Dr Shivam Shingla

Consultant Medical Oncologist
MBBS, MD, DNB Medical Oncology
MNAMS MRCP UK (SCE)
Lung Cancer Fellowship From
Zurich Switzerland

www.drshivamshingla.com

+91 98925 96286

drshivamshingla@gmail.com

#Reference From NCCN Guidelines

Contents

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) and NCCN Foundation
3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462 USA

1
CML basics

Chronic myeloid leukemia (CML) is caused by a single, specific abnormal gene that is created when a piece of chromosome 9 and a piece of chromosome 22 break off and trade places. The result is a fused gene called *BCR::ABL1* and a shortened chromosome 22 called the Philadelphia chromosome. If you do not have the Philadelphia chromosome or the *BCR::ABL1* gene, you do not have CML.

Blood

Chronic myeloid leukemia (CML) is a type of blood cancer. Blood is a tissue. A tissue is a group of cells that work together to perform a function. Blood's function is to move oxygen and nutrients throughout your body and carry away waste. Blood also plays an important role for the immune system and in preventing bleeding.

Blood cells

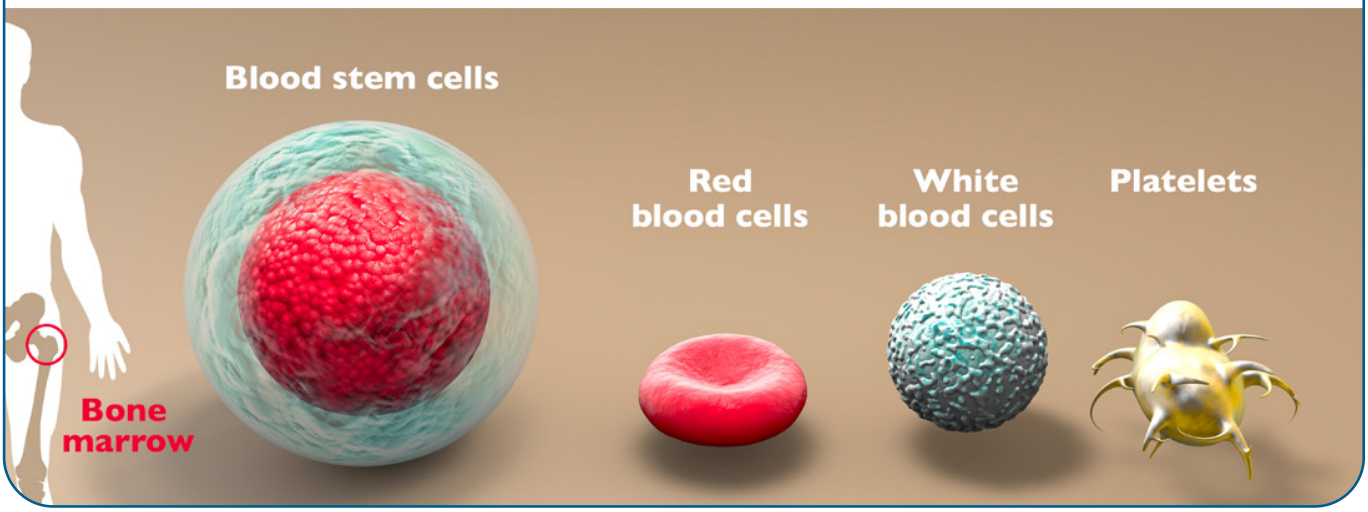
Your blood contains different types of cells that float in plasma. Plasma is a clear, yellowish fluid made up of mostly water. More than half of your blood is plasma.

There are 3 types of blood cells:

- Red blood cells (erythrocytes)
- White blood cells (leukocytes), which include granulocytes, monocytes, and lymphocytes
- Platelets (thrombocytes)

Blood stem cells

Bone marrow contains stem cells. A blood stem cell is an immature cell that can develop into a red blood cell, white blood cell, or platelet.



Blood cells have important jobs. Red blood cells (RBCs) carry oxygen throughout the body. White blood cells (WBCs) fight infections. Platelets (PLTs) help control bleeding.

Blood cells are being replaced in your body all the time. Many have a short lifespan. Some white blood cells live for less than one day. Your body makes one million red blood cells every second!

How blood cells are formed

Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are early blood-forming cells called blood (hematopoietic) stem cells. All types of blood cells are created from blood stem cells. At any given time, the bone marrow will have cells in various stages of development, from very immature to almost fully mature. This process is called differentiation. After a blood stem cell develops into a red blood cell, white blood cell, or platelet, it is released into your bloodstream as needed.

Blood stem cells can copy themselves or "self-renew." These cells are rare. The role of blood stem cells is to make cells that will become red blood cells, white blood cells, and platelets. These are called progenitor cells or precursor cells.

There are different types of progenitor cells:

- Lymphoid progenitor cells form into lymphoblasts that mature into lymphocytes
- Myeloid progenitor cells from into myeloblasts and other non-lymphoid blood cells

CML is thought to arise from myeloid progenitor cells. However, an advanced form of CML, called blast phase CML, can arise in either lymphoid or myeloid progenitor cells. The type of cell will affect treatment.

Chronic myeloid leukemia

Chronic myeloid leukemia (CML) is a type of myeloproliferative neoplasm (MPN). MPNs are a group of blood cancers that start in the myeloid progenitor cells. A neoplasm is any abnormal growth and typically refers to cancer. MPNs produce too many blood cells, making it difficult for blood to do its work. Usually in CML, there are too many white blood cells (granulocytes). Sometimes, there are too few or too many platelets, as well.

Granulocytes include:

- Neutrophils
- Eosinophils
- Basophils

Neutrophils appear in large numbers in CML. Basophil and eosinophil counts can also be high, and sometimes platelets will also be high. In some, the number of granulocytes is normal but the platelet count is high. “Chronic” means this cancer worsens slowly. The average age at diagnosis is about 65 years of age. However, CML occurs in all age groups.

The cause of CML can be traced to a single, specific abnormal gene (*BCR::ABL1*), which results from a fusion between parts of chromosomes 22 and 9 known as Philadelphia chromosome. Philadelphia chromosome is the hallmark of CML.

Philadelphia chromosome

All cells in our body contain genetic information organized into chromosomes. Most cells have 23 pairs of chromosomes. A cell must make a copy of its chromosomes before dividing into two cells. Sometimes, there are mistakes in the copies. One type of mistake happens when parts of two chromosomes break off and switch with each other. This is called a chromosome translocation. It can result in a fusion gene such as the *BCR::ABL1* gene found in CML. Genes tell cells what to become and what to do.

When a piece of chromosome 9 and a piece of chromosome 22 break off and switch places, it creates a new, abnormal chromosome 22 that contains a small part of chromosome 9. This new chromosome is referred to as the Philadelphia chromosome (Ph).

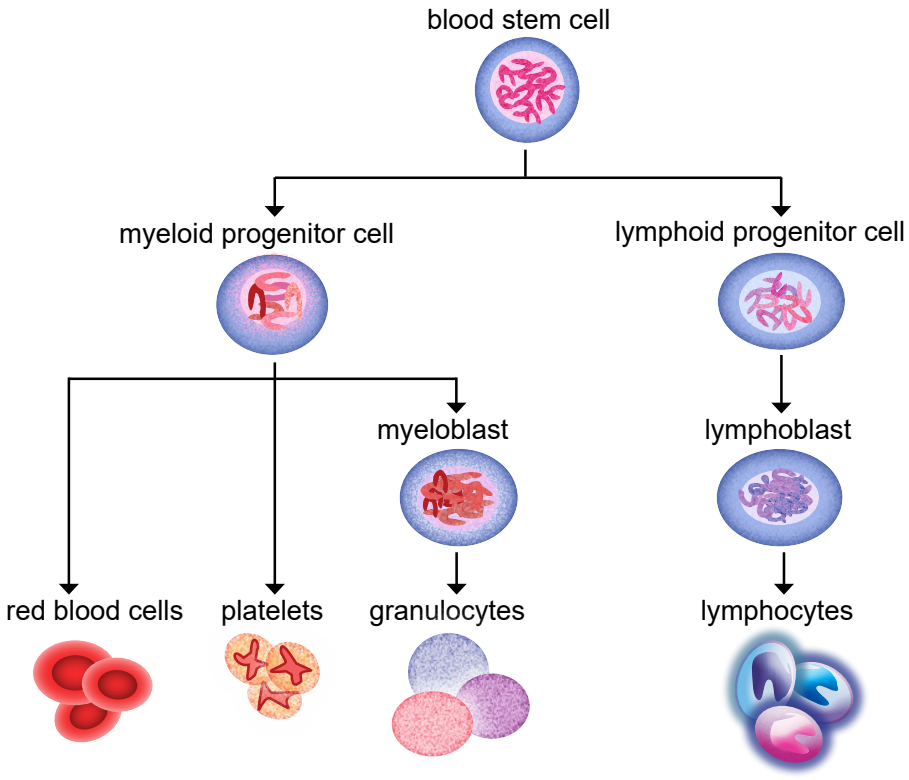
BCR::ABL1

Chromosomes have many genes. One piece of chromosome 9 contains a gene called *ABL1.* One piece of chromosome 22 contains a gene called *BCR*. When these genes fuse together on chromosome 22, a new *BCR::ABL1* gene is formed. This translocation is also shown as t(9;22). *BCR::ABL1* is not found in normal blood cells. It is not passed down from parents to children.

BCR::ABL1 makes a new protein that leads to uncontrolled cell growth. Treatment for CML aims to stop the activity of the BCR::ABL1 protein. Genes are italicized and are written like this: *BCR::ABL1*. Proteins are not italicized and are written like this: BCR::ABL1.

