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✓ Step-by-step guides to the cancer care options likely to have the best results
✓ Based on treatment guidelines used by health care providers worldwide
✓ Designed to help you discuss cancer treatment with your doctors

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Chronic myeloid leukemia (CML) is caused by a mutation 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 the abnormal chromosome 22 called the Philadelphia chromosome.

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

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

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.
**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 stem cells (hematopoietic stem cells). All types of blood cells start as blood stem cells. At any given time, bone marrow will have cells in various stages of development, from very immature to almost fully mature. With each stage, the blood stem cell changes and gets closer to what it is meant to be. After a blood stem cell develops into a red blood cell, white blood cell, or platelet, it is released in your bloodstream as needed.

Blood stem cells can copy themselves or self-renew. These cells are rare. Blood stem cells can also make new cells that are committed to becoming a certain type of blood cell. These are called progenitor cells or precursor cells. Progenitor cells are much more common than blood stem cells. Progenitor cells can become red blood cells, white blood cells, or platelets.

There are different types of progenitor cells:

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

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**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.
CML basics

Chronic myeloid leukemia

CML is thought to arise in a stem or early progenitor cell and lead to growth in myeloid progenitor cells. Blast phase CML can arise in either lymphoid or myeloid progenitor cells.

Blasts

A blast is an immature 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.

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. 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 form from myeloblasts.

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.

Philadelphia chromosome

The Philadelphia chromosome is formed by a translocation between parts of chromosomes 9 and 22. It contains the abnormal BCR-ABL1 fusion gene.
1 CML basics

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 the creation of the Philadelphia chromosome. Philadelphia chromosome is the hallmark of CML.

**Philadelphia chromosome**

All cells in our body contain genetic information organized in 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 translocation. It can result in a fusion gene. *BCR-ABL1* is a gene fusion 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). You might see it referred to as 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: *BCR-ABL1*. Proteins are not italicized: BCR-ABL1.

Some people have very low levels of *BCR-ABL1*, but do not have CML. If you do not have certain levels of the Philadelphia chromosome or the *BCR-ABL1* gene, you do not have CML. However, other chronic leukemias such as Philadelphia-negative (Ph-) myeloproliferative neoplasms are possible.

More information can be found in *NCCN Guidelines for Patients: Myeloproliferative Neoplasms*, available at NCCN.org/patientguidelines.
Three phases of CML

The 3 phases of CML are:

- Chronic
- Accelerated
- Blast

Phases are based on the number 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.

**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 3 out of every 20 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 tends to respond 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 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.

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 blast phase CML (BP-CML) is based on if the blasts are myeloid or lymphoid.
Review

- Chronic myeloid leukemia (CML) is a type of myeloproliferative neoplasm (MPN).
- Usually in CML, there are too many granulocytes. Granulocytes are a type of white blood cell that form from myeloblasts. Myeloblasts are an immature white blood cell. 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 chromosome 22. The abnormal chromosome 22 is 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 that 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.
2
Testing for CML

14  Test results
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Accurate testing is needed to diagnose and treat CML. This chapter presents an overview of possible tests and what to expect.

Test results

Test results will 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 test results.

Whether you are going for a second opinion, test, or office visit, keep these things in mind:

- 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 let 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 fridge or keep it in a place where someone can access it in an emergency.

Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer.
- Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and test results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments. You never know when you might need it!
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, herbs, or supplements you take. Tell your doctor about any symptoms you have. A medical 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 about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Guide 1
Testing for CML
Medical history and physical exam that includes spleen size
- CBC with differential
- Chemistry profile
- Bone marrow aspirate and biopsy
- Cytogenetic testing
- qPCR using IS for BCR-ABL1 found in blood
- Hepatitis B panel

Physical exam
During a physical exam a health care provider may:
- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you
- 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. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell the doctor if you have felt any lumps or have any pain.
- Feel below your ribcage to see if your spleen is enlarged. An enlarged spleen is one sign of CML.

Doctors should perform a thorough physical exam along with a complete health history. See Guide 1.
Fertility and pregnancy

CML survivors of both sexes are at risk for fertility issues. Fertility is the ability to have children. To preserve one’s fertility, action may be needed before starting cancer treatment. Your doctor should discuss fertility preservation with those of childbearing age before starting CML treatment.

You might be referred to a fertility specialist to discuss the options. More information can be found in NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer, available at NCCN.org/patientguidelines.

