that carries oxygen from the lungs to the rest of the body. Also called a red blood cell.
erthrocytosis
A high number of red blood cells.
erthromelalgia
A health condition that turns skin red and may cause painful, burning sensations.
erthropoiesis-stimulating agent
A drug that helps bone marrow to make more red blood cells.
erthropoietin (EPO)
A hormone made by the kidneys.
estential thrombocytopenia (ET)
A cancer of blood stem cells that make too many platelets. Also called essential thrombocytosis.
extramedullary hematopoiesis
The making of blood cells outside the bone marrow.
fatigue
A feeling of extreme tiredness, even with enough sleep, that limits a person’s functioning.
fibrosis
The scarring of supportive fibers in tissue.
fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal changes in a cell’s genes and chromosomes.
G-CSF
granulocyte colony-stimulating factor
gene
A set of coded instructions within cells that control cell behavior.
Words to know

**GM-CSF**
granulocyte-macrophage colony-stimulating factor

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

**granulocyte**
A type of white blood cell.

**hematocrit**
The percentage of red blood cells in blood.

**hematologist**
A doctor who’s an expert in diseases of the blood.

**hematopoietic stem cell**
A 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.

**hemorrhage**
Blood loss inside or on the outside of the body. Also called bleeding.

**hepatomegaly**
An abnormally large liver.

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

**hypercellularity**
A high number of cells.

**hypertension**
High blood pressure.

**IPSET-thrombosis**
International Prognostic Score of Thrombosis.

**iron**
A mineral needed to make new red blood cells.

**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.

**leukocyte**
A type of white blood cell.

**leukocytosis**
A high number of white blood cells.

**leukoerythroblastosis**
The presence of immature white blood cells and red blood cells with a nucleus in the bloodstream.

**leukopenia**
A low number of white blood cells.

**liver function tests (LFTs)**
Tests that measure chemicals made or processed by the liver.

**LMWH**
low-molecular-weight heparin

**lymphadenopathy**
One or more lymph nodes that are abnormally large.

**lymphoid cell**
A blood cell that is related to lymphocytes.

**MDS**
myelodysplastic syndromes

**medical history**
A report of all your health events and medications.

**megakaryocyte**
A bone marrow cell that makes blood-clotting platelets.
megakaryocytic hyperplasia
A high number of megakaryocytes in bone marrow.

MFSAF
Myelofibrosis Symptom Assessment Form

MIPPS
Mutation-Enhanced International Prognostic Score System

molecular genetic test
A lab test of an abnormal gene inside cells.

MPN-SAF
Myeloproliferative Neoplasm Symptom Assessment Form

MPN-SAF TSS
MPN Symptom Assessment Form Total Symptom Score

mutation
An abnormal set of coded instructions in cells (gene).

myeloid cell
A blood cell that is related to platelets, red blood cells, granulocytes, or monocytes.

myeloproliferative neoplasm (MPN)
A cancer of blood-forming cells that causes an excess of blood cells or bone marrow scarring.

MYSEC-PM
Myelofibrosis Secondary to PV and ET-Prognostic Model

neutrophilic hyperplasia
A high number of white blood cells called neutrophils.

NGS
next-generation sequencing

NOS
not otherwise specified

NSAID
non-steroidal anti-inflammatory drug

paresthesia
A burning or prickling sensation in the body.

partial remission
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.

peripheral smear
The study of a drop of blood using a microscope.

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.

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

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

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

prePMF
Prefibrotic primary myelofibrosis.
**Words to know**

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

**prognosis**
The likely course and outcome of a disease based on tests.

**progression**
A worsening of cancer.

**pruritus**
Itchy skin.

**pulmonary embolism**
A blockage of an artery in a lung by a blood clot that formed in a deep vein.

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

**reverse transcription polymerase chain reaction (RT-PCR)**
A lab test that detects a cancer marker even if it’s in a few cells.