Blood cell formation

All blood cells start as blood stem cells. A blood stem cell has to go through many stages to become a red blood cell, white blood cell, or platelet. CML affects the myeloid progenitor cells and causes too many granulocytes (a type of white blood cell). However, advanced CML can affect the lymphoid progenitor cells.



Three phases of CML

CML can have three phases. Most people are diagnosed in the chronic phase, but a small number can be diagnosed in accelerated or blast phase.

The 3 phases of CML are:

- Chronic
- Accelerated
- Blast

Phases are based on the percentage of immature white blood cells (blasts) found in the blood and bone marrow. Normal bone marrow contains 5 percent (5%) blasts. This means that it is normal to have 5 blasts for every 100 blood cells. In CML the number of blasts is higher than 5%, but usually less than 10%. Fifteen percent or more blasts is a sign of advanced phase CML. Accelerated and blast phase are considered advanced phases.

Chronic phase

The first phase of CML is called chronic phase (CP-CML). In this phase, there is an increased number of white blood cells in the blood, bone marrow, or both. Less than 1.5 out of every 10 blood cells are myeloblasts (<15%).

CML progresses very slowly in the chronic phase. It may take several months or years to reach the next phase. Compared to other phases, CP-CML typically responds better to treatment.

Accelerated phase

The second phase of CML is called accelerated phase (AP-CML). In this phase, the number of myeloblasts is higher than normal or there are chromosome changes that suggest that the number of myeloblasts is going to increase soon. The number of white blood cells may also be high. There may be a very low number of platelets in the blood caused by CML and not by treatment. In the accelerated phase, CML cells may grow fast.

In all phases, CML cells contain the Philadelphia chromosome (Ph+). However, in the accelerated phase, there may be new abnormal DNA changes (mutations) within Ph+ cells.

Blast phase

The third and final phase of CML is called blast phase (BP-CML). It is also referred to as “blast crisis.” Once CML is in blast phase, it can be life-threatening and very difficult to treat. As a result, a major focus of treatment of CML is to prevent blast phase. Blast phase happens after a series of events, including additional gene mutations and resistance to targeted drug therapy.

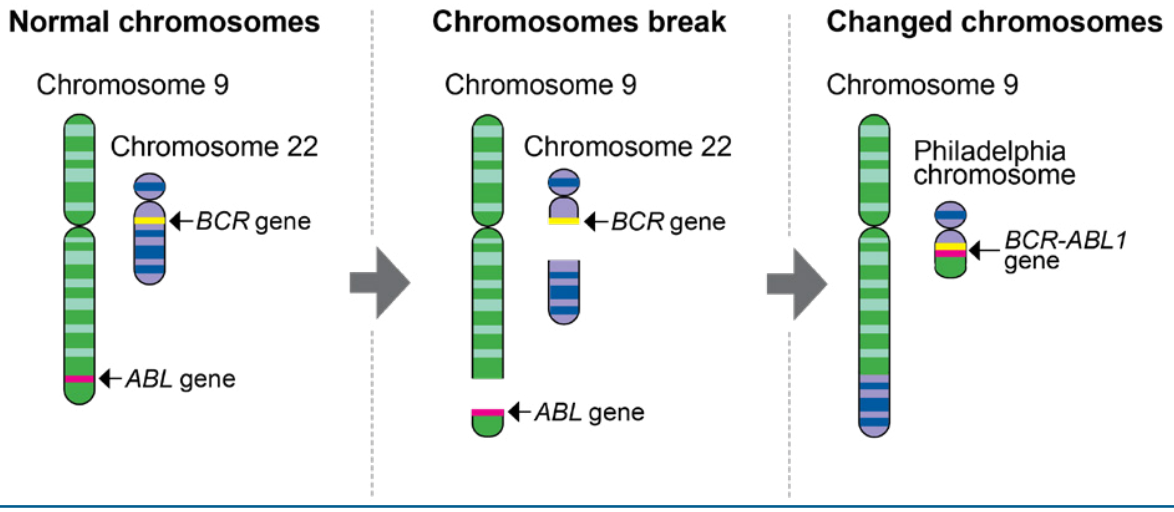
A blast is an immature white blood cell. There is more than one type of white blood cell. Both lymphoid and myeloid progenitor cells form into blast cells called lymphoblasts or myeloblasts depending on the type. Blasts are committed to becoming a type of blood cell. Lymphoblasts normally mature into lymphocytes, a type of white blood cell.

Myeloblasts are responsible for all other non-lymphoid blood cells in bone marrow, such as granulocytes, a type of white blood cell.

In the blast phase, the number of blasts is very high, at least 3 out of every 10 cells (30%). Blast cells may be found in tissues and organs outside the bone marrow or blood. Treatment for BP-CML is based on whether the blasts are myeloid or lymphoid.

Philadelphia chromosome

Chronic myeloid leukemia (CML) is caused by a single, specific abnormal gene that is created when a piece of chromosome 9 and a piece of chromosome 22 break off and trade places. The result is a fused gene called *BCR::ABL1* and a shortened chromosome 22 called the Philadelphia chromosome.



Key points

- Chronic myeloid leukemia (CML) is a type of myeloproliferative neoplasm (MPN). MPNs produce too many blood cells, making it difficult for blood to do its work.
- Usually in CML, there are too many granulocytes. Granulocytes are a type of white blood cell that forms from myeloblasts. Myeloblasts are immature white blood cells. Sometimes, there are too many or too few platelets, as well.
- The cause of CML can be traced to a single, specific abnormal gene (*BCR::ABL1*) found on an abnormal chromosome 22 called the Philadelphia chromosome.
- If you do not have the Philadelphia chromosome or the *BCR::ABL1* gene, you do not have CML.
- *BCR::ABL1* results in the production of the BCR::ABL1 protein, which leads to uncontrolled cell growth. Treatment for CML aims to stop the activity of the BCR::ABL1 fusion protein.
- There are 3 phases of CML. The chronic phase is the first phase. The accelerated phase is the second phase. The third and final phase is called the blast phase. Accelerated and blast phase are grouped into advanced CML.

Those with CML should be treated at experienced leukemia centers.

2
Tests

Treatment planning starts with testing. Accurate testing is needed to diagnose and treat CML. This chapter presents an overview of possible tests and what to expect.

Test results

Results from blood and bone marrow biopsy will be used to determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

Keep these things in mind:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment.
- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don’t be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP. They are great partners in care.
- Include in your contact list information on the exact type of cancer, as well as any treatment and the date it started.

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbals, or supplements you take. Some supplements interact and affect prescriptions that your doctor may give you. Tell your doctor about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer, or where the cancer started, and if it is in multiple locations.

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched.
- Feel for enlarged lymph nodes in your neck, underarm, and groin.
- Feel your abdomen and below your left ribcage to see if your spleen is enlarged. An enlarged spleen is one sign of CML.

Tests used to diagnose CML can be found in **Guide 1.**

Guide 1
Testing for CML

Medical history and physical exam that includes spleen size
Complete blood count (CBC) with differential
Chemistry profile
Bone marrow aspirate and biopsy
Cytogenetic and biomarker testing
qPCR using IS for *BCR::ABL1* found in blood
Hepatitis B panel

Testing takes time. It might take days or weeks for all test results to come in.

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of blood, which is removed through a needle placed into your vein. Some of the blood tests you might have are described next.

Blood clotting tests

Your body stops bleeding by turning blood into a gel-like form. The gel-like blood forms into a solid mass called a blood clot. Clotting is a process or series of events. Proteins, called coagulation factors, are needed for clotting. They are made by the liver. These tests are known together as a coagulation panel or disseminated intravascular coagulation (DIC) panel.

An impaired clotting process is common in leukemia. This is called coagulopathy. You may have bleeding and bruises or blood clots.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. RBCs carry oxygen throughout your body, WBCs fight infection, and PLTs control bleeding. CML often causes a high WBC count and/or PLT count, but can sometimes cause low counts of other blood cells.

Differential

There are 5 types of WBCs: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of WBC. It also checks if the counts are in balance with each other.

Chemistry profile

A chemistry profile or panel measures the levels of different substances released in your blood by the liver, bone, and other organs.

Creatinine

Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys aren't working as well as they were when someone had lower levels of creatinine.

Hepatitis B panel

Hepatitis is a virus that causes inflammation of the liver. Hepatitis B (HBV) is spread by contact with blood and other bodily fluids. A blood test will show if you had hepatitis in the past or if you have it today. Some treatments might cause HBV to reactivate, which can cause liver damage.

HLA typing

Human leukocyte antigens (HLAs) are proteins found on the surface of most cells. They play an important role in your body's immune response. HLAs are unique to each person. They mark your body's cells. Your body detects these markers to tell which cells are yours. In other words, all your cells have the same set of HLAs. Each person's set of HLAs is called the HLA type or tissue type.

HLA typing is a test that detects a person's HLA type. This test is done before a donor (allogeneic) blood stem cell transplant. To find a donor match, your proteins will be compared to the donor's proteins to see how many

proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood or tissue samples from you and your blood relatives will be tested first.

Liver function tests

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well.

Phosphate

Cells have a lot of phosphate in them. Therefore, when many cells are breaking down at the same time, the levels of phosphate in the blood can go up. Your kidneys help get rid of extra phosphate, but too much phosphate in the blood can also damage the kidneys, making it harder to get the levels back down to normal. Since we absorb phosphate from the foods that we eat, you might be given a medicine called a phosphate binder to prevent phosphate levels from rising too high.

Potassium

Blood plasma has a low level of potassium and a high level of sodium, but inside cells are high levels of potassium and low levels of sodium. When many cells are breaking down all at the same time, the level of potassium in the blood can go up. The differences in levels of potassium inside and outside of cells is very important to certain processes such as the electrical signals in the heart. Very high levels of potassium in the blood can cause dangerous heart rhythms.

