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Chronic Myeloid Leukemia

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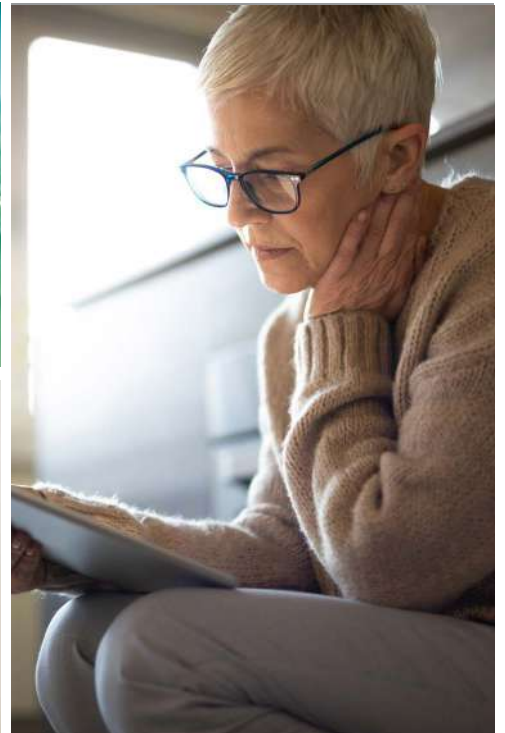
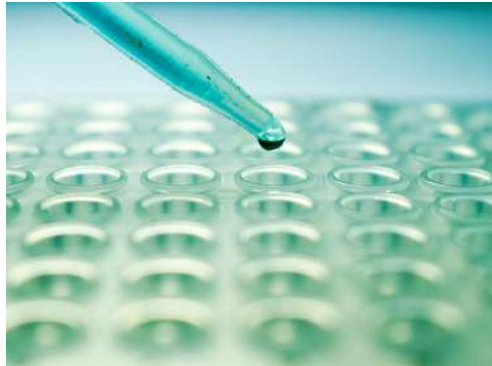
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CML basics

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Chronic myeloid leukemia (CML) is a slow-growing blood cancer that starts in the blood stem cells of bone marrow. In CML, there are too many white blood cells. A chromosome change called the Philadelphia chromosome is found in CML. This happens when a piece of chromosome 9 and a piece of chromosome 22 break off and trade places with each other. The result is a fused gene called *BCR-ABL1*.

Blood

Chronic myeloid leukemia (CML) is a slow-growing 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. 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.

Blood cells

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 germs. Platelets help control bleeding.

Blood cells don't live forever. Many have a short lifespan. Some white blood cells live less than one day. Your blood cells are being replaced in your body all the time.

How blood cells are formed

Bone marrow is the sponge-like tissue in the center of most bones. Inside your bone marrow are cells that make blood. These cells are called blood stem cells (hematopoietic stem cells). All types of blood cells start as blood stem cells.

A blood stem cell has to mature or go through many stages to become a red blood cell, white blood cell, or platelet. 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 do 2 things:

- Make exact copies of themselves
- Make new cells that have the potential to become blood cells

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 being a certain type of blood cell. These are called progenitor 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 2 types of blood progenitor cells:

- Lymphoid
- Myeloid

Lymphoid refers to lymphocyte, a type of white blood cell. Myeloid refers to bone marrow. 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 white blood cell.

Lymphoid progenitor cells

Lymphoid progenitor cells develop into a type of white blood cell called lymphocytes. Lymphocytes are released from bone marrow into the bloodstream.

Myeloid progenitor cells

Myeloid progenitor cells develop into white blood cells, red blood cells, and platelets. These cells are released from bone marrow into the bloodstream.

White blood cells, called granulocytes, are different than the white blood cells produced by lymphoid progenitor cells. CML produces too many granulocytes.

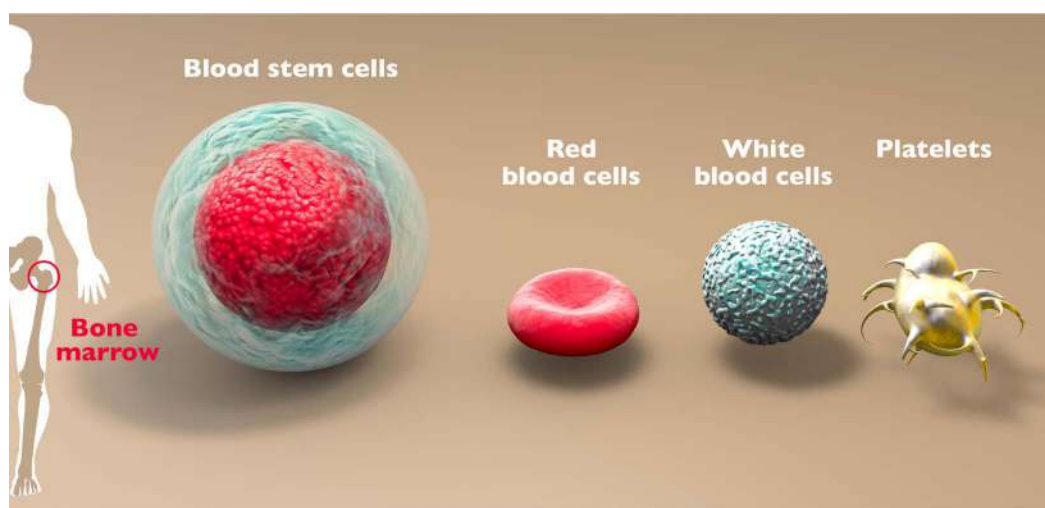
Granulocytes include:

- Neutrophils
- Eosinophils
- Basophils

CML starts in the myeloid progenitor cells. However, blast phase CML can start in either lymphoid or myeloid progenitor cells.

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.



Chronic myeloid leukemia

Cancer is a disease that starts in the cells of your body. Leukemia is cancer of the white blood cells.

There are different types of leukemia, which include:

- Acute lymphocytic leukemia (ALL)
- Acute myeloid leukemia (AML)
- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)

CML is a type of myeloproliferative neoplasm (MPN). MPNs are a group of rare blood cancers that start in the myeloid progenitor cells. “Myelo” means marrow. “Proliferative” means growing and refers to making too many cells. A neoplasm is any abnormal growth. MPNs make too many blood cells, making it difficult for blood to do its work.