Those with ovaries
Those who can have children will have a pregnancy test before starting treatment. Cancer treatment can hurt the baby if you are or become pregnant during treatment. Some types of treatment can also cause a miscarriage. Therefore, birth control to prevent pregnancy during and after treatment is recommended. Hormonal birth control may not be recommended, so ask your doctor about options.

Those with testicles
Cancer and cancer treatment can damage sperm. However, the best available evidence indicates that most of the standard treatments for chronic phase CML do not affect male fertility or result in birth defects in the children of men who are on these treatments. If you think you want children in the future, talk to your doctor now. Sperm banking may be an option.

Infertility
Infertility is the complete loss of the ability to have children. The actual risk of infertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Chemotherapy with alkylating agents has a higher risk of infertility. Sometimes, there isn’t time for fertility preservation before you start treatment. Talk to your doctor about your concerns.

Planning a pregnancy
Talk with your doctor if you are planning to become pregnant now or in the future. This might affect treatment options. Certain treatments for CML will need to be avoided if you are pregnant or breastfeeding.

Treatment during pregnancy
Certain treatments for CML will need to be avoided if you are pregnant or breastfeeding.

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.
Testing for CML

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

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. Red blood cells carry oxygen throughout your body, while white blood cells fight infection, and platelets control bleeding. CML often causes a high WBC count and/or platelet count, but can sometimes cause low counts of other blood cells.

Differential
There are 5 types of white blood cells: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of white blood cell (WBC). It also checks if the counts are in balance with each other.

Chemistry profile
A chemistry profile or panel measures different substances in your blood. The liver, bone, and other organs release chemicals in your blood. A chemistry profile measures these levels.

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 hepatitis B to reactivate, which can cause liver damage.

HLA typing
A human leukocyte antigen (HLA) is a protein found on the surface of most cells. It plays 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 white blood cells 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 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.
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.

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.

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.

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.

Uric acid
Uric acid is released by cells when DNA breaks down. It is a normal waste product that dissolves in your 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. High uric acid might be a side effect of chemotherapy. Very high levels of uric acid in the blood can damage the kidneys.

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.

**Tissue tests**

A biopsy is the removal of a sample of tissue or group of cells for testing. Your 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.

**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

**Bone marrow biopsy**

Samples of bone and marrow are removed in a 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 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.

**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 path 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 tell cells what to do and what to become.

CML can cause changes in genes and chromosomes in blood cells. Genetic tests look for these changes or abnormalities. 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, re-arranged, or extra chromosomes. One of the two copies of chromosome 22 is abnormal in CML cells. Testing looks for this abnormal chromosome (Philadelphia chromosome), which is used to diagnose and to help determine the CML phase. Results help confirm CML and predict the path it will take. This is called a prognosis.

Bone marrow cytogenetics is recommended at diagnosis, if treatment milestones aren't reached, or with any sign of relapse.
There are 2 types of cytogenetic tests used in CML:

- **Karyotype**
- **FISH**

### Karyotype

A karyotype is a picture of chromosomes. Doctors look for whether 46 chromosomes or 23 pairs are present. They also look for extra, missing, or abnormal pieces of chromosomes, such as the **BCR-ABL1** gene. Since a karyotype usually requires growing cells, a sample of bone marrow is needed. Sometimes (especially with newly diagnosed CML), enough growing cells can be found in the peripheral blood to allow a karyotype.

### 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. Sometimes, a bone marrow sample is needed to get all the information your doctor needs to help plan your care.
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 lab process that can make millions or billions of copies of DNA (genetic information). PCR is very sensitive. It can find 1 leukemia cell among more than 100,000 normal cells. This test can be performed on either blood or bone marrow.

qPCR (IS)
A special PCR called quantitative reverse transcriptase polymerase chain reaction (qPCR) is used in CML. It measures the number of cells with 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 doctor 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
Mutation testing includes tests of genes or their products (proteins). 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.

Mutation testing can be performed on blood or bone marrow. It should be done prior to starting treatment for advanced phase CML or if the qPCR (IS) results increase more than 10 times the lowest measured level.

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. 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.