Pregnancy test

Those who can become pregnant will be given a pregnancy test before treatment begins.

Tumor lysis syndrome panel

Cancer treatment causes cell death. In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. TLS is rare. Changes in creatinine, potassium, phosphate, and uric acid levels can be signs of TLS.

Uric acid

Uric acid is released by cells when DNA breaks down. It is a normal waste product that dissolves in the blood and is filtered by the kidneys where it leaves the body in the urine. Too much uric acid in the body is called hyperuricemia. With CML, it can be caused by a fast turnover of white blood cells (WBCs). High uric acid might be a side effect of treatment. Very high levels of uric acid in the blood can damage the kidneys.

Fertility (all genders)

Treatment with targeted therapy and other forms of systemic therapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your care team how cancer and cancer treatment might change your fertility.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren't really sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation can be found at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Performance status

Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health will be rated using a PS scale called Eastern Cooperative Oncology Group (ECOG). PS is one factor taken into consideration when choosing a treatment plan. Your preferences about treatment are always important.

The ECOG PS scores range from 0 to 5.

- **PS 0** means the person is fully active.
- **PS 1** means the person is still able to perform light to moderate activity, but with some limitations.
- **PS 2** means the person is limited to the chair or bed less than half of the time and still able to care for self.
- **PS 3** means the person is limited to the chair or bed more than half of the time.
- **PS 4** means the person is totally confined to the bed or chair and completely unable to care for self.
- **PS 5** means the person is not alive.

Good PS is usually PS 0 or PS 1.

Bone marrow tests

Leukemia starts in the bone marrow. To diagnose CML and determine the CML phase, samples of bone marrow must be removed and tested before starting any treatment. For many, this is a painful procedure. Your care team will try to make you as comfortable as possible. Usually, you will only have this test once at diagnosis. However, you might have another during or after treatment, if needed.

There are 2 types of bone marrow tests that are often done at the same time:

- Bone marrow aspirate
- Bone marrow biopsy

Your bone marrow is like a sponge holding liquid and cells. An aspirate takes some of the liquid and cells out of the sponge, and a biopsy takes a piece of the sponge.

The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. Your doctors will first clean and give sedation and/or numb your skin and outer surface of your bone. For an aspirate, a hollow needle will be pushed through your skin and into the bone. Liquid bone marrow will then be drawn into a syringe. For the biopsy, a wider needle will be used to remove a core sample. You may feel bone pain at your hip for a few days. Your skin may bruise.

Your bone marrow sample should be reviewed by a pathologist who is an expert in the diagnosis of CML. This review is often referred to as histology, histopathology, or hematopathology review. The pathologist will note the overall appearance and the size, shape, and type of your cells. Tests will be done on the biopsied cells. Ask questions about your biopsy results and what it means for your treatment.

Be prepared to have many blood tests.

Flow cytometry

Flow cytometry is a laboratory method used to detect, identify, and count specific cells. Flow cytometry involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine measures the number of cells, things like the size and shape of the cells, and proteins like BCR::ABL1 on the surface of thousands of cells.

Flow cytometry may be used on cells from circulating (peripheral) blood or from a bone marrow aspirate. A blood test can count the number of white blood cells, but it cannot detect the subtle differences between different types of blood cancers. Flow cytometry can detect these subtle differences.

Genetic tests

Genetic tests are used to learn more about your type of CML, to target treatment, and to determine the likely course your cancer will take (prognosis). This testing is different from family history genetic testing.

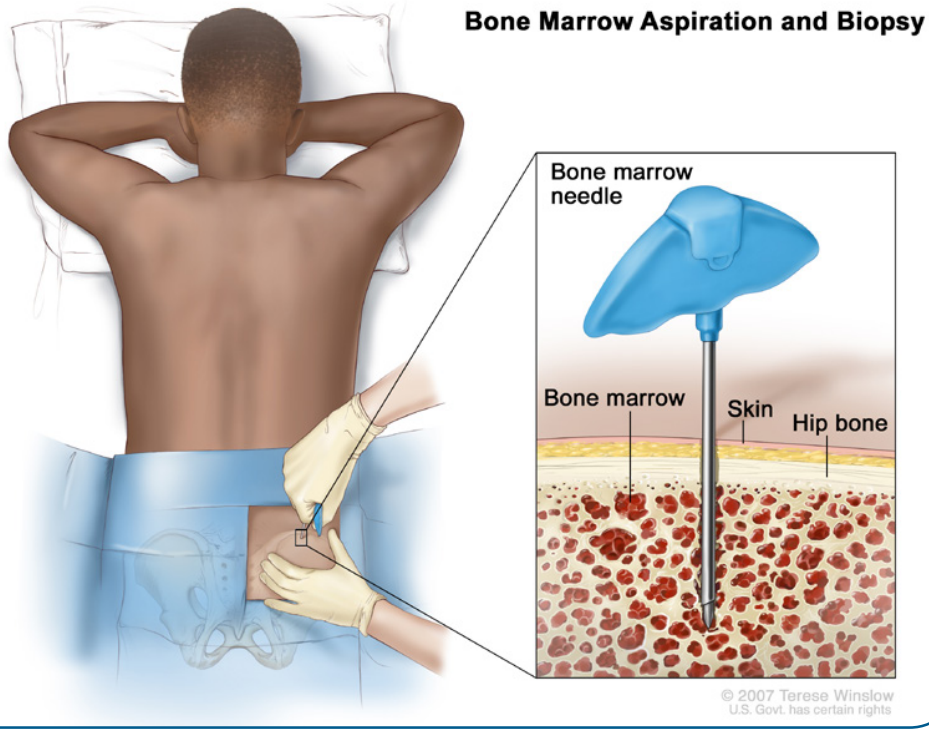
Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes are coded instructions for the proteins your cells make. A mutation is when something goes wrong in the genetic code. Proteins are written like this: BCR::ABL1. Genes are written in italics like this: *BCR::ABL1*.

CML can cause changes in genes and chromosomes in blood cells. Genetic tests look for these changes or abnormalities. Testing will look for the Philadelphia chromosome, which is used to diagnose and to help determine the CML phase. You may be placed into a risk group based on the types of genetic abnormalities found.

Cytogenetics

Cytogenetics is the study of chromosomes, which contain most of the genetic information in a cell. Cytogenetics involves testing samples of blood, tissue, and bone marrow to look for broken, missing, rearranged, or extra chromosomes.

Samples of bone and marrow are removed in a bone marrow biopsy. A bone marrow aspirate and biopsy is needed to diagnose CML.



There are 2 types of cytogenetic tests used in CML:

- Karyotype
- Fluorescence in situ hybridization (FISH)

Karyotype

A karyotype is a picture of chromosomes. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. A karyotype will show extra, missing, rearranged, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow or blood must be used.

FISH

Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. For example, the probes attach to the *BCR* gene and the *ABL1* gene. The *BCR::ABL1* gene is detected when the colors of the probes overlap by translocation. A translocation is the switching of parts between two chromosomes. The *BCR::ABL1* translocation can also be written as t(9;22).

FISH can look for translocations that are too small to be seen with other methods. It can only be used for known changes. It cannot detect all the possible changes found with a karyotype. Since this test doesn't need growing cells, it can be performed on either a bone marrow or blood sample. Most commonly, a bone marrow sample is needed to get all the information your care team needs to help plan your care.

Biomarker tests

Biomarker testing is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing. It includes tests of genes or their products (proteins) and identifies the presence or absence of mutations and certain proteins.

Next-generation sequencing

Next-generation sequencing (NGS) is a high-throughput method used to determine a portion of a person's DNA sequence.

PCR

A polymerase chain reaction (PCR) is a technique that can make millions or billions of copies of your DNA or RNA (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for NGS.

qPCR (IS)

A special PCR called quantitative reverse transcriptase polymerase chain reaction (qPCR) is used in CML. It measures the number of cells within the *BCR::ABL1* gene. The number found in your blood is compared to an international standard or baseline called the International Scale (IS). This is the most important test for monitoring response to treatment. Ask your care team if they are using qPCR (IS). It is the gold standard for detecting and measuring *BCR::ABL1*.

A qPCR (IS) should be done at initial diagnosis to look for the presence of the *BCR::ABL1* gene on the Philadelphia chromosome. You will have this test often after starting treatment. This test might be referred to as real-time or reverse transcriptase (RT) PCR.

Mutation testing

A sample of your blood or bone marrow will be used to see if the CML cancer cells have any specific mutations. This is separate from the genetic testing for mutations that you may have inherited from your parents.

Subtle new drug-resistant mutations in the *BCR::ABL1* gene may occur over time. They can happen as CML progresses to advanced phases such as accelerated or blast phase. Mutations can also happen during treatment for CML. Mutation testing is used to look for these new mutations. Some mutations lead to resistance to certain targeted therapies. There are many possible mutations.

Heart tests

Heart or cardiac tests are used to see how well your heart works. These tests might be used to monitor treatment side effects. You might be referred to a cardiologist.

Electrocardiogram

An electrocardiogram (ECG or EKG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged corrected QT interval (or QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an ECG. Certain treatments for CML can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

Echocardiogram

An echocardiogram (or echo) uses sound waves to make pictures. It is a type of ultrasound. For this test, small patches will be placed on your chest to track your heartbeat. Next, a wand with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen on a screen. The pictures will be recorded for future viewing.

An echocardiogram is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart every time it beats. In low ejection fraction, the amount of blood pumping from the left side of the heart is lower than normal.

Cardiac nuclear medicine scan

A nuclear heart scan is an imaging test that uses special cameras and a radioactive substance called a tracer to create pictures of your heart. The tracer is injected into your blood and travels to your heart. This test can also be used to measure the ejection fraction.