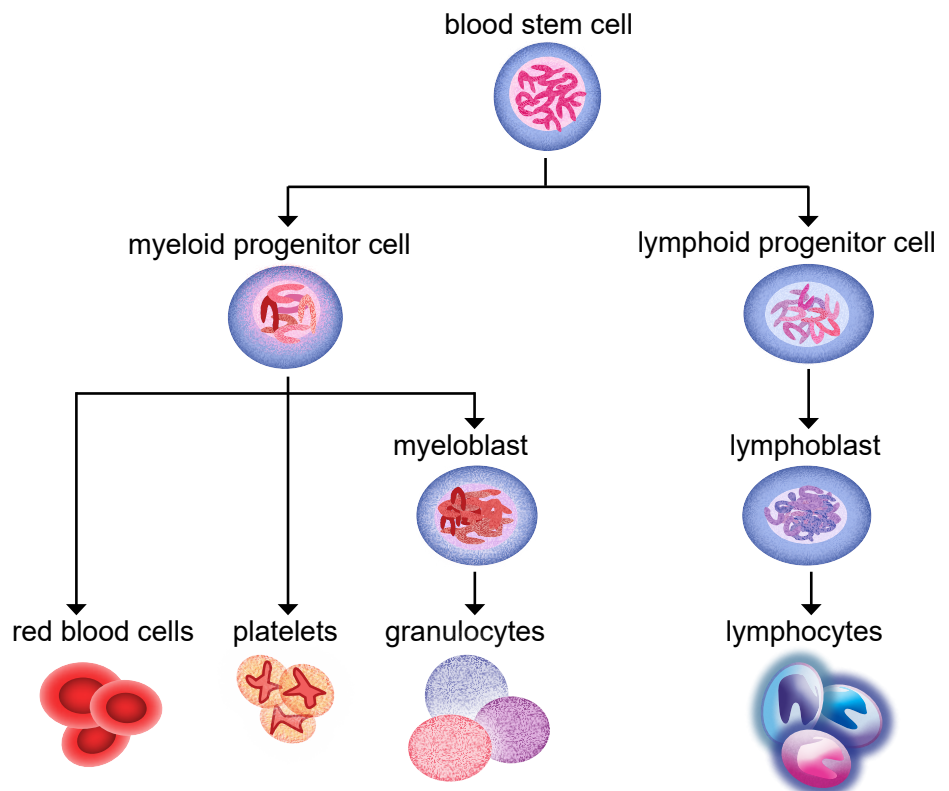
In CML, there are too many granulocytes, in particular neutrophils. Other cell counts that can be high include basophils and eosinophils. “Chronic” means this cancer worsens slowly.

The average age at diagnosis is about 67 years of age. However, CML occurs in all age groups.

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.

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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 is when parts of two chromosomes break off and switch with each other. This is called a translocation. It can result in a fusion gene. Genes tell cells what to become and what to do.

In the Philadelphia chromosome, a piece of chromosome 9 and a piece of chromosome 22 break off and trade places with each other. These pieces then fuse together on chromosome 22. This new, abnormal chromosome 22 is referred to as the Philadelphia chromosome. You might see it written as Ph-positive (Ph+).

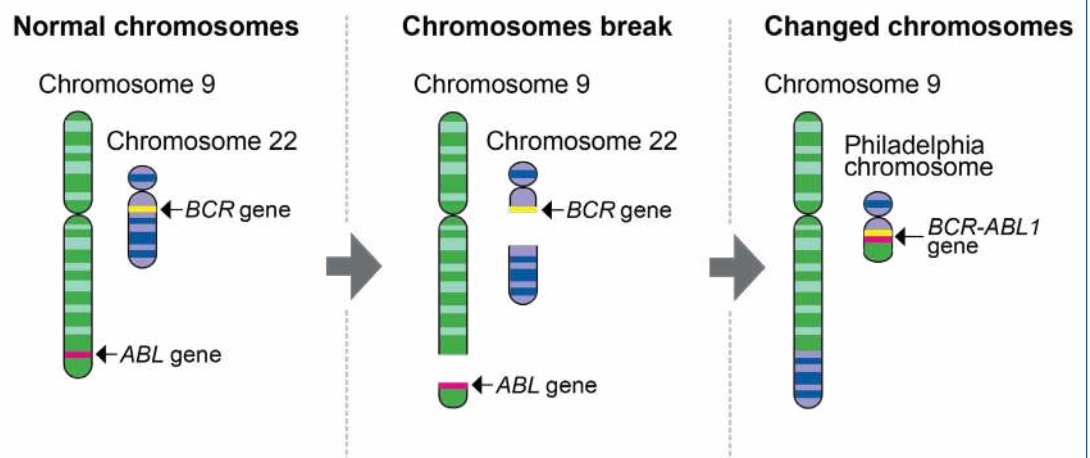
The piece of chromosome 9 is a gene called *ABL*. The piece of chromosome 22 is a gene called *BCR*. When these genes fuse together on chromosome 22, the *BCR-ABL1* gene is formed. *BCR-ABL1* is a fusion gene. It is not found in normal blood cells. It is not passed down from parents to children.

BCR-ABL1 makes a new protein that leads to uncontrolled cell growth. Treatment for CML aims to stop the activity of the BCR-ABL fusion protein. Genes are written like this: *BCR-ABL*. Proteins are written like this: BCR-ABL.

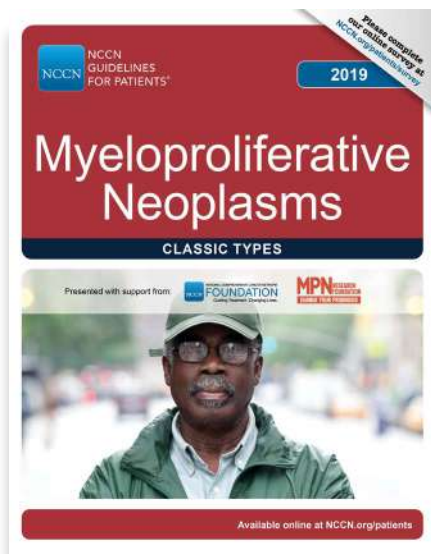
The Philadelphia chromosome is the hallmark of CML. It contains the *BCR-ABL1* gene. Some people have very low levels of *BCR-ABL1*, but do not have CML. If you do not have certain levels of the Philadelphia chromosome or the *BCR-ABL1* gene, you do not have CML. However, you might have another chronic leukemia such as a Ph- myeloproliferative neoplasm.

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.



More information can be found in *NCCN Guidelines for Patients®: Myeloproliferative Neoplasms*, available at [NCCN.org/patientguidelines](https://www.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) in the blood and 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%. A higher number of 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, marrow, or both. Less than 1 out of every 10 blood cells are myeloblasts (<10%).

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. The number of white blood cells is also high. There may be a very low number of platelets in the blood. In the accelerated phase, CML cells may grow fast.

In all phases, CML cells contain the Philadelphia chromosome. However, in the accelerated phase, there may be new abnormal changes within chromosomes.

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. The 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%). At this phase, 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 (granulocytes) or lymphoid (lymphocytes). This is different than chronic phase CML (CP-CML) or accelerated phase CML (AP-CML) where the blasts are myeloid (myeloblasts).