Lumbar puncture
A lumbar puncture (LP) or spinal tap is a procedure that removes spinal fluid. It is also used to inject chemotherapy into the spinal fluid called intrathecal (IT) chemotherapy. Sometimes, CML can travel to the cerebrospinal fluid (CSF) that surrounds the spine or brain. A lumbar puncture might be used to rule out leukemia cells in the CSF or to prevent central nervous system (CNS) disease. When IT therapy is given together to prevent CNS disease, it is called CNS prophylaxis. An LP is usually reserved for those with blast phase (blast crisis).
Review

- Blood tests check for signs of disease, how well organs are working, and treatment results.
- Those who can become pregnant will be given a pregnancy test before treatment begins.
- Treatment may affect fertility or the ability to have children.
- Talk to your doctor if you are or plan to become pregnant. Certain treatments for CML will need to be avoided if you are pregnant or breastfeeding.
- A biopsy is the removal of a sample of tissue or group of cells for testing. A diagnosis of CML is confirmed using either a bone marrow aspirate or bone marrow biopsy.
- Genetic tests are used to learn more about your CML, to target treatment, and to determine the likely path your cancer will take (prognosis).
- As CML progresses, it can mutate. Therefore, you might have mutation testing before treatment for advanced CML.
- 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.
- Heart or cardiac tests are used to see how well your heart works. These tests might be used to monitor treatment side effects.
- Leukemia can travel to the cerebrospinal fluid (CSF) that surrounds the spine or brain.

A bone marrow aspirate or biopsy is needed to diagnose CML.
3 Treatment options

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28 Chemotherapy
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29 Stem cell transplant
31 Clinical trials
32 Supportive care
35 Review
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.

Targeted therapy

Targeted therapy is a form of systemic therapy that travels throughout your body. It is a drug 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):

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

TKIs are divided into first, second, and even third generation. Each generation of a drug gets more specific and better at targeting certain mutations. This means that next-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 doctor. 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 doctor 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 problems, liver problems, and kidney failure. Do not take TKIs while pregnant or breastfeeding. Talk to your doctor first before stopping any TKI.

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.

Did you know?
The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

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.

### 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 medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is very important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. **Bring a list with you to every visit.**

### Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. All chemotherapies affect the instructions (genes) that tell cancer cells how and when to grow and divide. 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.
Stem cell transplant

A stem cell transplant (SCT) replaces bone marrow stem cells. You might hear it called a hematopoietic cell transplant (HCT) or a bone marrow transplant (BMT). This book will refer to it as SCT.

There are 2 types of SCTs:

- 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 SCT (allo-SCT) is used as a treatment option for CML. It is usually reserved for those with blast phase (blast crisis). An SCT depends upon donor availability and your health at the time of potential SCT. The steps of an allo-SCT are described next.

**Conditioning**

Before an SCT, 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 won’t kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

Transfusions

A transfusion is a common procedure to replace blood or blood components (red blood cells or platelets). It is given to you 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 people 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 doctor for specific information about your risks.
- Chemotherapy 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.
Transplanting stem cells
After conditioning, you will receive the healthy stem cells through a transfusion. 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 about the possible side effects or complications of SCT and how this might affect your quality of life.

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
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 treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your treatment team about whether a clinical trial might make sense for you.

Phases
Most cancer clinical trials focus on treatment. Treatment trials are done in phases that build on one another.

- **Phase I trials** study the safety and side effects of an investigational drug or treatment approach.
- **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.

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 treatment is as safe as possible.

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. This information is also described in detail in an informed consent form. Giving informed consent means that you understand the possible benefits and risks and agree to join. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others 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 doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

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.

What if I get the placebo?
A placebo is an inactive version of a real medicine. Placebos are almost never used alone in cancer clinical trials. All participants receive cancer treatment. You may receive a commonly used treatment, the investigational drug, or both.

Do I have to pay to be in a clinical trial?
Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.

Supportive care
Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves your quality of life. 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. Some common side effects are described next.

Depression
Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt. Talk to your doctor and with those whom you feel most comfortable about how you are feeling. There are services and people who can help you. Support and counseling are available.

For more information, read NCCN Guidelines for Patients: Distress During Cancer Care, available at NCCN.org/patientguidelines.
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.

Fatigue
Fatigue is common in those undergoing cancer treatments and can be worsened by some types of chemotherapy. Exercise, yoga, and massage therapy can help. You might be referred to a nutritionist or dietician. Talk to your care team about your fatigue.

Infection
You will be monitored for infection. In 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 chemotherapy.

For more information, read the NCCN Guidelines for Patients: Anemia and Neutropenia, available at NCCN.org/patientguidelines.