Key points

- Blood tests check for signs of disease, and how well organs are working.
- Those who can become pregnant will be given a pregnancy test before treatment begins.
- Talk to your care team if you are or plan to become pregnant. Certain treatments for CML will need to be avoided if you are pregnant or breastfeeding.
- A diagnosis of CML is confirmed using a bone marrow aspirate and bone marrow biopsy.
- Cytogenetic and biomarker tests are used to learn more about your CML, to target treatment, and to determine the likely course your cancer will take called a prognosis.
- A special PCR called quantitative reverse transcriptase polymerase chain reaction (qPCR) using the International Scale (IS) measures the number of cells with the *BCR::ABL1* gene mutation.
- As CML progresses, it can mutate. Therefore, you might have mutation testing before treatment for advanced CML.
- Heart or cardiac tests might be used to monitor treatment side effects.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

3
Treatment options

This chapter provides a general overview of therapies you might receive. CML is usually treated with targeted therapy. A targeted therapy focuses on specific or unique features of cancer cells such as the protein made by the *BCR::ABL1* gene.

Chronic myeloid leukemia (CML) is highly treatable and may be curable in certain circumstances. It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

Care team

Treating CML takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team might include the following:

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **A diagnostic radiologist** interprets the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places intravenous (IV) ports for treatment.
- **A medical oncologist** treats cancer in adults using systemic therapy.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners and physician assistants** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Oncology pharmacists** provide medicines used to treat cancer and to manage symptoms and side effects.
- **Palliative care nurses, advanced practice providers (APPs), and physicians** help provide an extra layer of support with your cancer-related care.

- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **A research team** helps to collect research data and coordinate care if you are participating in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

Your physical, mental, and emotional well-being are important. You know yourself better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

Tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. Bring a list with you to every visit.

Systemic therapy

Systemic therapy is drug therapy that works throughout the body. Systemic therapy includes chemotherapy, targeted therapy, and immunotherapy. CML is usually treated with targeted therapy. Goals of systemic therapy should be discussed before starting treatment. The choice of therapy takes into consideration many factors, including age, other serious health issues, and future treatment possibilities like a hematopoietic cell transplant. Your preferences about treatment are important. If you have any religious or personal beliefs about certain kinds of treatment, now would be the time to share them with your care team.

Warnings!

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction. It is critical to speak with your care team about any supplements you may be taking.

Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- St. John's Wort

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. Bring a list with you to every visit.

Get to know your care team and help them get to know you.

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and normal cells. Omacetaxine (Synribo) is an example of chemotherapy used to treat CML.

Steroids

Steroid is the short name for corticosteroid. Steroids are man-made versions of hormones made by the adrenal glands. The adrenal glands are small structures found near the kidneys, which help regulate blood pressure and reduce inflammation. Steroids also are toxic to lymphoid cells and may be part of a treatment. Steroids can cause short-term and long-term side effects. Corticosteroids are not the same as the steroids used by some athletes.

Targeted therapy

Targeted therapy is a form of systemic therapy that focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive.

Tyrosine kinase inhibitor

A tyrosine kinase inhibitor (TKI) is a type of targeted therapy that blocks the signals that cause cancer to grow and spread. TKIs might be used alone or in combination with other systemic therapies like chemotherapy.

Tyrosine kinases are proteins in cells that are important for many cell functions. The protein made by the *BCR::ABL1* gene is a tyrosine kinase. It moves or transfers chemicals, called phosphates, from one molecule to another. TKIs block this transfer, which stops the uncontrolled cell growth in CML.

TKIs are slightly different from one another, but they generally work in a similar way. They may cause different side effects. You might not be given a certain TKI if you have a health condition, such as lung or heart issues, or certain mutations. Sometimes, a TKI will stop working when there's a new mutation in CML cells. Switching to a different TKI can often help.

TKIs used to treat CML

TKIs that might be used to treat CML (listed in alphabetical order):

- Asciminib (Scemblix)
- Bosutinib (Bosulif)
- Dasatinib (Sprycel)
- Imatinib (Gleevec)
- Nilotinib (Tasigna)
- Ponatinib (Iclusig)

TKIs are divided into first, second, and even third generation. In general, each generation of a drug gets more specific and better at targeting certain mutations. This means that second- and third-generation TKIs are usually more effective and faster at creating a response. However, they might have more side effects.

Imatinib is the only first-generation TKI. Since it is less toxic than second-generation TKIs, it is a good option for those who are older or who have other more serious health issues. Risks of each TKI are considered for your specific situation.

If CML doesn't seem to be responding to one TKI, then another TKI will be tried. Certain drugs may work better and be less toxic. Dose might be increased or decreased depending on how CML is responding to treatment. You will be closely monitored during treatment.

Breastfeeding

Certain types of drug treatment can end up in your breast milk. If you are breastfeeding or plan to breastfeed, talk to your care team. There are options. Those on TKI therapy should not breastfeed. TKIs can pass into human breast milk.

TKI side effects

A side effect is an unwanted health issue. If you feel unwell or a side effect is interfering with your ability to do daily tasks, tell your treatment team. There may be ways to help you feel better. It is very important to continue to take your medicine even if you do not feel well. Speak to your care team before making any changes!

Side effects are common among TKIs. These include low blood counts, fatigue, and musculoskeletal pain. You may feel nauseated, have diarrhea, and vomit. Changes in your skin may occur, such as a rash. You may feel tired and get headaches and fevers. Fluid buildup in limbs (edema) or around certain organs may occur. Severe side effects include heart and liver issues, and kidney failure. Do not take TKIs while pregnant or breastfeeding. Talk to your care team first before stopping any TKI.

Asciminib

Asciminib is in a separate class because it targets a different area of *BCR::ABL1*. It can be used in those who have taken at least two prior treatments. It may not be preferred in those who have had pancreatitis.

Bosutinib

Bosutinib is a second-generation TKI. It may not be preferred for those who have liver or stomach and digestion (gastrointestinal) issues.

Dasatinib

Dasatinib is a second-generation TKI. Dasatinib is more potent than imatinib. It may not be prescribed if you have lung (pulmonary) disease or breathing issues.

Imatinib

Imatinib was the first TKI approved by the U.S. FDA (Food and Drug Administration) to treat CML. Imatinib has been studied for a long time and is still a very good treatment option. Imatinib is an option for those who are older or who have other more serious health issues. It is also an option for those who have low-risk chronic phase CML where an aggressive treatment might not be needed.

Nilotinib

Nilotinib is a second-generation TKI. It works in almost the same way as imatinib. However, nilotinib is more potent. Sudden deaths have occurred in those taking nilotinib. Nilotinib may not be best for those who have heart (cardiovascular) issues, are at risk for heart issues, or who have electrolyte abnormalities. Nilotinib may cause increased blood sugar or worsen peripheral vascular disease. Nilotinib prolongs the QT interval, which is detectable on an electrocardiogram (ECG or EKG). You will likely have ECGs to monitor your heart.

Ponatinib

Ponatinib is a third-generation TKI. It is the only effective treatment for those with a *BCR::ABL1* gene mutation called *T315I,* but may be used as a third-line treatment option in those without *T315I.* Ponatinib can have some serious side effects and is not used as a first-line therapy. You might be referred to a cardiologist to monitor your heart if you receive this treatment.

Hematopoietic cell transplant

A hematopoietic cell transplant (HCT) replaces hematopoietic stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy as part of the transplant process. A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. You might hear it called a stem cell transplant (SCT) or a bone marrow transplant (BMT). This book will refer to it as HCT. HCTs are performed in specialized centers. Most people with CML do not need an HCT.

There are 2 types of HCTs:

- **Autologous** – stem cells come from you
- **Allogeneic** – stem cells come from a donor who may or may not be related to you. Only an allogeneic HCT is used as a possible treatment option in CML.

Allogeneic transplant

An allogeneic transplant (alloHCT) uses healthy stem cells from a donor. The donor may or may not be related to you. Before an HCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune system so your body will accept and won't kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

After conditioning, you will receive a transfusion of the healthy stem cells from a donor that has been matched to you. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. Transfusions are also possible. A red blood cell transfusion is used to prevent bleeding and to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding. While waiting for the cells to engraft, you will likely feel tired and weak.

Possible side effects

Every treatment has side effects. You will be monitored for infections, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack your normal, healthy tissue. There are treatments for GVHD. Ask your care team about the possible side effects or complications of HCT and how this might affect your quality of life.

More information on GVHD can be found at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Clinical trials

A clinical trial is a type of medical research study. After being developed and 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).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your care team about whether a clinical trial may make sense for you.

Phases

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

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

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.

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 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.

Start the conversation

Don't wait for your care team 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.

Your preferences about treatment are always important. Talk to your care team and make your wishes known.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

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 for this care that are not covered by your insurance.

Supportive care

Supportive care is health care given during all cancer stages. It aims to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Best supportive care, supportive care, and palliative care are often used interchangeably.

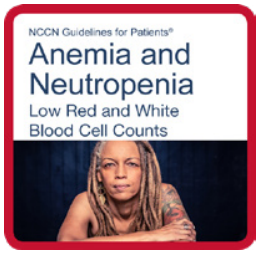
It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment. Some potential side effects and procedures are described next. They are not listed in order of importance. Some side effects are very rare.

Anemia, neutropenia, and thrombocytopenia

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not have enough healthy blood cells, resulting in less oxygen being carried to your cells. You might tire easily if you are anemic.
- **Neutropenia** is a decrease in neutrophils, the most common type of white blood cell. This puts you at risk for infection.
- **Thrombocytopenia** is a condition where there are not enough platelets found in the blood. This puts you at risk for bleeding.