Review

- There are 3 types of blood cells: red blood cells (erythrocytes) carry oxygen, white blood cells (leukocytes) fight infection, and platelets (thrombocytes) help blood to clot.
- Chronic myeloid leukemia (CML) is a blood cancer of the myeloid progenitor cells. Myeloid progenitor cells develop into red blood cells, granulocytes (a type of white blood cell), and platelets. CML causes too many granulocytes.
- CML is a type of myeloproliferative neoplasm (MPN). MPNs make too many blood cells, making it difficult for blood to do its work.
- The Philadelphia chromosome (Ph) is the hallmark of CML. It contains the *BCR-ABL1* gene. If you do not have the Philadelphia chromosome or the *BCR-ABL1* gene, you do not have CML.
- 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

Testing for CML

14 General health tests

15 Blood tests

16 HLA typing

16 Tissue tests

18 Chromosome tests

20 Heart tests

20 Spinal fluid tests

21 Review



Accurate testing is needed to diagnose and treat CML. This chapter presents an overview of tests you might receive and what to expect.

Test results will determine your treatment plan and measure how well treatment is working. 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.

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

- Bring someone with you to doctor visits. Encourage this person to ask questions and take notes.
- Write down questions and take notes during appointments. Don't be afraid to ask 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. It will be helpful when getting a second opinion.
- Organize your papers into a medical binder or notebook. 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 binder or notebook. Hang the list on your fridge or keep it by the phone.

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 other 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. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Physical exam

A physical exam is a study of your body. A doctor will check your body for signs of disease.

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.](#)

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*

Hepatitis panel

Blood tests

Blood tests are useful for diagnosing CML. They can help to find other diseases, too. In a blood test, a sample of your blood is removed through a needle placed into your vein.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Remember, all of these cells are made in your bone marrow. Cancer and other diseases can cause levels that are too high or too low. CBC is a key test that gives a picture of your overall health.

CML often causes a high white blood cell count, but can sometimes cause low counts of other healthy blood cells.

CBC with differential

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

Chemistry profile

Chemicals in your blood come from your liver, bone, and other organs. A chemistry profile measures the levels of these chemicals. Abnormal results may be a sign that organs such as your liver or kidneys aren't working well. This test may be repeated during and after treatment.

Hepatitis panel

Hepatitis B is a virus that causes inflammation of the liver. Hepatitis B can become active during CML or some of its treatments. Tell your treatment team if you've ever been infected with hepatitis. If you're unsure, testing is advised. A sample of your blood is needed for testing.

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 blood stem cell transplant. Your proteins will be compared to the donor's white blood cells to see how many proteins are the same in order to find the best match. 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.

Tissue tests

A biopsy is the removal of a sample of tissue for testing.

Bone marrow tests

Leukemia starts in the bone marrow. To diagnose CML, samples of bone marrow must be removed. Lab results will be used to confirm the disease. 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 usually done at the same time:

- Bone marrow aspiration
- Bone marrow biopsy

The samples are usually taken from the back of the hip bone (pelvis). Ask your doctor about the type of bone marrow test you might have, where the sample will be taken, and what you will be given to help you relax. For many, this is a painful procedure. Your care team will try to make you as comfortable as possible.

A doctor who specializes in the study of blood diseases and cancers is called a hematologist. A hematopathologist is a doctor who specializes in blood diseases by looking at cells under a microscope. The hematopathologist will study the results of various blood and bone marrow tests and write a report that will be sent to your doctor.

Aspiration and biopsy

A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a core of bone.

You will likely lie on your belly. Your doctor will first clean and numb your skin. The outer surface of your bone will be numbed, too.

For aspiration, 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. The samples will be sent to a lab for testing. You may feel bone pain at your hip for a few days. Your skin may bruise.

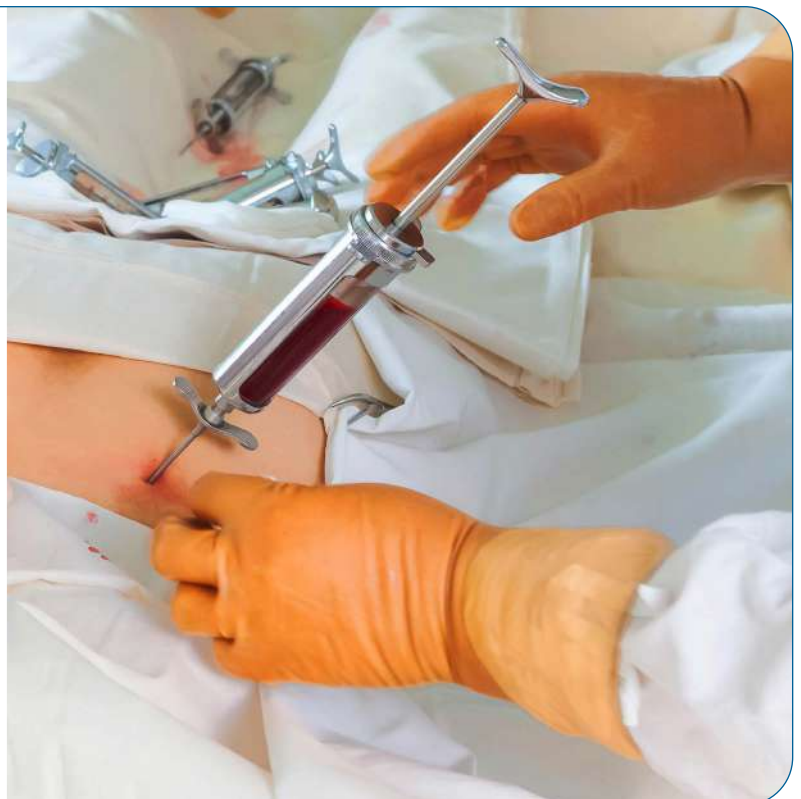
Flow cytometry

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 on the surface of thousands of cells.

A complete 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. It can show if the leukemia cells are mostly myeloid cells or lymphoid cells. This test is important because the cell type may affect which treatment is best for you.

Bone marrow biopsy

Samples of bone and marrow are removed in a biopsy.



Chromosome tests

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome.

Normal human cells contain 23 pairs of chromosomes. Each chromosome contains thousands of genes. Genes tell cells what to do and what to become.

CML cells have chromosome changes that can be seen under a microscope or found with other tests.