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.

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

For more information, read the NCCN Guidelines for Patients: Nausea and Vomiting, available at NCCN.org/patientguidelines.
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.

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
• Describe 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?
• Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt).
• Does pain get in the way of doing the things you enjoy?
Review

- Targeted therapy focuses on specific or unique features of cancer cells.
- 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-growing cells throughout the body, including cancer cells and normal cells.
- An allogeneic stem cell transplant (SCT) replaces bone marrow stem cells with healthy cells from a donor who may or may not be related to you.
- 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.
- All cancer treatments can cause unwanted health issues called side effects.

Tell your doctor about any medicines, vitamins, over-the-counter drugs, herbals, or supplements you are taking.
4 Risk groups

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37 Risk groups
38 Primary treatment
38 Monitoring
39 Response types
40 Response milestones
41 Second-line treatment
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NCCN Guidelines for Patients®:
Chronic Myeloid Leukemia, 2021
In chronic phase CML (CP-CML), there is an increased number of granulocytes in the blood, bone marrow, or both. Chronic phase CML is treatable. Together, you and your doctor 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 3 out of every 20 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 is with 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 your doctor 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

Your doctor will also consider:

- If you have any other serious health issues called comorbidities
- Side effects and toxicity of a 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 preference

### 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 TKIs (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 possible. However, imatinib is generally not favored.

### 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 $BCR-ABL1$. You will have a qPCR (IS) at diagnosis and every 3 months once you start treatment. After $BCR-ABL1$ (IS) is 1% or less, qPCR (IS) is recommended every 3 months for 2 years, then every 3 to 6 months. It is very important to keep up with testing and doctor visits.
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 0.11% would be a 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) • 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) • 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) • 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 a 3-log or more decrease in BCR-ABL1 if qPCR (IS) not used
• 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 means $BCR-ABL1$ is 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. $BCR-ABL1$ is at 0.01% or less.

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 skipped any doses
- Are taking any medicines, over-the-counter drugs, herbals, or supplements

It is very important to tell your doctor about any teas you drink and any supplements you take. It might be one reason your treatment is not working. Another reason might be that your CML has a new gene mutation. You doctor will consider this and order any mutation or cytogenetic 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.

In the guide below:

- Green shows milestones have been reached.
- Light green milestone is based on the treatment goal.
- Yellow shows areas of concern.
- Red shows failure to reach milestones.

### Guide 4
**Treatment milestones using BCR-ABL1 (IS)**

<table>
<thead>
<tr>
<th></th>
<th>at 3 months</th>
<th>at 6 months</th>
<th>at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BCR-ABL1 (IS) is more than 10%</strong></td>
<td>Possible TKI resistance</td>
<td>TKI resistance</td>
<td>TKI resistance</td>
</tr>
<tr>
<td><strong>BCR-ABL1 (IS) is between 10% and 1% (EMR)</strong></td>
<td>Milestone met</td>
<td>Milestone met</td>
<td>Possible TKI resistance</td>
</tr>
</tbody>
</table>
| **BCR-ABL1 (IS) is between 1% and 0.1% (CCyR)** | Milestone met | Milestone met | • 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)** | Milestone met | Milestone met | Milestone met |
Possible TKI resistance (yellow)
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 genetic and mutation testing before continuing treatment.

Treatment options are:

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

TKI resistance (red)
If the number of $BCR-ABL1$ (IS) cells is more than 10% after 6 or 12 months, it means that treatment milestones were not met or maintained. The option is to switch to another TKI and discuss if SCT is right for you. You may talk with a transplant expert. You might have additional mutation testing.

Milestones reached (green)
If milestones have been reached, you will stay on your TKI. It’s very important not to stop or skip taking your medicine. Missing doses allows the leukemia cells to grow. Monitoring will continue.

Milestones might have been reached (light green)
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
- Treatment-free remission (TFR), then milestone is not met.

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 doctor 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.