More information on anemia, neutropenia, and thrombocytopenia is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



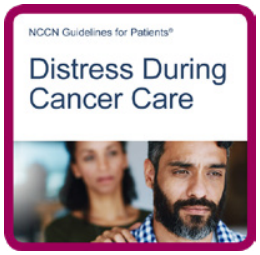
Diarrhea

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It is important to drink lots of fluids.

Distress

Depression, anxiety, and sleeping problems are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

More information on distress is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

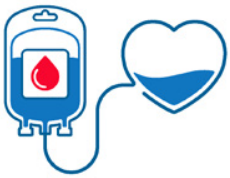
Infection

Infections occur more frequently and are more severe in those with a weakened immune system. Drug treatment for CML can weaken the body's natural defense against infections. If not treated early, infections can be fatal.

Neutropenia, a low number of white blood cells, can lead to frequent or severe infections. When someone with neutropenia also develops a fever, it is called febrile neutropenia (FN). With FN, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections. FN is a side effect of some types of systemic therapy.

Hand-foot syndrome

Hand-foot syndrome is a common side effect of chemotherapy. Small amounts of chemotherapy leak out of very small blood vessels called capillaries in the palms of the hands and soles of the feet. It causes redness, swelling, and pain. Sometimes blisters appear. You will want to protect your hands and feet by applying moisturizer or lotion, using gloves when washing dishes, and spreading yard work over several days.



Transfusions

A transfusion is a common procedure to replace blood or blood components (red blood cells or platelets). It is given through an intravenous line (IV), a tiny tube that is inserted into a vein with a small needle.

- ✓ The whole process can take about 1 to 4 hours, depending on how much blood is needed.
- ✓ Most transfusions use blood from a donor. Some choose a family member or friend to donate blood.
- ✓ Blood transfusions are usually very safe. Donated blood is carefully tested, handled, and stored.
- ✓ Most people's bodies handle blood transfusions very well. But, like any medical procedure, there are some risks. Speak with your care team for specific information about your risks.
- ✓ Systemic therapy can affect how bone marrow makes new blood cells. Some people getting treatment for cancer might need a transfusion of red blood cells or platelets.

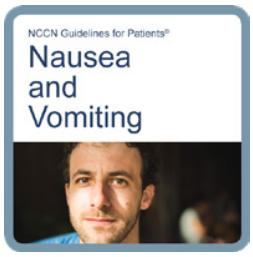
Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social health concerns, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You will be given medicine to prevent nausea and vomiting.

More information on nausea and vomiting is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Neuropathy

Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by cancer or cancer treatment.

Neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Seizures and confusion can occur.

Pain

Tell your care team about any pain or discomfort. Bone or muscle pain are possible. You might meet with a palliative care specialist to manage pain.

Side effects

All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant. Cancer treatment can cause a number of side effects. Some are very serious.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

Key points

- Treatment decisions should involve a multidisciplinary team (MDT) of doctors, health care workers, and social care professionals from different fields of medicine who have knowledge (expertise) and experience with your type of cancer.
- Targeted therapy focuses on specific or unique features of cancer cells. CML is usually treated with targeted therapy.
- A tyrosine kinase inhibitor (TKI) is a type of targeted therapy that blocks the signals that cause certain cancers to grow and spread.
- Those on TKI therapy should not breastfeed. TKIs can pass into human breast milk.
- Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and normal cells.
- A hematopoietic cell transplant (HCT) replaces damaged bone marrow stem cells with healthy stem cells. You might hear it called a stem cell transplant (SCT) or bone marrow transplant (BMT).
- A clinical trial is a type of medical research study.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves your quality of life. Supportive care is always given.
- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.
- Eating a balanced diet, drinking enough fluids, exercise, yoga, and massage therapy can help manage side effects.
- Some side effects, called late effects, may take years to appear. Risk for late effects will depend on the type(s) of cancer treatment you had, and the dose and the length of time you were treated. It is important to keep follow-up appointments.

4
Chronic phase

In chronic phase CML (CP-CML), there is an increased number of granulocytes in the blood, bone marrow, or both. CP-CML is treatable. Together, you and your care team will choose a treatment plan that is best for you.

Overview

CML is often diagnosed during the chronic phase of the disease. In this phase, there is an increased number of white blood cells called granulocytes in the blood, marrow, or both. Less than 1.5 out of every 10 blood cells are blasts (<15%) in chronic phase CML (CP-CML).

CP-CML responds well to treatment. However, if left untreated, CP-CML can progress to accelerated phase or blast phase CML, which is more difficult to cure.

CP-CML is highly treatable. Treatment includes targeted therapy or TKIs. It is very important to take all medicine exactly as prescribed and not miss or skip doses. Also, keep up with follow-up visits and testing. You can expect a near-normal to normal life expectancy if CML goes into remission and you continue to take medicine as prescribed.

Not everyone responds to treatment in the same way. Some people will do better than expected. Others will do worse. Factors such as your general health or if you have serious health conditions are also very important.

Risk groups

People in the same risk group will likely respond to treatment in the same way. As a result, doctors often use risk groups to help plan treatment. Ask how your risk group will affect your treatment. **See Guide 2.**

Guide 2
Risk groups

Low	• Sokal score is less than 0.8 • Hasford score is 780 or less • EUTOS long-term survival score is 1.5680 or less
Intermediate	• Sokal score is between 0.8 and 1.2 • Hasford score is between 781 and 1480 • EUTOS score is between 1.5680 and 2.2185
High	• Sokal score is more than 1.2 • Hasford score is more than 1480 • EUTOS score is more than 2.2185

In CML, risk is calculated using:

- Age
- Spleen size on physical exam
- Blood counts

Based on this information, you will receive one of the following:

- Sokal score
- Hasford (EURO) score
- EUTOS long-term survival (ELTS) score

This score places you into a risk group:

- Low
- Intermediate
- High

In addition to your risk score, these factors are important:

- If you have any other serious health issues called comorbidities
- Side effects and toxicity of a tyrosine kinase inhibitor (TKI)
- Possible drug interactions between a chosen TKI and any medicines, herbals, supplements, and over-the-counter (OTC) drugs you are taking
- Whether your insurance plan will cover a particular TKI
- Your wishes or preferences about treatment options

Primary treatment

The first or main treatment given is called primary treatment. It is based on your risk group.

Low risk

For low risk, the preferred treatment options are:

- Imatinib or generic imatinib (generic imatinib is the same in dosage, safety, strength, quality, and performance as imatinib)
- Second-generation TKI (bosutinib, dasatinib, or nilotinib)
- Clinical trial

Intermediate or high risk

For intermediate or high risk, the preferred treatment option is a second-generation TKI (bosutinib, dasatinib, or nilotinib). Imatinib or generic imatinib and a clinical trial are also recommended options.

Monitoring

To see how well CML is responding to targeted therapy, you will be monitored with qPCR using IS. A qPCR (IS) is the only tool sensitive enough to detect very low levels of *BCR::ABL1.*

qPCR (IS) scores

The qPCR (IS) score uses a standard baseline of 100%. This is the starting point or value that your results are measured against. It is the average of what is observed in untreated individuals; it is possible to have a value of greater than 100%. Changes in qPCR (IS) scores are often described in terms of

"log changes." Log changes can decrease or increase. A log increase means that the value has gone up at least 10 times from the lowest it has been. For example, an increase of *BCR::ABL1* to 1.2% from a previous value of 0.12% would be a one log increase. A log increase while being treated is cause for concern.

Response types

There are 3 response types:

- **A hematologic response** measures your blood cell counts.
- **A cytogenetic response** measures your chromosomes. Treatment aims to reduce the number of cells with the Philadelphia chromosome (Ph+) to near zero. Some cells with *BCR::ABL1* may remain in a complete cytogenetic response (CCyR).
- **A molecular response** measures your molecules. Treatment aims to reduce the number of cells with the *BCR::ABL1* gene mutation to as close to zero as possible.

For definitions of different response types, **see Guide 3.**

Guide 3
Response types and definitions

Complete hematologic (blood) response (CHR)	• Blood counts are normal • No immature cells, such as myelocytes, promyelocytes, or blasts in blood • No signs and symptoms of disease (spleen is normal size)
Cytogenetic (Philadelphia chromosome or Ph) response	• Complete cytogenetic response (CCyR): No Philadelphia chromosomes (Ph-) • Major cytogenetic response (MCyR): Ph+ are between 0% and 35% • Partial cytogenetic response (PCyR): Ph+ are between 1% and 35% • Minor cytogenetic response: Ph+ are between 36% and 65%
Molecular *(BCR::ABL1)* response	• Early molecular response (EMR): *BCR::ABL1* (IS) is 10% or less at 3 and 6 months • Major molecular response (MMR): *BCR::ABL1* (IS) is 0.1% or less • Deep molecular response (DMR): *BCR::ABL1* (IS) is 0.01% or less (MR4.0) or *BCR::ABL1* (IS) is 0.0032% or less (MR4.5)
Relapse	• Any sign of loss of response

Response milestones

For CML, treatment results are discussed in terms of response milestones. The goal is to hit certain response milestones within a specific timeframe and maintain those milestones.

There are 2 very important milestones:

- **Early molecular response (EMR)** is defined as *BCR::ABL1* between 10% and 1% at 3 months and 6 months. It is a sign of how well treatment will work long term. The next milestone is complete cytogenetic response by 12 months.
- **Complete cytogenetic response (CCyR)** is the absence of the Philadelphia chromosome (Ph-). It is equal to a *BCR::ABL1* value of 1% or less. It should be achieved within 12 months.