**risk stratification**
An assessment of the likelihood of an event based on proven predictors.

**satiety**
A feeling of fullness from eating.

**SM-AHN**
Systemic mastocytosis with an associated hematologic neoplasm

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

**splenomegaly**
An abnormally large spleen.

**SSRI**
Selective serotonin reuptake inhibitor

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

**thrombosis**
A blockage of blood flow in blood vessels caused by a blood clot.

**tinnitus**
Sounds that are produced by the body and not heard by others, such as high-pitched ringing.

**tumor lysis syndrome (TLS)**
A health condition caused by the rapid death of many cancer cells.

**uric acid**
A chemical that is in most cells.

**vein**
A blood vessel that moves blood back to the heart.

**venous thromboembolism (VTE)**
A blood clot that formed in a deep vein and may now be stuck in a lung artery.

**von Willebrand disease (VWD)**
A blood disorder that causes blood not to clot.
This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms, Version 1.2022. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS  
Senior Director  
Patient Information Operations

Laura J. Hanisch, PsyD  
Patient Information Program Manager  
Patient Information Operations

Susan Kidney  
Senior Graphic Design Specialist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms, Version 1.2022 were developed by the following NCCN Panel Members:

*Aaron T. Gerds, MD, MS/Chair  
Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

*Tracy I. George, MD  
Huntsman Cancer Institute at the University of Utah

Animesh Pardanani, MBBS, PhD  
Mayo Clinic Cancer Center

Brady L. Stein, MD, MHS  
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

*Elizabeth Hexner, MD  
Abramson Cancer Center at the University of Pennsylvania

*Gabriela S. Hobbs, MD  
Massachusetts General Hospital Cancer Center

*Ken P. Johnson, MD  
Massachusetts General Hospital Cancer Center

Krishna Gundabolu, MBBS  
Fred & Pamela Buffett Cancer Center

Mary Anne Bergman  
Guidelines Coordinator

Laura J. Hanisch, PsyD  
Patient Information Program Manager  
Patient Information Operations

Sanjay R. Mohan, MD  
Vanderbilt-Ingram Cancer Center

Brady L. Stein, MD, MHS  
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Amro Elshoury, MD  
Roswell Park Comprehensive Cancer Center

* reviewed this patient guide. For disclosures, visit NCCN.org/disclosures.
Index

acute myeloid leukemia (AML) 9, 11, 41, 52, 54, 59, 69

allogeneic hemopoietic stem cell transplant 46–48, 50, 52, 54, 69

anemia 11, 41, 48, 50, 54, 56, 59, 69

anticoagulant 33, 35–37, 69

aspirin 30, 32–33, 36–37, 39, 56–58, 61

bone marrow aspiration 16, 39, 50, 69

bone marrow biopsy 16, 20, 39, 41, 50, 63, 69

CALR mutation 15, 17, 19–22

chemotherapy 47, 52, 54, 59, 61

chronic myeloid leukemia (CML) 8, 15, 17, 69

clinical trial 40, 46, 49, 52–54, 65, 69

coagulation 57, 69

complete blood count (CBC) 15–16, 69

cytopreductive therapy 30, 33, 38–42, 47, 56, 70

essential thrombocythemia (ET) 8–9, 11–12, 14, 17–20, 24–26, 29–30, 32–35, 38, 40–42, 44–45, 56–57, 59, 61, 70, 72

human leukocyte antigen (HLA) 71

JAK inhibitor 40, 52, 54

JAK mutation 48

medical history 14, 71

MPL mutation 15, 17, 19–22

myelodysplastic syndromes (MDS) 9, 20, 22

MPN-10 23, 25–27, 38, 50

NCCN Cancer Centers 75

NCCN Contributors 74

phlebotomy 34, 41, 58, 59, 72

plateletpheresis 36, 42, 57, 72


post-ET myelofibrosis 9, 25, 34, 41, 44–45, 72

post-PV myelofibrosis 9, 41, 44–45, 50, 72

primary myelofibrosis (PMF) 8–9, 12, 14, 17–18, 20–22, 44, 47, 72

second opinion 62

shared decision–making 61

supportive care 56, 62, 64, 73

triple negative 20, 22

von Willebrand disease (VWD) 32, 73

watch and wait 46–47, 49, 54
Myeloproliferative Neoplasms

2022

NCCN Foundation gratefully acknowledges our advocacy supporter MPN Research Foundation and the following corporate supporters for helping to make available these NCCN Guidelines for Patients: AbbVie, Bristol Myers Squibb, and Incyte Corporation. NCCN independently adapts, updates, and hosts the NCCN Guidelines for Patients. Our corporate supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.

To support the NCCN Guidelines for Patients

DONATE NOW

Visit NCCNFoundation.org/Donate

NCCN.org/patients – For Patients | NCCN.org – For Clinicians