To stop TKI therapy, you must meet all the following conditions:

- 18 years of age or over
- In chronic phase CML with no history of accelerated or blast phase CML
- Taking a TKI for at least 3 years
- Tests showed that you had the $BCR-ABL1$ gene at one time
- Stable molecular response (MR4) with $BCR-ABL1$ of 0.01% or less for 2 or more years on at least 4 tests, done at least 3 months apart
- Access to a reliable qPCR test using IS with at least a MR4.5 sensitivity (0.00316% or better), that can provide test results within 2 weeks
- Regular monitoring starting with once a month
Frequent monitoring is needed for those in remission who have stopped taking TKI therapy. You will have tests more often than before. This is to make sure that your \( BCR-ABL1 \) levels stay low. If the \( BCR-ABL1 \) level increases past 0.1%, you will restart treatment. There is a chance that your cancer might return (relapse) if you stop taking the targeted therapy. Ask your doctor about the risks.

**Review**

- 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 3 out of every 20 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.
5

Advanced phase

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46 Accelerated phase
47 Blast phase
48 Stem cell transplant
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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 stem cell transplant (SCT) would follow any treatment for the best chance of remission. Together, you and your doctor will choose a treatment plan that is best for you.

**Testing**

For advanced phase CML, specific tests are required. Some of these tests will reveal more about the CML you have. Other tests are needed for certain treatments. You will have flow cytometry to determine the type of blast (myeloid or lymphoid), mutation testing, and HLA testing if a blood stem cell transplant (SCT) is an option. A lumbar puncture will be considered. This is to rule out lymphoid-blast phase CML.

Before treatment, you will have tests to confirm the phase of CML. For definitions of advanced phase CML, see Guide 5.

### Guide 5

**Definition of advanced phase CML**

<table>
<thead>
<tr>
<th>Accelerated</th>
<th>Any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Blood myeloblasts are between 15% and 29%</td>
</tr>
<tr>
<td></td>
<td>• Blood myeloblast and promyelocyte total 30% or more</td>
</tr>
<tr>
<td></td>
<td>• Blood basophils are 20% or more</td>
</tr>
<tr>
<td></td>
<td>• Platelet count is 100 x 10⁹/L or less</td>
</tr>
<tr>
<td></td>
<td>• Additional mutations are found in Ph+ cells</td>
</tr>
<tr>
<td></td>
<td>• Any increase in lymphoblasts is a concern that blast phase is beginning</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blast</th>
<th>Any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• 30% or more blasts are found in blood, marrow, or both</td>
</tr>
<tr>
<td></td>
<td>• Blast cells are found in tissues and organs outside the bone marrow or blood</td>
</tr>
</tbody>
</table>
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. Some targeted therapies will work on certain mutations, while others will not. Therefore, the TKI chosen will be based on the type of gene mutation(s). Ask your doctor 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 doctor 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 stem cell transplant (SCT)?
- Is there any leukemia in your central nervous system (CNS)?
- What gene 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 blasts and white blood cells is also 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 SCT is likely needed. For treatment options, see Guide 6.

Guide 6
Treatment options: Accelerated phase

Clinical trial

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<table>
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<th>Used in some cases</th>
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<tbody>
<tr>
<td>• Omacetaxine</td>
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</table>
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 and CNS prophylaxis is recommended for lymphoid blast phase.

An allogeneic (donor) stem cell transplant would follow blast phase treatment. Treatment options can be found in Guide 7.

More information on ALL-type induction therapies can be found in NCCN Guidelines for Patients: Acute Lymphoblastic Leukemia, available at NCCN.org/patientguidelines.

More information on AML-type induction therapies can be found in NCCN Guidelines for Patients: Acute Myeloid Leukemia, available at NCCN.org/patientguidelines.

Guide 7
Treatment options: Blast phase

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<td>• TKI with steroids</td>
<td>• TKI</td>
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Stem cell transplant

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

How your body responds to an allo-SCT is based on age, if you have other serious health issues (comorbidities), donor type, and transplant center. You will have qPCR (IS) after an SCT 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 means $BCR-ABL1$ is 1% or less.

CCyR
If the stem cell transplant causes CCyR, then 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 if you had accelerated or blast phase CML before.

Not in CCyR or in relapse
If Philadelphia chromosomes or $BCR-ABL1$ genes remain, or CML has returned, then treatment options include:

- TKI
- TKI with donor lymphocyte infusion (DLI) or omacetaxine
- Clinical trial

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

- 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 the 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) blood stem cell transplant (SCT) 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 SCT as part of the overall plan.

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
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 doctor.

It’s your choice

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

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

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

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from school, family, 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 doctor. 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. With telehealth, it is easier than ever to get a second opinion without leaving your home.

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 resources listed in this book.