Although not a response milestone, another treatment result is a major molecular response (MMR). In MMR, *BCR::ABL1* is less than 0.1% and can predict a deep molecular response (DMR). A DMR is when *BCR::ABL1* can't be detected except by the most sensitive of tests, or cannot be detected at all. In a DMR, *BCR::ABL1* is at 0.01% or less.

It is very important to continue to take your medicine as prescribed and not miss or skip any doses.

Not meeting milestones

If treatment is not meeting certain milestones, then it is possible your CML is resistant to the TKI you are taking.

If this is the case, you will be asked if you:

- Missed or forgot to take any doses
- Are taking any medicines, over-the-counter (OTC) drugs, herbals, or supplements, or if there were any changes to other medicines you might take for your heart, allergies, or digestion.

It is very important to tell your care team about any teas you drink like green tea and any supplements you take such as turmeric. It might be one reason your treatment is not working. Another reason might be that your CML has a new drug-resistant mutation. Your care team will consider this and order any mutation or biomarker testing as needed.

Second-line treatment

Second-line treatment options are based on qPCR (IS) results and if primary treatment milestones were met. Response milestones are measured as the percentage of cells with *BCR::ABL1* using qPCR (IS). The goal is to reduce the number of CML cells with *BCR::ABL1* to less than 1% within 12 months.

For treatment milestones, **see Guide 4.**

Guide 4
Treatment milestones using *BCR::ABL1 (IS)*

If at 3 months	*BCR::ABL1* (IS) is more than 10%, then possible TKI resistance
	BCR::ABL1 (IS) is between 10% and 1% (EMR), then milestone met
	BCR::ABL1 (IS) is between 1% and 0.1% (CCyR), then milestone met
	BCR::ABL1 (IS) is 0.1% or less (DMR), then milestone met
If at 6 months	*BCR::ABL1* (IS) is more than 10%, then TKI resistance
	BCR::ABL1 (IS) is between 10% and 1% (EMR), then milestone met
	BCR::ABL1 (IS) is between 1% and 0.1% (CCyR), then milestone met
	BCR::ABL1 (IS) is 0.1% or less (DMR), then milestone met
If at 12 months	*BCR::ABL1* (IS) is more than 10% , then TKI resistance
	BCR::ABL1 (IS) is between 10% and 1% (EMR), then possible TKI resistance
	BCR::ABL1 (IS) is between 1% and 0.1% (CCyR), then milestone met if goal is long-term survival. Milestone not met if goal is treatment-free remission.
	BCR::ABL1 (IS) is 0.1% or less (DMR), then milestone met

- Red shows milestone not met.
- Yellow shows area of concern and possible TKI resistance.
- Light green milestone is based on the treatment goal.
- Green shows milestone goal met.

Milestone not met

If the *BCR::ABL1* (IS) level is more than 10% after 6 or 12 months, it means that treatment milestones were not met or maintained. If you have been taking your medication regularly, the next option is to switch to another TKI and discuss if hematopoietic cell transplant (HCT) is right for you. You might talk with a transplant expert.

Possible TKI resistance

You might have possible TKI resistance if the number of *BCR::ABL1* (IS) cells:

- Is more than 10% after 3 months
- Is greater than 1% after 12 months

You might have additional biomarker and mutation testing before continuing treatment.

Treatment options are:

- Switch to another TKI
- Stay on the same TKI or increase the dose, unless it is imatinib
- Discuss if allogeneic HCT is right for you. You might talk with a transplant expert.

Milestone might have been reached

For those with *BCR::ABL1* (IS) between 0.1% and 1% at 12 months, if the treatment goal is:

- Long-term survival, then the milestone is met and you will continue with the same TKI.
- Treatment-free remission (TFR), then the milestone is not met. You might switch to a different TKI, be referred to a center that specializes in CML, or be recommended for a clinical trial.

Treatment-free remission

For some, it may be possible to discontinue or stop TKI therapy if all milestones have been met. This is called treatment-free remission (TFR). Your care team should consult with a CML specialist and review with you in detail the potential risks and benefits. You will need to agree (consent) to stop therapy and be aware of the TKI withdrawal side effects.

Frequent monitoring is needed for those in remission who have stopped taking TKI therapy. You will need to have frequent blood tests. This is to make sure that your *BCR::ABL1* levels stay low. If the *BCR::ABL1* level increases above 0.1%, you will need to restart treatment. There is a chance that your cancer might return (relapse) if you stop taking the targeted therapy. Ask your care team about the risks.

Milestone met

If milestones have been reached, you will stay on your TKI. It's very important not to stop your medication without your physician's advice or skip doses of your medicine. Missing doses allows the leukemia cells to grow. Monitoring will continue indefinitely.

Key points

- In chronic phase CML (CP-CML), there is an increased number of white blood cells called granulocytes found in blood, bone marrow, or both. Less than 1.5 out of every 10 blood cells are blasts (<15%).
- CP-CML is highly treatable.
- Treatment for CP-CML is based on risk groups using age, spleen size, and blood counts.
- Treatment results are discussed in terms of milestones. The goal is to hit and maintain certain treatment milestones within a specific timeframe.
- Two very important milestones are early molecular response (EMR) at 3 months and 6 months and complete cytogenetic response (CCyR) by 12 months.
- The minimal goal of treatment is to reduce the number of CML cells with *BCR::ABL1* to less than 1% within 12 months.
- It is very important to take your medicine exactly as prescribed and not miss any doses.

Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- ✓ The time and dose of all medicines
- ✓ When pain starts and ends or lessens
- ✓ Where you feel pain
- ✓ A description of your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- ✓ Does the pain change at different times of day? When?
- ✓ Does the pain get worse before or after meals? Does certain food or drink make it better?
- ✓ Does the pain get better or worse with activity? What kind of activity?
- ✓ Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- ✓ A rating your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- ✓ Does pain get in the way of you doing the things you enjoy?

5
Advanced phase

Accelerated phase (AP) and blast phase (BP) are known as advanced phase CML. These phases are defined by an increase in blasts, additional gene mutations, and leukemia that is spreading. A hematopoietic cell transplant (HCT) would follow blast phase treatment for the best chance of remission. Together, you and your care team will choose a treatment plan that is best for you.

Testing

In accelerated phase CML (AP-CML), the blasts are myeloid. In blast phase CML (BP-CML), the blasts can be myeloid or lymphoid. This is different from chronic phase CML (CP-CML) where all of the blasts are myeloid. HLA testing might be done if a hematopoietic cell transplant (HCT) is planned.

Before treatment, you will have tests to confirm the advanced phase of CML—accelerated or blast phase. The phase is based on the number and type of blasts, if there are any new mutations, and if CML has spread to tissues and organs outside of the bone marrow or blood.

- In AP-CML, the number of blasts and white blood cells is higher than normal.
- In BP-CML, myeloblasts or lymphoblasts may be found in tissues and organs outside the bone marrow or blood.

Guide 5
Definitions of advanced phase CML

Accelerated	Any of the following: • Blood myeloblasts are between 15% and 29% • Blood myeloblasts and promyelocytes total 30% or more • Blood basophils are 20% or more • Platelet count is 100 x 109/L or less • Additional mutations are found in Ph+ cells • Any increase in lymphoblasts is a concern that blast phase is beginning
Blast	Any of the following: • 30% or more blasts are found in blood, marrow, or both • Blast cells are found in tissues and organs outside the bone marrow or blood

For definitions of advanced phase CML, **see Guide 5.**

Mutation testing

New mutations in the *BCR::ABL1* gene may occur over time. This can happen as CML progresses to advanced phases or it can happen during treatment for CML.

Mutation testing is used to look for these new mutations. Testing can be performed on blood or bone marrow. It should be done prior to starting treatment for advanced phase CML and for any convincing evidence of loss of response to treatment. Some targeted therapies will work on certain mutations, while others will not. Therefore, the tyrosine kinase inhibitor (TKI) chosen will be based on the type of gene mutation(s). Ask your care team why a certain treatment is being chosen and how it might work better for your type and phase of CML.

Treatment planning

Factors such as your age, medical history, test results, and any prior TKI therapy will be used for treatment planning. The goal of treatment is to stop CML from progressing to accelerated or blast phase.

Your care team will consider the following when planning treatment for advanced phase CML:

- Did your CML progress while being treated using TKI therapy?
- Did your CML progress while not being treated?
- Are you a candidate for a hematopoietic cell transplant (HCT)?
- Is there any leukemia in your central nervous system (CNS)?
- What mutations does your CML have?
- What TKIs did you take before? Did your CML not respond or was it resistant to certain TKIs?

Accelerated phase

In accelerated phase CML (AP-CML), the number of myeloblasts and white blood cells is high. Platelet count might be low. In all phases, CML cells contain the Philadelphia chromosome (Ph). However, in the accelerated phase, there may be new abnormal changes within chromosomes.

Treatment options

The treatment goal is to stop CML from progressing to blast phase. For long-term control, an allogeneic (donor) HCT is likely needed. For treatment options, **see Guide 6.**

Guide 6
Treatment options: Accelerated phase

Clinical trial

Preferred TKIs
- Bosutinib
- Dasatinib
- Nilotinib
- Ponatinib

Used in some cases
- Imatinib or generic imatinib
- Omacetaxine

Blast phase

In the blast phase, at least 3 out of every 10 cells (30%) are blasts. Blasts can be lymphoid (lymphoblasts) or myeloid (myeloblasts). Blasts may be found in tissues and organs outside the bone marrow or blood. A lumbar puncture (LP) and central nervous system (CNS) prophylaxis is recommended for lymphoid blast phase.

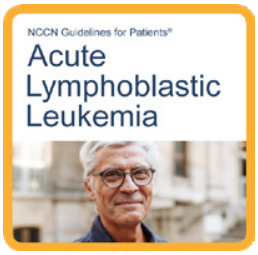
An allogeneic (donor) HCT would follow treatment for blast phase CML.