Cytogenetic testing

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 chromosome, in particular, is abnormal in CML cells. Testing is done to look for the Philadelphia chromosome (Ph) and 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:

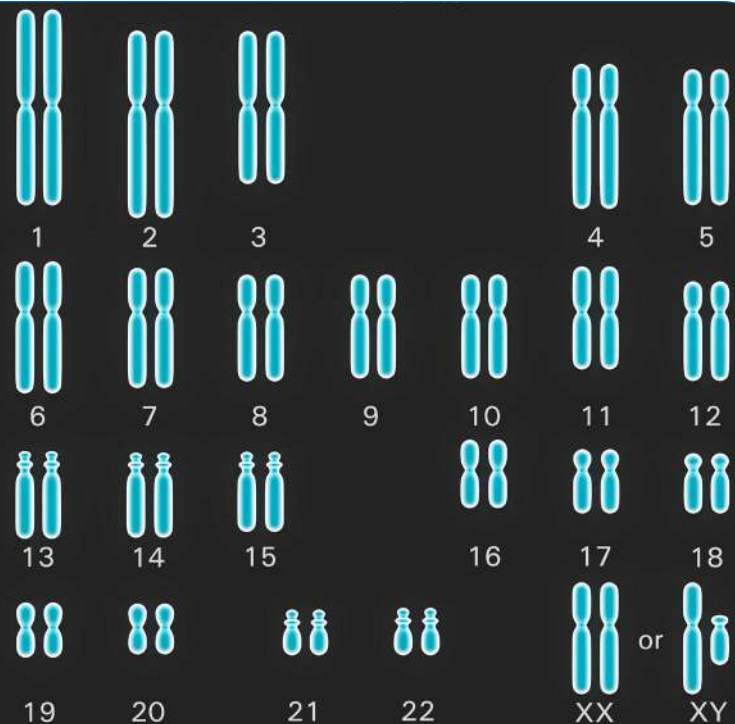
- Karyotype
- FISH

Karyotype

A karyotype is a picture of chromosomes. It is produced in about a week at a special lab. Doctors look for whether 23 pairs of chromosomes are present. They also look for

Karyotype

A karyotype is a picture of the chromosomes. In the Philadelphia chromosome, a piece of chromosome 9 and a piece of chromosome 22 break off and trade places with each other, called a translocation.



missing or abnormal pieces of chromosomes, such as the *BCR-ABL1* gene. Since a karyotype requires growing cells, a sample of bone marrow must be used.

FISH

A fluorescence in situ hybridization (FISH) is a method that involves special dyes, called probes, that attach to pieces of DNA. The probes attach to the *BCR* gene and the *ABL* gene. The *BCR-ABL1* gene is detected when the colors of the probes overlap. Since this test doesn't need growing cells, it can be performed on either a bone marrow or blood sample. However, FISH can only be used for known changes. It cannot detect all the possible changes found with a karyotype. Sometimes, a bone marrow sample will still be needed to get all of the information your doctor needs to help plan your care.

PCR

A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA (genetic information) in just a few hours, but results can take days. PCR is very sensitive, more sensitive than cytogenetic tests. It can find 1 leukemia cell among more than 100,000 normal cells. This is important when testing for treatment response or remission.

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 important. 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, about every 3 months for 2 years and every 3 to 6 months thereafter. It is done using a blood sample.

Mutation testing

Mutation testing includes tests of genes or their products (proteins). New 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.

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) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged 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.

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.

Spinal fluid tests

Leukemia can travel to the fluid that surrounds the spine or brain. This may cause symptoms. In order to know for sure leukemia cells are in your spinal fluid, a sample must be taken and tested.

A lumbar puncture is a procedure that removes spinal fluid. It is also called a spinal tap. A lumbar puncture may also be used to inject cancer drugs into spinal fluid. This is called intrathecal chemotherapy.

A lumbar puncture might be used to rule out a central nervous system (CNS) disease.

Review

- Blood tests check for signs of disease, how well organs are working, and treatment results.
- A bone marrow aspiration and biopsy are procedures that remove bone and marrow samples. Your marrow will be tested at diagnosis to confirm CML.
- Chromosome tests look at the genetic information inside cells. As CML progresses, it can mutate. Therefore, you might have mutation gene 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. Ask if qPCR (IS) is being used.
- HLA typing will be done if an allogeneic (donor) blood stem cell transplant is an option. Those with advanced CML usually have a transplant.
- A lumbar puncture might be used to rule out a central nervous system (CNS) disease.
- Heart or cardiac tests might be needed to test how well your heart pumps blood. It might be used to monitor for side effects.



Create a medical binder

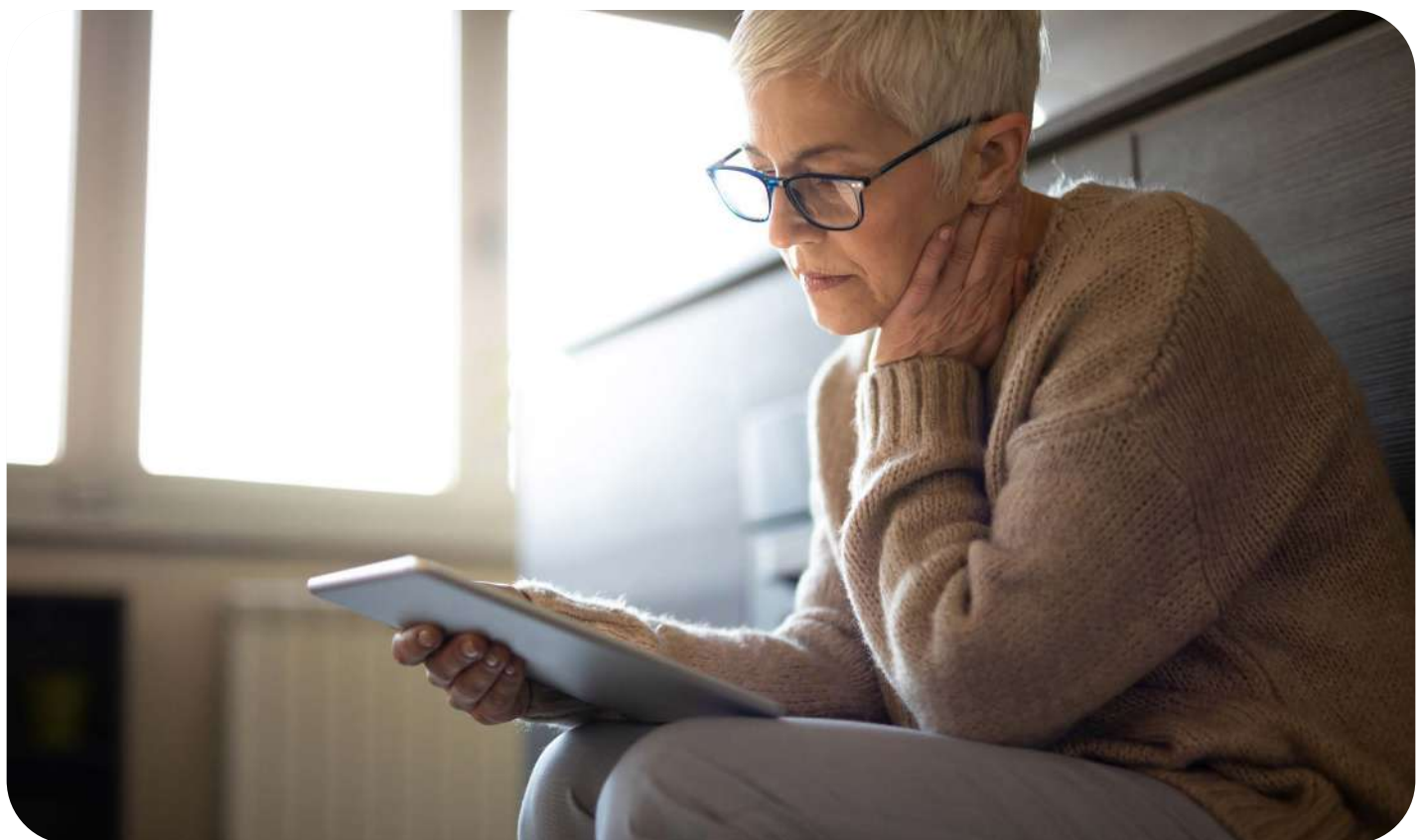
A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- 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 tests 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!