Questions to ask your doctors

Possible questions to ask your doctors 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 to ask 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 are they done?
Questions to ask your doctors about their experience

1. What is your experience treating CML?

2. What is the experience of those on your team?

3. Do you only treat CML? What else do you treat?

4. I would like to get a second opinion. Is there someone you recommend?

5. I would like another pathologist or hematopathologist to review the blood samples. Is there someone you recommend?

6. How many patients like me (of the same age, gender, race) have you treated?

7. Will you be consulting with CML experts to discuss my care? Whom will you consult?

8. How many procedures like the one you’re suggesting have you done?

9. Is this treatment a major part of your practice?

10. How many of your patients have had complications? What were the complications?
Questions to ask about options

1. What will happen if I do nothing?

2. How do age, white blood cell (WBC) count, health, and other factors affect the options?

3. How will treatment affect my fertility? Should I see a fertility specialist before starting treatment?

4. Am I a candidate for a stem cell transplant (SCT)? What are my options if I don’t want an SCT? Will I have more than one SCT?

5. Am I candidate for a clinical trial?

6. Which option is proven to work best for my risk group, age, and other factors?

7. 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?

8. How do you know if treatment is working? How will I know if treatment is working?

9. What are my options if the treatment stops working?

10. Are there any life-threatening side effects of this treatment? How will these be monitored?

11. What should I expect from this treatment? How long will treatment last?

12. Can I stop treatment at any time? What will happen? How will I know when to stop blood transfusions or other treatments?
Questions to ask about treatment

1. What are the treatment choices? What are the benefits and risks?

2. Which treatment do you recommend and why?

3. How long do I have to decide?

4. 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?

5. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?

6. How much will the treatment hurt? What will you do to make me comfortable?

7. How much will this treatment cost? What does my insurance cover? Are there any programs to help pay for treatment?

8. What kind of treatment will I do at home? What can I do to prepare our home to ensure my safety or the safety of other family members in the household?

9. What can I do to prevent or relieve side effects? What will you do?

10. Which treatment will give me the best quality of life? Which treatment will extend life? By how long?

11. Will I miss school or work?

12. What should be avoided or taken with caution while receiving treatment?
Questions to ask about fertility preservation

1. What can I do now to preserve my fertility?

2. What are my fertility preservation options?

3. Will any of the options affect my cancer treatment?

4. Which options will delay cancer treatment? If so, for how long?

5. Will fertility treatments increase the risk that the cancer may return?

6. How much will these fertility preservation options cost?

7. Which fertility preservation options are covered by insurance?

8. Can you refer me to a specialist who can help preserve my fertility?

9. Are there other ways to treat this cancer that will not affect my fertility?

10. How will I know if I am fertile when treatment is over? Are there tests that I can take?

11. What will be done to protect my fertility during treatment?

12. Where can I find support for coping with fertility issues?
Questions to ask about pregnancy

1. What should I do to protect from pregnancy during treatment?

2. Is there anything I need to do after treatment to protect from 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 to ask about clinical trials

1. What clinical trials are available? Are we eligible for any of them? Why or why not?

2. What are the treatments used in the clinical trial?

3. What does the treatment do?

4. Has the treatment been used before? Has it been used for other types of cancer?

5. What are the risks and benefits of this treatment?

6. What side effects should I expect? How will the side effects be controlled?

7. How long will I be on the clinical trial?

8. Will I be able to have other treatment if this doesn’t work?

9. How will you know the treatment is working?

10. Will the clinical trial cost me anything? If so, how much?
Resources

American Association for Clinical Chemistry
labtestsonline.org
labtestsonline.org/tests/bcr-abl1

American Cancer Society
cancer.org/cancer/chronic-myeloid-leukemia
cancer.org/content/dam/cancer-org/cancer-control/en/worksheets/pain-diary.pdf

Be The Match®
bethematch.org

Bone Marrow & Transplant Information Network
bmtinfonet.org

CancerCare
cancercare.org

Chemocare
chemocare.com

Leukemia & Lymphoma Society
LLS.org/leukemia

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

OncoLink
oncolink.org

Radiological Society of North America
radiologyinfo.org

share with us.

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

NCCN.org/patients/comments
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 (allo-HCT)**
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-growing 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 the patient receives white blood cells from the same person who donated blood-forming cells for the stem 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).
**Words to know**

**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.

**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
A type of blood cell that helps fight infections in the body.
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Chronic Myeloid Leukemia

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