Treatment options

Options for lymphoid blast phase include:

- Clinical trial
- ALL-type induction chemotherapy with a tyrosine kinase inhibitor (TKI) (preferred)
- TKI with steroids

More information on ALL-type induction therapies is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Options for myeloid blast phase include:

- Clinical trial
- AML-type induction chemotherapy with a TKI (preferred)
- TKI

More information on AML-type induction therapies is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

After an HCT

A hematopoietic cell transplant (HCT) is used to prevent CML from progressing. It is a treatment given to cure CML. However, this does not always happen. An allogeneic HCT (alloHCT) uses healthy blood (hematopoietic) stem cells from a donor who may or may not be related to you.

How your body responds to an alloHCT is based on age, if you have other serious health issues (comorbidities), donor type, and transplant center. You will have qPCR (IS) after an HCT to see if any cells with the Philadelphia chromosome (Ph) or *BCR::ABL1* gene remain.

In a complete cytogenetic response (CCyR), no Philadelphia chromosomes (Ph-) remain. It is equal to a *BCR::ABL1* level of 1% or less.

CCyR

Following an HCT, you will be monitored with qPCR. This is done with blood, not bone marrow. qPCR will be done every 3 months for 2 years, then every 3 to 6 months. If qPCR is negative, then you will continue to be monitored. You might have TKI therapy for at least one year after transplant if you had accelerated or blast phase CML before.

In a complete cytogenetic response (CCyR), no Philadelphia chromosomes (Ph-) remain.

Not in CCyR or in relapse

If Philadelphia chromosomes or *BCR::ABL1* genes remain after the hematopoietic cell transplant (HCT), or CML has returned, then treatment options include:

- TKI
- TKI with donor lymphocyte infusion (DLI)
- Omacetaxine
- Clinical trial

In a DLI you will receive white blood cells from the same person who donated blood-forming cells for the HCT. Treatment options are based on the type(s) of TKI you had before, your current health, *BCR::ABL1* mutations, and other factors. Your wishes are also important.

Key points

- Accelerated phase and blast phase are known as advanced phase CML. These phases are defined by an increase in blasts, additional gene mutations, and leukemia that is spreading.
- Before treatment, you will have tests to confirm the phase of CML.
- In all phases, CML cells contain the Philadelphia chromosome. However, in the accelerated phase, there may be new abnormal changes within chromosomes (gene mutations).
- Treatment options are based on prior TKI therapy, gene mutations in CML cells, and your health.
- In accelerated phase CML (AP-CML), the number of blasts and white blood cells are also high. Platelet count might be low.
- TKIs are often used to treat advanced phase CML. Chemotherapy or steroids may be added if in blast phase. For long-term control, an allogeneic (donor) or hematopoietic cell transplant (HCT) is needed.
- The goal of treatment for AP-CML is to stop CML from progressing to blast phase.
- Blast phase CML (BP-CML) happens after a series of events, including additional gene mutations and resistance to targeted therapy.
- Treatment for BP-CML is based on if the blasts are myeloid (granulocytes) or lymphoid (lymphocytes).
- Treatment for BP-CML usually includes an allogeneic HCT as part of the overall plan.

6
Making treatment decisions

It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

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

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
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or 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 care team. If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't 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.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Some possible questions to ask your care team are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Questions about diagnosis and testing

1. What tests are needed? What other tests do you recommend?
2. How soon will I know the results and who will explain them to me?
3. Where will the tests take place? How long will the tests take?
4. Is there a cancer center or hospital nearby that specializes in this type of cancer?
5. What will you do to make me comfortable during testing?
6. How do I prepare for testing? How will the test be done? What can I expect?
7. Would you give me a copy of the pathology report and other test results?
8. Who will talk with me about the next steps? When?
9. Will treatment start before the test results are in?
10. How many bone marrow tests are needed? When will they be done?

Questions about your care team's experience

1. What is your experience treating CML? What else do you treat?
2. What is the experience of those on your team?
3. I would like to get a second opinion. Is there someone you recommend? Who can help me gather all of my records for a second opinion?
4. I would like another pathologist or hematopathologist to review the blood samples. Is there someone you recommend?
5. How many patients like me (of the same age, gender, race) have you treated?
6. Will you be consulting with CML experts to discuss my care? Whom will you consult?
7. How many procedures like the one you're suggesting have you done?
8. Is this treatment a major part of your practice?
9. How often is a complication expected? What are the complications?
10. Who will manage my day-to-day care?

Questions about options

1. What will happen if I do nothing?
2. Which option is proven to work best for my risk group, age, and other factors?
3. Does any option offer a cure or long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?
4. How will treatment affect my fertility? Should I see a fertility specialist before starting treatment?
5. Am I a candidate for a hematopoietic cell transplant (HCT)? What are my options if I don't want an HCT? Will I have more than one HCT?
6. Am I candidate for a clinical trial?
7. What are my options if the treatment stops working?
8. What should I expect from this treatment? How long will treatment last?
9. What will happen if I stop treatment?
10. How will I know when to stop blood transfusions or other treatments?

Questions about treatment

1. What are the treatment choices? What are the benefits and risks?
2. Which treatment will give me the best quality of life? Which treatment will extend life? By how long?
3. Which treatment do you recommend and why?
4. How long do I have to decide? Is there a social worker or someone who can help me decide?
5. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?
6. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
7. How much will the treatment hurt? What will you do to make me comfortable?
8. How much will this treatment cost? What does my insurance cover? Are there any programs to help pay for treatment?
9. How long will treatment take? Will I miss school or work?
10. What should be avoided or taken with caution while receiving treatment?

Questions about side effects

1. What are the side effects of treatment?
2. What can I do to lessen or prevent side effects? What will you do?
3. Are there any life-threatening side effects of this treatment? How will these be monitored?
4. How long will these side effects last? Do any side effects lessen or worsen in severity over time?
5. What side effects should I watch for? What side effects should I expect?
6. When should I call the doctor? Can I text? What should I do on weekends and during non-office hours?
7. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?
8. Will you stop treatment or change treatment if there are side effects?
9. What medicines may worsen side effects of treatment?
10. What are some of the likely permanent side effects that I might have from the treatment?

Questions about pregnancy

1. What should I do to prevent pregnancy during treatment?
2. Is there anything I need to do after treatment to prevent pregnancy?
3. After treatment is over, how long will it take for menstrual periods to begin again?
4. If I am not having periods, should I still use contraceptives?
5. Is pregnancy safe for me after treatment? If so, how long should I wait after treatment to become pregnant?
6. Will I have to stop treatment if I become pregnant? For how long? Are there other treatment options?
7. Can I breastfeed? Will I have to stop treatment while I breastfeed?
8. If I stop treatment during pregnancy or breastfeeding, what does this mean in terms of my survival? Are there other treatment options?

Questions about hematopoietic cell transplants

1. Is a hematopoietic cell transplant an option for me?
2. What do I need to do to prepare?
3. What will you do to prepare?
4. What are the risks to myself and/or the donor?
5. How will the transplant affect my prognosis?
6. How will a transplant affect the quality and length of my life?
7. How long should I expect to be in the hospital?
8. How will I feel before, during, and after the transplant?
9. How many transplants has this center done for CML?
10. What is my risk of developing graft-versus-host disease (GVHD)?

Questions about clinical trials

1. What clinical trials are available for my type of cancer? Are they at your center or office? If they are not at your center or office, will you still follow my care during and after the clinical trial?
2. What are the treatments used in the clinical trial?
3. Has the treatment been used before? Has it been used for other types of leukemia?
4. What are the risks and benefits of this treatment?
5. What side effects should I expect? How will the side effects be controlled?
6. How long will I be in the clinical trial?
7. Will I be able to get other treatments if this doesn't work?
8. How will you know the treatment is working?
9. Will the clinical trial cost me anything? If so, how much?
10. How do I find out about clinical trials that I can participate in? Are there online sources that I can search?

Resources

American Cancer Society (ACS)
cancer.org/cancer/chronic-myeloid-leukemia

cancer.org/content/dam/cancer-org/cancer-control/en/worksheets/pain-diary.pdf

Be The Match®
bethematch.org

Blood & Marrow Transplant Information Network (BMT InfoNet)
bmtinfonet.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

Chemocare
chemocare.com

Leukemia & Lymphoma Society
lls.org/PatientSupport

MedlinePlus
medlineplus.gov/chronicmyeloidleukemia

National Bone Marrow Transplant Link
nbmtlink.org

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

National CML Society
nationalcmlsociety.org

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox

National Financial Resource Directory - Patient Advocate Foundation
patientadvocate.org/explore-our-resources/national-financial-resource-directory

OncoLink
oncolink.org

Patient Access Network Foundation
panfoundation.org

Radiological Society of North America
radiologyinfo.org

Testing.com
testing.com

testing.com/tests/bcr-abl1

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

Words to know

accelerated phase (AP-CML)
The second phase of chronic myeloid leukemia progression, when the number of blast cells is increased.

acute lymphoblastic leukemia (ALL)
A fast-growing cancer that causes too many immature white blood cells called lymphoblasts to be made.

acute myeloid leukemia (AML)
A fast-growing cancer that causes too many immature white blood cells called myeloblasts to be made.

adherence
The extent to which you take your medicine the right way, as explained by your doctor.

advanced phase
A rating of chronic myeloid leukemia, when the number of immature blood cells (blast cells) is high and it is causing symptoms.

allogeneic hematopoietic cell transplant (alloHCT)
A treatment in which the patient receives healthy, immature blood-forming cells from another person to replace damaged or diseased cells in the bone marrow. Also called allogeneic stem cell transplant (SCT).