3

Treatment options

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- 26 Chemotherapy
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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.

Targeted therapy

Targeted therapy works throughout the body. It is drug therapy that focuses on specific or unique features of cancer cells.

Targeted therapies target 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. As a result, targeted therapies are less likely to damage healthy cells.

Tyrosine kinase inhibitors

Tyrosine kinase inhibitors (TKIs) are a type of targeted therapy used to treat CML.

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 cell growth.

Each TKI works in a slightly different way. You might not be given a certain TKI if you have a health condition, such as lung or heart issues. Sometimes, a TKI will stop working when there's a new mutation in CML cells. Switching to a different TKI may help.

TKIs used to treat CML

TKIs used to treat CML include:

- Bosutinib
- Dasatinib
- Imatinib
- Nilotinib
- Ponatinib

TKIs are divided into first, second, and even third generation. Each generation of 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. It is also an option for those who have low-risk chronic phase CML where a stronger TKI might not be needed. For intermediate- or high-risk chronic phase CML, other TKIs will be tried before imatinib. 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. Your doctor will consider many things when treatment planning, including test results, risk score, overall health, and your wishes.

Side effects

All cancer treatments can cause unwanted health issues. Such health issues are 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.

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

Bosutinib

Bosutinib is a second-generation TKI. It is not used for those who have stomach and digestion (gastrointestinal) issues.

Dasatinib

Dasatinib is a second-generation TKI. Dasatinib is more potent than imatinib. It will 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. Thus, it is called a “first-generation” TKI. 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 is not for those who have heart (cardiovascular) issues, are at risk for heart issues, or who have electrolyte abnormalities. Nilotinib may cause increased blood sugars or worsen peripheral vascular disease.

Nilotinib prolongs the QT interval. You will likely have electrocardiograms to monitor your heart.

Ponatinib

Ponatinib is a third-generation TKI. It is often used in those with a 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.

Life-threatening side effects include:

- Heart failure
- Liver failure
- Blood clots

Warnings!

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

These include:

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

Even certain medicines can affect the ability of a TKI to do its job. Antacids, heart medicine, and anti-depressants are just some of the medicines that might interact with a targeted therapy. This is why it is important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbs, or supplements you are taking. **Bring a list with you to every visit.**

Drug interactions are common with TKIs. Don't worry! Doctors are aware of these drug interactions and are prepared to make adjustments. You will still receive excellent care! **Tell your doctor about any OTC medicines, herbs, or supplements you use, including any teas you drink.**

Tell your doctor about any medications, vitamins, over-the-counter drugs, herbs, or supplements you are taking.

Chemotherapy

Chemotherapy is a drug therapy used to treat cancer. Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. All chemotherapy drugs affect the instructions (genes) that tell cancer cells how and when to grow and divide. This disrupts the life cycle of cancer cells.

Most chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which chemotherapy is used. You will have tests to see how well treatment is working.

Omacetaxine

Omacetaxine (Synribo™) is a type of chemotherapy used to treat chronic or accelerated phase CML that is resistant and/or intolerant to 2 or more TKIs.

Monitoring

Side effects are part of any treatment. A side effect is an unhealthy or unpleasant condition caused by treatment. Chemotherapy can be toxic or harmful to your body. Sometimes, treatment with omacetaxine may be stopped or delayed until any issues are resolved.

Complete blood count

If you are receiving omacetaxine you have complete blood counts (CBCs):

- Every week during induction and initial maintenance cycles
- Every 2 weeks, or as needed, after initial maintenance

Hyperglycemia

If you are taking omacetaxine, you will be monitored for hyperglycemia or too much blood sugar (glucose). Those with diabetes or who are at risk for diabetes should be watched closely. Omacetaxine may not be an option if you have diabetes that is not under control.

Blood stem cell transplant

A blood stem cell transplant replaces damaged or destroyed stem cells with healthy stem cells. The healthy stem cells form new marrow and blood cells. It is also called a hematopoietic cell transplant (HCT). You might know it as a stem cell transplant (SCT) or bone marrow transplant (BMT).

There are 2 types of blood stem cell transplants:

- Autologous – stem cells come from you
- Allogeneic – stem cells come from a donor

Only an allogeneic SCT is used as a treatment option for CML. It is the main treatment for advanced CML. The steps of an allogeneic SCT are described next.

Conditioning

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

There are 2 main types of conditioning treatment:

- High-dose conditioning consists of high doses of strong chemotherapy. High-dose conditioning can cause life-threatening side effects. Also, not everybody can tolerate it.
- Reduced-intensity conditioning consists of low doses of strong chemotherapy. It may also consist of low-intensity drugs. Reduced-intensity conditioning may be used for people who are older or less healthy overall. However, the chance for a cancer relapse is greater.

Radiation therapy may also be given as part of conditioning treatment.

Transplanting stem cells

After chemotherapy, 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. You may be given antibiotics to prevent or treat infection. You may also be given a red blood cell transfusion to prevent bleeding and to treat anemia (below normal red blood cell count). Platelet transfusion may be 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 doctor about the possible side effects or complications of SCT and how this might affect your quality of life.

Clinical trials

Clinical trials study how safe and helpful tests and treatments are for people. Clinical trials find out how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve your care and treatment of cancer.

Clinical trials have 4 phases.

- Phase I trials aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects.
- Phase II trials assess if a drug works for a specific type of cancer.
- Phase III trials compare a new drug to a standard treatment.
- Phase IV trials test drugs approved by the U.S. FDA (Food and Drug Administration) to learn more about side effects with long-term use.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often are alike in terms of their cancer and general health. This helps to ensure that any change is from the treatment and not because of differences between patients.

If you decide to join a clinical trial, you will need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits. Even after you sign a consent form, you can stop taking part in a clinical trial at any time.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or

at other treatment centers nearby. Discuss the risks and benefits of joining a clinical trial with your care team. Together, decide if a clinical trial is right for you.

NCCN experts encourage patients to join a clinical trial, when possible.



Finding a clinical trial

- Search the National Institutes of Health (NIH) database for clinical trials. It includes publicly and privately funded clinical trials, who to contact, and how to enroll. Look for an open clinical trial for your specific type of cancer. Go to ClinicalTrials.gov.
- The National Cancer Institute's Cancer Information Service (CIS) provides up-to-date information on clinical trials. You can call, e-mail, or chat live. Call 1.800.4.CANCER (800.422.6237) or go to cancer.gov.

Review

- Targeted therapies seek out how cancer cells grow, divide, and move in the body. Tyrosine kinase inhibitors (TKIs) are a type of targeted therapy used to treat CML.
- TKIs are a standard treatment of CML. They target the *BCR-ABL1* gene.
- TKIs interact with prescribed drugs and other medicines, such as over-the-counter (OTC) drugs, herbal supplements, and vitamins. Tell your doctor about any OTC medicines, herbs, or supplements you use, including any teas you drink.
- Chemotherapy stops the life cycle of cancer cells so they can't increase in number. Omacetaxine (Synribo™) is a type of chemotherapy used to treat chronic or accelerated phase CML that is resistant and/or intolerant to 2 or more TKIs.
- All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Ask your care team about the side effects of treatment and what can be done to prevent them.
- A blood stem cell transplant (SCT) or hematopoietic cell transplant (HCT) replaces damaged stem cells with healthy stem cells. An allogeneic (donor) SCT is used to treat advanced CML.
- NCCN experts encourage patients to join a clinical trial, when possible.

Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted chemotherapy, and immunotherapy are all types of systemic therapy. Systemic therapies work throughout the body.

4

Chronic phase CML

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In chronic phase CML, there is an increased number of white blood cells called granulocytes. Treatment is based on risk groups. 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 1 out of every 10 blood cells are blasts (<10%) in chronic phase CML (CP-CML).

CP-CML responds well to treatment. However, if 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.

Granulocytes

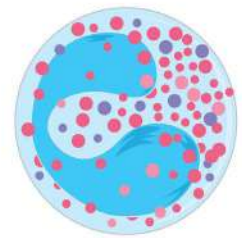
Three types of granulocytes include neutrophil, basophil, and eosinophil.



Neutrophil



Basophil



Eosinophil

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.](#)

In CML, risk is calculated using:

- Age
- Spleen size
- 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, herbs, supplements, and over-the-counter (OTC) drugs you are taking
- Your wishes or preference

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

First-line treatment

The primary or first-line treatment is the first treatment you have. TKIs are the preferred first-line treatment for chronic phase CML. The goal of treatment is to control CML by putting it into remission called a complete response.

There are different types of complete response. The goal is to reduce the number of CML cells to as close to zero as possible and keep it there. This is called a complete molecular response (CMR).

You will have a qPCR using IS to see how well CML is responding to treatment and what response milestones have been achieved.

Low-risk group

Treatment will be based on risk score, how toxic a specific TKI is, your age, ability to tolerate therapy, and any other serious health issues.

The preferred options for low risk are:

- Imatinib
- Bosutinib
- Dasatinib
- Nilotinib
- Clinical trial

A preferred treatment is one that has a proven track record of having the best result or being the most effective.

Intermediate- or high-risk group

With intermediate or high risk, the goal is to control the cancer at a faster rate. Therefore, a second-generation TKI is preferred. These TKIs are faster at cytogenetic and molecular responses. The goal is to prevent disease progression to advanced phase CML.

Treatment will be based on risk score, how toxic a specific TKI is, your age, your body's ability to tolerate therapy, and any other serious health issues you might have.

The preferred treatment options for intermediate or high risk are:

- Bosutinib
- Dasatinib
- Nilotinib

Other recommendation options include:

- Imatinib
- Clinical trial

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 *BCR-ABL1* after a complete cytogenetic response (CCyR) is achieved. In CCyR, *BCR-ABL1* is less than 1%.

After starting first-line treatment, you will have a qPCR (IS) every 3 months. Once a CCyR has been achieved, 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.

Treatment milestones are measured as the percentage of cells with *BCR-ABL1* that remain after treatment. The goal is to reduce the number of CML cells with the Philadelphia chromosome (Ph+) to as close to zero as possible.

Changes in qPCR (IS) scores are often described in terms of “log changes.”

For example:

- 1-log reduction is 10 times lower
- 2-log reduction is 100 times lower
- 1-log increase is 10 times higher

If your doctor says that you have had a 1-log reduction, it means that the amount of *BCR-ABL1* has dropped to around 10%.

- **Partial cytogenetic response (PCyR)**
When *BCR-ABL1* is between 10% and 1% (1-log reduction)
- **Complete cytogenetic response (CCyR)**
When *BCR-ABL1* is between 1.0% and 0.1% (2-log reduction)
- **Major molecular response (MMR or MR3.0)** – When *BCR-ABL1* is 0.1% (3-log reduction)
- **Complete molecular response (CMR)**
When *BCR-ABL1* is 0.0032%. A good lab can detect a 4.5-log reduction.

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. For definitions of different response types, [see Guide 3](#).

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. In a CCyR, *BCR-ABL1* is 1% or less. It should be achieved within 12 months.

Although not a response milestone, another treatment result is a complete molecular response (CMR). A CMR is when *BCR-ABL1* can't be detected. For this response, a PCR test that can detect at least a 4.5-log reduction is needed.

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, supplements, or herbs

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. Your doctor will consider this and order any mutation or cytogenetic testing as needed.

It's very important to take your medicine on time and exactly as prescribed. Don't miss or skip a dose!

Guide 3 Response types and definitions

| | |
|-------------------------------------|--|
| Complete hematologic (blood) | <ul style="list-style-type: none"> • 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 | <p>4 types</p> <ul style="list-style-type: none"> • Complete cytogenetic response (CCyR) - No Philadelphia chromosomes (Ph) are found • 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 | <p>3 types</p> <ul style="list-style-type: none"> • Early molecular response (EMR) - <i>BCR-ABL1</i> (IS) is 10% or less at 3 and 6 months • Major molecular response (MMR) - <i>BCR-ABL1</i> (IS) is 0.1% or a 3-log or more decrease in <i>BCR-ABL1</i> if qPCR (IS) not used • Complete molecular response (CMR) - is based on how sensitive the test is. The more sensitive the test, the better it is at finding <i>BCR-ABL1</i> |

Second-line treatment

Second-line treatment options are based on qPCR (IS) results and if first-line treatment milestones were met. For treatment milestones, see [Guide 4](#).

- Green shows when milestones have been reached.
- Yellow shows when scores are of concern.
- Red shows scores failing to reach milestones.