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

***BCR::ABL1* gene**
An abnormal gene that is formed when the *BCR* gene and *ABL* gene join on the Philadelphia chromosome. Also called *BCR::ABL1* fusion gene.

BCR::ABL1 protein
An abnormal protein that is made by the *BCR::ABL1* fusion gene and causes too many abnormal white blood cells to be made.

blast cell
An immature white blood cell. Can be myeloid or lymphoid.

blast phase (BP-CML)
The final phase of chronic myeloid leukemia, which has the highest number of blast cells in the blood and bone marrow and can be life-threatening. Also called blast crisis.

blood chemistry profile
A test that measures the amounts of many different chemicals in a sample of blood.

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

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

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

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

chemotherapy
Drugs that kill fast-dividing cells, including cancer cells and normal cells.

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

chronic myeloid leukemia (CML)
A slow-growing cancer that starts in the bone marrow and causes too many granulocytes to form.

chronic phase
The first phase of chronic myeloid leukemia, when the number of white blood cells is higher than normal but may not cause symptoms.

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

complete blood count (CBC) with differential
A test of the number of blood cells as well as the different types of white blood cells in a sample.

complete cytogenetic response (CCyR)
When tests don't find any copies of the Philadelphia chromosome.

cytogenetics
The study of chromosomes.

deep complete molecular response (DMR)
No copies of the abnormal *BCR::ABL1* gene are found using a very sensitive test.

donor lymphocyte infusion (DLI)
Procedure in which a person receives white blood cells from the same person who donated blood-forming cells for the hematopoietic cell transplant.

drug interaction
A change in the way a drug acts or works in the body when it is taken with another drug or substance.

drug resistance
When cancer does not respond to a drug treatment.

early molecular response (EMR)
When *BCR::ABL1* is between 10% and 1% at 3 months and 6 months.

flow cytometry
A test that looks at certain substances on the surface of cells to identify the type of cells present.

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

fusion gene
A gene that is made when parts of two separate genes join.

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

graft-versus-host disease (GVHD)
A disease that occurs when transplanted blood stem cells attack a patient's normal cells.

granulocyte
A type of white blood cell that has small particles (granules).

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

hematopathologist
A doctor who specializes in blood diseases by looking at cells under a microscope.

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

hematopoietic cell transplant (HCT)
A treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

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

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

International Scale (IS)
A standardized scale for measuring and reporting results of a very sensitive test that measures the number of cells that have the *BCR::ABL1* gene.

intolerance
When treatment with a drug must be stopped due to severe side effects.

log reduction
A decrease in the number of cells that have the *BCR::ABL1* gene.

lumbar puncture (LP)
A procedure that removes spinal fluid. Also called a spinal tap.

lymphoid
Referring to a type of white blood cell called a lymphocyte.

major molecular response (MMR)
An improvement related to treatment, when tests detect a 3-log reduction in *BCR::ABL1* levels. It means that there are 1,000 times fewer cells with the *BCR::ABL1* gene than the standardized baseline level.

molecular response
An improvement related to treatment, when tests detect a decrease in the number of cells that have the *BCR::ABL1* gene.

mutation testing
A test that looks for abnormal changes in genes (the coded instructions in cells for making and controlling cells).

myeloid
Referring to a type of white blood cell called a granulocyte.

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

Philadelphia chromosome (Ph)
An abnormal, short chromosome 22 that is formed when parts of chromosomes 9 and 22 switch with each other. It is the hallmark of chronic myeloid leukemia and contains the *BCR::ABL1* gene.

prognosis
The likely or expected course and outcome of a disease.

quantitative reverse transcriptase polymerase chain reaction (qPCR)
A very sensitive test that measures the number of cells in the blood or bone marrow that have the *BCR::ABL1* gene.

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

remission
There are minor or no signs of a disease.

resistance
When cancer does not respond to a drug treatment.

secondary resistance
When cancer responds to a drug at first, but then stops responding after a period of time.

second-line treatment
The next treatment used against a disease after the first treatment failed or had to be stopped.

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

spleen
An organ to the left of the stomach that helps protect the body from disease.

stem cell transplant (SCT)
A treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells.

steroid
A drug used to reduce swelling, pain, and redness.

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

targeted therapy
Treatment with drugs that target a specific or unique feature of cancer cells.

transfusion
Replacing lost blood with new blood.

translocation
When pieces of two chromosomes (long strands of coded instructions for controlling cells) break off and switch with each other.

treatment response
An outcome or improvement in disease that is caused by treatment.

tyrosine kinase
A type of protein in cells that sends signals that tell cells when to grow and divide to make new cells.

tyrosine kinase inhibitor (TKI)
A type of drug that attaches to the BCR::ABL1 protein so that it can't send growth signals.

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

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

NCCN.org/patients/comments

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Myeloid Leukemia, Version 1.2023. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

Tanya Fischer, MEd, MSLIS
Senior Medical Writer

Susan Kidney
Senior Graphic Design Specialist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Myeloid Leukemia, Version 1.2023 were developed by the following NCCN Panel Members:

*Neil P. Shah, MD, PhD/Chair
UCSF Helen Diller Family Comprehensive Cancer Center

Ravi Bhatia, MD/Vice-Chair
O'Neal Comprehensive Cancer Center at UAB

Jessica K. Altman, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Maria Amaya, MD, PhD
University of Colorado Cancer Center

Kebede H. Begna, MD
Mayo Clinic Cancer Center

Ellin Berman, MD
Memorial Sloan Kettering Cancer Center

Robert H. Collins, Jr., MD
UT Southwestern Simmons Comprehensive Cancer Center

Peter T. Curtin, MD
City of Hope National Medical Center

Daniel J. DeAngelo, MD, PhD
Dana-Farber/Brigham and Women's Cancer Center

Jason Gotlib, MD, MS
Stanford Cancer Institute

*Gabriela Hobbs, MD
Massachusetts General Hospital Cancer Center

Hagop M. Kantarjian, MD
The University of Texas MD Anderson Cancer Center

Lori Maness, MD
Fred and Pamela Buffett Cancer Center

Monica Mead, MD
UCLA Jonsson Comprehensive Cancer Center

Leland Metheny, MD
Case Comprehensive Cancer Center University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Sanjay Mohan, MD, MSCI
Vanderbilt-Ingram Cancer Center

Joseph O. Moore, MD
Duke Cancer Institute

Vivian Oehler, MD
Fred Hutchinson Cancer Center

Keith Pratz, MD
Abramson Cancer Center at the University of Pennsylvania

Iskra Pusic, MD, MSCL
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Michal G. Rose, MD
Yale Cancer Center/ Smilow Cancer Hospital

*B. Douglas Smith, MD
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Kendra L. Sweet, MD, MS
Moffitt Cancer Center

Moshe Talpaz, MD
University of Michigan Rogel Cancer Center

Tiffany N. Tanaka, MD
UC San Diego Moores Cancer Center

James Thompson, MD, MS
Roswell Park Comprehensive Cancer Center

Jennifer Vaughn, MD, MSPH
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Jeanna Welborn, MD
UC Davis Comprehensive Cancer Center

David T. Yang, MD
University of Wisconsin Carbone Cancer Center

NCCN Staff

Kristina Gregory, RN, MSN, OCN
Vice President, Clinical Information Programs

Hema Sundar, PhD
Manager, Global Clinical Content

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

NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • *pennmedicine.org/cancer*

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • *cityofhope.org*

Dana-Farber/Brigham and Women's
Cancer Center | Massachusetts
General Hospital Cancer Center
Boston, Massachusetts
617.732.5500 • *youhaveus.org*
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • *dukecancerinstitute.org*

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • *foxchase.org*

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • *unmc.edu/cancercenter*

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • *fredhutch.org*

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073 • *huntsmancancer.org*

Indiana University
Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • *www.cancer.iu.edu*

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • *moffitt.org*

O'Neal Comprehensive
Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • *uab.edu/onealcancercenter*

Robert H. Lurie Comprehensive Cancer
Center of Northwestern University
Chicago, Illinois
866.587.4322 • *cancer.northwestern.edu*

Roswell Park Comprehensive
Cancer Center
Buffalo, New York
877.275.7724 • *roswellpark.org*

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

St. Jude Children's
Research Hospital/
The University of Tennessee
Health Science Center
Memphis, Tennessee
866.278.5833 • *stjude.org*
901.448.5500 • *uthsc.edu*

Stanford Cancer Institute
Stanford, California
877.668.7535 • *cancer.stanford.edu*

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

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The University of Texas
MD Anderson Cancer Center
Houston, Texas
844.269.5922 • *mdanderson.org*

UC Davis
Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • *cancer.ucsd.edu*

UCLA Jonsson
Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • *cancer.ucla.edu*

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • *cancer.ucsf.edu*

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • *coloradocancercenter.org*

University of Michigan
Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • *rogelcancercenter.org*

University of Wisconsin
Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • *uwhealth.org/cancer*

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • *utsouthwestern.edu/simmons*

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • *vicc.org*

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • *yalecancercenter.org*

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DR SHIVAM SHINGLA

BSES MG Hospital (Andheri):
9 am to 10 am (Monday to Friday)
Nanavati Max Hospital (Vile Parle):
10 am to 12 pm (Monday to Saturday)
S. L. Raheja Hospital (Mahim):
12 pm to 4 pm (Monday to Saturday)
Suvarna Hospital (Borivali):
5 pm to 6 pm (Monday and Friday)
Sushrut Hospital (Chembur):
By appointment
Hinduja Hospital (Khar): By appointment
Galaxy Healthcare (Borivali): By appointment

www.drshivamshingla.com

drshivamshingla@gmail.com

+91 98925 96286

#Reference From NCCN Guidelines