Scores of concern (yellow)

Where you see yellow in the guide below, it is possible that your CML has TKI resistance. You might need to have additional genetic and mutation testing.

Second-line 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.

Scores missing milestones (red)

Where you see red in the guide below, it means that first-line 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 need to have additional mutation testing.

| Guide 4 Treatment milestones | | | | |
|--|-------------------------|----------------|-------------------------|----------------------|
| | at 3 months | at 6 months | at 12 months | at 15 months or more |
| Number of Ph+ cells are more than 10% | Possible TKI resistance | TKI resistance | TKI resistance | TKI resistance |
| Number of Ph+ cells are between 10% and 1% (EMR) | Milestone met | Milestone met | Possible TKI resistance | TKI resistance |
| Number of Ph+ cells are 1% or less (CCyR) | Milestone met | Milestone met | Milestone met | Milestone met |

Milestones reached (green)

Where you see green in the guide, these milestones have been reached. 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.

Remission

For some people, it may be possible to discontinue or stop TKI therapy. Your doctor should consult with a CML specialist and review with you in detail the potential risks and benefits if targeted therapy is discontinued. You will need to agree (consent) to discontinuing therapy and be aware of the TKI withdrawal side effects.

In order to discontinue TKI therapy, you must meet all of 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, that can provide test results within 2 weeks

Frequent monitoring is needed. 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% (major molecular response), 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.

For those who remain in major molecular response (MMR), tests are every month for one year, every 2 months for the second year, and every 3 months thereafter.

Review

- In chronic phase CML (CP-CML), there is an increased number of white blood cells called granulocytes. Less than 1 out of every 10 blood cells are blasts (<10%). Blasts are immature blood cells.
- Treatment for CP-CML is based on risk groups using age, spleen size, and blood counts.
- The goal of treatment is to put cancer in remission. CP-CML is highly treatable.
- For CML, treatment results are discussed in terms of milestones. The goal is to hit certain milestones within a specific timeframe.
- The 2 very important milestones are early molecular response (EMR) at 3 months and 6 months and complete cytogenetic response (CCyR) by 12 months.
- Treatment milestones are measured as the percentage of cells with *BCR-ABL1* that remain after treatment. The goal is to reduce the number of CML cells with the Philadelphia chromosome (Ph+) to as close to zero as possible.

5

Advanced phase

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- 41 Accelerated phase
- 42 Blast phase
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- 45 Review



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. Treatment is usually a clinical trial, targeted therapy, or a combined therapy. A blood 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](#).

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 or if the qPCR (IS) results increase more

Guide 5 Definition of advanced phase CML

Accelerated

Any of the following:

- Blood myeloblasts are between 15% and 29%
- Blood myeloblast and promyleocyte totals are 30% or more
- Blood basophils are 20% or more
- Platelet count is $100 \times 10^9/L$ 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

than 10 times the lowest measured level. 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.

Your doctor should 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 blood 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 the leukemia from progressing to blast phase. For long-term control, an allogeneic SCT is frequently needed. For treatment options before an SCT, see [Guide 6](#).

Guide 6 Accelerated phase treatment options

Clinical trial

Preferred TKIs

- Bosutinib
 - Dasatinib
 - Nilotinib
 - Ponatinib
-

Other recommended TKI

- Imatinib
-

Used in some cases

- Omacetaxine
-

Allogeneic SCT

An allogeneic SCT is an option after:

- Clinical trial
- Preferred TKIs - Bosutinib, dasatinib, nilotinib, ponatinib
- Other recommended TKI – Imatinib
- Used in some cases – Omacetaxine

For monitoring and treatment options after an SCT, [see Guide 7](#).

Blast phase

Blast phase CML (BP-CML) happens after a series of events, including additional gene mutations and resistance to targeted therapy. The number and type of blasts matters. Blasts may have spread outside the blood or marrow to other tissues.

Treatment options

Treatment for BP-CML is based on if the blasts are myeloid (granulocytes) or lymphoid (lymphocytes).

BP-CML can act like an acute leukemia. Acute leukemias include acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML). Your treatment will be based on whether the leukemia cells are mostly lymphoid or myeloid. [See Guide 8](#).

Guide 7

After an allogeneic blood stem cell transplant (SCT)

| | | |
|-----------------------|--|---|
| Allogeneic SCT | <p>If in CCyR, then monitor with qPCR every 3 months for 2 years, and then every 3 to 6 months</p> | <p>If qPCR doesn't find CML, then consider a TKI for at least 1 year in those who had AP-CML or BP-CML before</p> <hr/> <p>➔ If qPCR finds CML, then discuss the following with the transplant team:</p> <ul style="list-style-type: none"> • TKI • TKI with DLI or omacetaxine • Clinical trial |
| | <p>If not in CCyR or in relapse, then discuss the following options with the transplant team:</p> <ul style="list-style-type: none"> • TKI • TKI with DLI or omacetaxine • Clinical trial | |

For long-term control, an allogeneic (donor) blood stem cell transplant (SCT) is needed.

Steroid

Steroid is the short name for corticosteroid. It is a type of drug that is often used to relieve inflammation. Steroids also are toxic to lymphoid cells. Therefore, a steroid may be added to TKI treatment for lymphoid type blast phase CML.

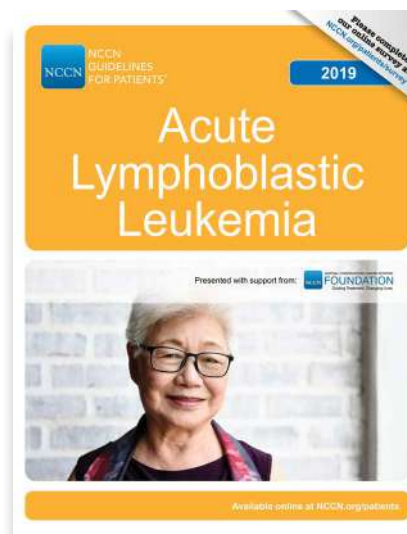
CNS treatment

Sometimes CML travels to or relapses in the central nervous system (CNS). In this case, special treatment is needed. CNS treatment may include chemotherapy injected into spinal fluid, which is called intrathecal chemotherapy.

Chemotherapy

Chemotherapy may be added to TKI treatment. The type of chemotherapy depends on if the blasts are myeloid or lymphoid. If lymphoid, you will have chemotherapy that is used for ALL. If myeloid, you will have chemotherapy that is used for AML.

More information can be found in *NCCN Guidelines for Patients®: Acute Lymphoblastic Leukemia*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Guide 8 Blast phase treatment options

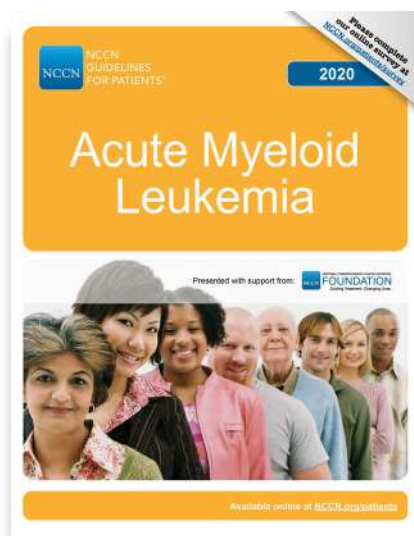
Lymphoid

- Clinical trial
- ALL-type induction chemotherapy with a TKI
- TKI with steroids

Myeloid

- Clinical trial
- AML-type induction chemotherapy with a TKI
- TKI

More information can be found in *NCCN Guidelines for Patients®: Acute Myeloid Leukemia*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



After allogeneic SCT

An allogeneic SCT will help keep your CML in remission. After an allogeneic SCT, you will be tested to see if a complete cytogenetic response (CCyR) was achieved. In CCyR, no Philadelphia chromosomes are found and *BCR-ABL1* is usually less than 1%. [See Guide 7.](#)

In a donor lymphocyte infusion (DLI) you will receive lymphocytes from the same person who donated the blood stem cells for the SCT. A DLI with TKI may cause a fast drop in *BCR-ABL1*.

Omacetaxine is used for CML that is resistant to targeted therapy (TKI) and/or CML that progressed after 2 or more TKIs were tried.

If CCyR achieved

If CCyR was achieved, then you be monitored with a qPCR every 3 months for 2 years, and every 3 to 6 months thereafter.

If qPCR doesn't find CML, then your doctor will consider a TKI for at least 1 year in those who had AP-CML or BP-CML before.

If qPCR finds CML, then your doctor will discuss with the transplant team the following options:

- TKI
- TKI with DLI or omacetaxine
- Clinical trial

If not in CCyR or CML has relapsed

Relapse is any sign of loss of response (relapse). If there is a 1-log increase in *BCR-ABL1* with loss of major molecular response (MMR), then a bone marrow biopsy will be done to see if a CCyR was also lost.

If tests results show CML is not in CCyR or has relapsed, then your doctor will discuss with the transplant team the following options:

- TKI
- TKI with DLI or omacetaxine
- Clinical trial

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 the 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 the leukemia 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).
- BP-CML is usually treated with an allogeneic SCT.

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

6

Making treatment decisions

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It is 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 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 decisions:

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

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the

time to build a relationship with your doctor, it will help you feel supported 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 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 prognosis

1. What is the CML phase? What does this mean in terms of my prognosis?
2. Where did the cancer start? In what type of cell (myeloid or lymphoid)?
3. What tests do I need? What other tests do you recommend?
4. How soon will I know the results and who will explain them to me?
5. Is there a cancer center or hospital nearby that specializes in my type and subtype of cancer?
6. What will you do to make me comfortable during testing?
7. How do I prepare for testing?
8. Would you give me a copy of the pathology report and other test results?
9. Who will talk with me about the next steps? When?
10. Will I start treatment before the test results are in?

Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, health, and other factors affect my options?
3. What if I am pregnant? What if I'm planning to become pregnant in the near future?
4. Am I a candidate for a blood stem cell transplant (SCT)? What if a SCT is not an option?
5. Am I a candidate for a clinical trial?
6. Which option is proven to work best for the CML phase, my age, and other factors?
7. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
8. What can be done to prevent or relieve the side effects of treatment?
9. Are there any life-threatening side effects of this treatment? How will I be monitored?
10. How do you know if treatment is working? How will I know if treatment is working?
11. What are my options if my treatment stops working?
12. Can I stop treatment at any time? If I do, what will happen?

Questions to ask about treatment

1. What are my 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? Should I bring someone with me?
6. How much will the treatment hurt? What will you do to make me comfortable?
7. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?
8. Will I miss work or school? Will I be able to drive?
9. What type of home care will I need? What kind of treatment will I need to do at home?
10. What can I do to prevent side effects? What will you do?
11. When will I be able to return to my normal activities?
12. Which treatment will give me the best quality of life? Which treatment will extend my life? By how long?

Questions to ask about blood stem cell transplants

1. How do you find a donor?
2. How long will I have to wait for a blood stem cell transplant (SCT)?
3. What do I need to do to prepare?
4. What will you do to prepare?
5. What are the risks to myself and/or the donor?
6. How will the transplant affect my prognosis?
7. How will a transplant affect the quality and length of my life?
8. What should I expect?
9. How long should I expect to be in the hospital?
10. How will I feel before, during, and after the transplant?
11. How many SCTs has this center done for those with CML?
12. Will I have more than one SCT?

Websites

Be The Match®

bethematch.org

Bone Marrow & Transplant Information Network

bmtinfonet.org

Leukemia & Lymphoma Society

LLS.org/patientsupport

National Cancer Institute (NCI)

cancer.gov/types/leukemia

National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

National Bone Marrow Transplant Link

nbmtlink.org

NCCN for Patients®

NCCN.org/patients

NCCN Reimbursement Virtual Resource

NCCN.org/reimbursement_resource_room/default.aspx



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 (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 together 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.

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.

blood stem cell transplant (SCT)

A treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells.

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.

complete molecular response (CMR)

No copies of the abnormal *BCR-ABL1* gene are found using a very sensitive test.

cytogenetics

The study of chromosomes.

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 together.

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.

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).

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.

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.

NCCN Contributors

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

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Abramson Cancer Center
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Philadelphia, Pennsylvania
800.789.7366
penmedicine.org/cancer

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
800.999.5465
nebraskamed.com/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
Los Angeles, California
800.826.4673
cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
877.332.4294
dfbwc.org
massgeneral.org/cancer

Duke Cancer Institute
Durham, North Carolina
888.275.3853
dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427
foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

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

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

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/departments-centers/mayo-clinic-cancer-center

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

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

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

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

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
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

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

UC San Diego Moores Cancer Center
La Jolla, California
858.657.7000
cancer.ucsd.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

The University of Texas
MD Anderson Cancer Center
Houston, Texas
800.392.1611
mdanderson.org

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

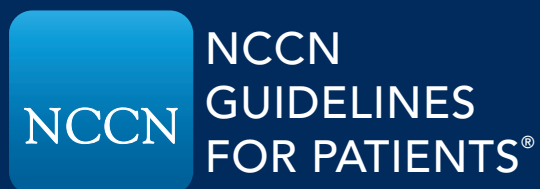
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480
vicc.org

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

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Chronic Myeloid Leukemia

2020

NCCN Foundation® gratefully acknowledges our industry supporters, Novartis Pharmaceuticals Corporation and Pfizer Inc, in making available these NCCN Guidelines for Patients®. NCCN independently develops and distributes the NCCN Guidelines for Patients. Our industry supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.

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